ADULT HUMAN EXOCRINE PANCREAS CONTAINS
MESENCHYAL STEM CELLS

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Up to now mesenchymal stem cells (MSC) have only been isolated from the bone marrow, adipose tissue, umbilical cord blood and veins, muscle and placenta but not from endodermal organs. In this study, we investigate if MSC can be isolated from human exocrine pancreas.

We cultured human exocrine pancreas tissue obtained after purification of pancreateic islets for human transplantation in expansion media for human MSC (IMDM + 10% FCS + PDGF-FB) until adherent cells appeared. After 2 passages, these cells were characterized by FACs analysis and compared to human MSC isolated from bone marrow. Mesenchymal differentiation potential was tested by culturing these cells in adipogenic, chondrogenic differentiation media.

In 10 of 11 human pancreas exocrine fractions with a purity of 99% adherent fibroblast-like cells were identified and expanded. Cells were grown for up to 36 population doublings (16 passages) maintaining a fibroblast-like morphology. FACs analysis showed that these cells were negative for CD31, CD34, CD45, CD106, MHC class 1, CD54low, and positive for CD44, CD90, CD105. Culturing these cells in adipogenic and chondrogenic differentiation media allowed them to differentiate into adipocyte-like and chondrocyte-like cells, demonstrating their mesenchymal phenotype.

Our data show that mesenchymal stem cells are present in the exocrine fraction of human pancreas. These cells are phenotypically similar to MSC from the bone marrow. Ongoing studies are needed to show if these cells are an endodermal progenitor cell and a potential source of hepatocytes and beta cells for clinical transplantation.

Poster Presentations

Cell Transplant

PO-001 ADULT HUMAN EXOCRINE PANCREATE CONTAINS MESENCHYAL STEM CELLS

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RE-ASSEMBLAGE OF DISSOCIATED LIVER CELLS INTO THE SUBCUTANEOUS ADIPOSE TISSUE OF RAT ABDOMEN

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Purpose: New prospects in a therapy of severe hepatic failure will be opened if the subcutaneous transplantation of the functional liver cells can be successfully performed. In this study the possibility of the subcutaneous transplantation of the liver cells fell into necrosis due to the rejection. The average tissue expression induced by gene expression of human liver cells.

Results: Considerably large organoid was formed from transplanted liver cells. Capillaries, cell nests and duct-like structures appeared in 24, 48 and 72 hours in the subcutaneous adipose tissue, respectively. Glycogen granules were identified in the transplanted liver cells, however, the expression of AFP was confirmed only in a small number of cells. After 30 days, almost transplanted liver cells fell into necrosis due to the rejection. The average tissue weight occupied by liver cells was 20mm long, 4mm thickness and 8 mm width. Conclusion: Considerably large organoid was formed from transplanted liver cells. The adipose tissue is an suitable environment for the generation of human liver cells.
MONOCYTE-DERIVED CELLS TO RE-INDUCE UMBILICAL CORD (UC): A POSSIBLE SOURCE OF STEM HEPATOCYTE TRANSPLANTATION AS A TREATMENT FOR LIVER DISEASES

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We recently generated monocytic-derived (Md) cells that might play a role in re-inducing self-tolerance in autoimmune diseases. Here, we tested Md-cells in a mouse model of chronic colitis. MCNs were isolated from spleen, blood and bone marrow of BabB mice. They were used without modification (control cells) or cultured with M-CSF and challenged with γ-INF (Md-cells). Chronic colitis was induced with dextran-sodium-sulfate (DSS). 24h after DSS treatment, 5 x 10^6 Md-cells (n=14) or control cells (n=20) were injected i.v.; a control group received no cells (n=10). Inflammation in the colon was scored histologically, where 0-2 represents mild and 3-4 massive inflammation. Lymphocytes from mice with DSS colitis were CFSE-labelled, co-cultivated with Md-cells (or control cells), and counted at 48h. The colon inflammatory score was reduced from 3.3±0.2 in untreated controls to 2.5±0.3 with Md-cells (p<0.001). No reduction was observed with control cells (2.6±0.3). Md-cells eliminated lymphocytes from mice with colitis nearly completely when co-cultured. Only 13.5±5.1% of colitis lymphocytes survived. This effect was not observed with control cells (96.8±9.9%) or with Md-cells in trans-well plates (121±22%). Lymphocytes surviving in Md-cell co-cultures were highly enriched for CD4+CD25+ cells that showed a >30-fold up-regulation of Foxp3 mRNA.

PO-008 HEPATOCYTE TRANSPLANTATION IN GUNN RATS: IMPROVEMENT IN BILIRUBIN METABOLISM

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The shortage of donor organs for liver transplantation has led to research of alternatives including transplant of stem cells. Mesenchymal stem cells (MSC) have a pluripotent ability to differentiate into a variety of cell lineages. Aims: To demonstrate that UC is a possible source of MSC and that they can differentiate into hepatocytes.

Methods: The cells were collected from UC within 24 hours after deliveries. After expansion, they were characterized as negative for CD34, CD38, CD45, FcγRI, CD11b and positive for CD73. The heterogeneous population was then immunoseparated using specific markers for MSC. The cell plasticity was then tested by differentiation of mesenchymal derived cells. Then this population was differentiated into hepatocytes by using hepatocyte growth factors. Cells differentiation was assessed by immunocytochemistry.

Results: Myogenic differentiation: MiF was positive at 7th and MyoD at 12th day of culture. Adipogenic differentiation: oil red staining was positive at 9th day of culture. Osteogenic differentiation: von Kossa staining was positive at 7th days of culture. Hepatic differentiation: alphaFP and HNF-4alpha were positive at 14th and albumin and c-met at 30th day of culture.

Conclusion: Umbilical cord represent a potential alternative source of MSC. The high plasticity of these cells was demonstrated by differentiation of mesenchymal derived cells. The differentiation into hepatocyte-like cells seem to be promising for future research and clinical applications.

PO-010 HEPATOCYTE TRANSPLANTATION AS A TREATMENT FOR GLYCOCEN STORAGE DISEASE TYPE 1B

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Hepatocyte transplantation is a promising new approach for the treatment of damaged heart function after MI. Besides i.m. transplantation systemic application reveals comparable improvement of LV function. In combination with superior availability, transplantation of PCMO promises an effective alternative clinical option to other cell-based therapies.
of liver-based inborn errors of metabolism. We report successful hepatocyte transplantation in an 18-year-old boy with glycogen storage disease type IIb (body weight 35 kg, height 1.48 m). Clinical signs include severe hypoglycemia 3–4 h after eating, increased production of lactate, triglycerides, and lactic acid, and development of hepatic anomalies. He required carn- Urbane meals every 6 h to maintain blood glucose levels. Hepatocytes were isolated from the whole liver of donor using two step collagenase perfusion method. Hepatocytes, approximating 2x10^6 (2% of the estimated recipient's to- tal hepatocytes) were infused into his portal vein through a percutaneous trans- hepatic catheter. He received 1x10^7 cryopreserved hepatocytes from same donor at 7 days later. He showed no hypoglycemia even after 8 hours fasting at 12 days later. Liver biopsy showed normal level of glucose-6-phosphatase ac- tivity (before transplantation, it was nearly zero) at posttransplantation 3 weeks. He received 3x10^7 cells from another donor at 1 month after first transplantation. He showed no hypoglycemia without eating carn-starch until now (4 month after first transplantation). This is the first and successful clinical hepatocyte trans- plantation in Korea. Hepatocyte transplantation is a safe and promising tech- nique in the treatment of rare inborn errors of metabolism.

**PO-011 KERATINOCYTES SURVIVE FOR MONTHS IN NaCl AND CAN BE SUCCESSFULLY TRANSPLANTED**

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**Introduction:** We searched for methods of long-term preservation of skin for subsequent tx. Since epidermis and dermis are, resistant to ischemia and de- hydration, we tried to use dehydration method for preservation of skin frag- ments for tx.

**Aim:** Study was carried out to prove that skin fragments dehydrated in pow- dered sodium chloride can retain their vital properties and can be successfully transplanted.

**Methods:** Human skin fragments (30) from lower limbs were harvested during elective vascular surgery (consent of ethical committee). They were placed in heat-dried fine sodium chloride powder (1 part skin 9 parts of NaCl), kept at room temperature for 3 to 6 months. They were desalinated and fragments 1x1 cm were transplanted to the dorsum of dorsal mice (60). After 3 weeks, the grafts were harvested.

**Results:** Skin grafts were taken by the recipient. On histology, keratinocytes looked normal. They were all HLA class I. Staining with monoclonal anti- human p63 (stem cells), CD29 (transient cells), PCNA (proliferating cell nuclear antigen) revealed normal pictures of basal layer cells. In mice receiving BdUr selective vascular surgery (consent of ethical committee). They were placed in dehydration method. Hepatocytes, approximating 2x10^9 (2% of the estimated recipient's to- tal hepatocytes) were infused into his portal vein through a percutaneous trans- hepatic catheter. He received 1x10^7 cryopreserved hepatocytes from same donor at 7 days later. He showed no hypoglycemia even after 8 hours fasting at 12 days later. Liver biopsy showed normal level of glucose-6-phosphatase ac- tivity (before transplantation, it was nearly zero) at posttransplantation 3 weeks. He received 3x10^7 cells from another donor at 1 month after first transplantation. He showed no hypoglycemia without eating carn-starch until now (4 month after first transplantation). This is the first and successful clinical hepatocyte trans- plantation in Korea. Hepatocyte transplantation is a safe and promising tech- nique in the treatment of rare inborn errors of metabolism.
LIVER RECOVERY IN RATS WITH CCL4-INDUCED CIRRHOSIS AFTER STEM CELL TRANSPLANTATION

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Chronic liver failure results in the decrease of the number of functioning hepatocytes. It dictates the necessity of using the exogenous viable cells or/and the agents that can stimulate regenerative processes. Fetal liver contains both hepatic and hematopoietic stem cells with high proliferative potential. Also, immature cells produce fetal specific factors that may have positive effect on an injured liver.

The aim of this study was to test the ability of human fetal liver cell (FLC) and cell-free extract (CFE) of human fetal tissues to stimulate recovery processes in an experimental model of carbon tetrachloride (CCl4)-induced cirrhosis in rats.

Fetal liver cells were isolated from 8-12-weeks human fetuses. For extraction preparation we used mesodermal fetal tissues. Liver cirrhosis in rats was induced by administration of low dose CCl4 for 3 months. Cirrhotic rats were intrasplenically injected with FLC or CFE. Animals were sacrificed on the day 15.

Human FLC transplantation was shown to prevent the death of cirrhotic animals almost completely. Cell transplantation normalized several biochemical indices in blood serum, as well as restored mitochondrial function and liver detoxification. Also, morphological patterns of liver recovery after FLC transplantation were demonstrated by the 15th day.

Biochemical and histological results demonstrated that CFE of non-hepatic origin as well as FLC transplantation activated recovery processes in rat cirrhotic liver; while morphological differences were present in rat livers depending on the treatment scheme.

Total positive effect of FLC and CFE on rat cirrhotic livers is thought to be due to the presence in FLC and CFE of highly-active stage-specific factors promoting activation of cellular repair mechanisms.

ULTRASTRUCTURAL LIVER CHANGES AFTER BONE MARROW TRANSPLANTATION IN MURINE SCHISTOSOMIASIS

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The efficiency of differentiation of bone marrow cells into hepatocytes in vivo and its importance in physiopathologic processes is still debated. Using the murine model of schistosomiasis, unfractionated male bone marrow cells were transplanted into non irradiated female mice chronically infected with Schistosoma mansoni without immunosuppression therapy. Two weeks after intraperitoneal transplantation, mice were sacrificed on the 8th week of the experiment. Their livers were subjected to electron microscopic examination.

A relative increase in circulating small progenitor cells with large nuclei was seen. These cells were detected also in between the hepatocytes facing the sinusoids, which showed congestion. Many inflammatory cells especially eosinophils were observed. The livers of the normal non injured, bone marrow transplanted mice displayed congestion of the sinusoids and the presence of oval cells with large nuclei showing marginal heterochromatin, in addition to some small mononuclear cells in the vicinity of hypertrophied kupffer cell. Binucleated hepatocytes with prominent nuclei were detected denoting regenerative signs.

Accordingly, we suggest that unfractionated bone marrow cells can add to the regeneration of the injured schistosomiasis liver and non injured liver to a lesser extent. However, further immune electron microscopic studies are needed to reveal the nature of these small cells.

MICROBIOLOGICAL ECOLOGY OF HUMAN ISLET ISOLATION CONTAMINATION FOR TRANSPLANTATION

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Introduction: Available procedure for human islet preparation and transplantation do not allow for formal sterility assessment. Implementation of stringent preventive measures are therefore mandatory to limit the risk of recipient contamination. In this study we analysed prospectively the result of microbial biological ecology of human islet isolation and transplantation in our clinical islet transplant program from march 2003 to march 2005.

MICROBIOLOGICAL ECOLOGY OF HUMAN ISLET ISOLATION AND TRANSPLANTATION

Isabelle Martinache, Rodrigue Dessein, Rimed Ezzouaoui, B. Sendid, Daniel Poulain, Brigitte Vandewalle, Valery Gmyr, Marie-Christine Vantyghem, Julie Kerr-Conte, Francois Pattou. INSERM ERIT-M 0106 Diabetes Cell Therapy, Biotechnologie, Parasitologie and Mycology, University Hospital of Lille, Lille, France.

Available procedures for human islet preparation do not formally assess the sterility of cell preparations. Stringent measures are therefore mandatory to limit the risk of microbiological contamination.

Methods: We prospectively monitored the microbiological ecology of clinical islet transplantation from 3/2003 to 3/2005. Pancreata were cold stored for 4-8 hours, and processed according to state of the art procedures (ISO 9001-2000 quality management system). Specific procedures to limit microbiological contamination included: 1) Iodin Polyvidon gastroduodenal instillation in the donor, 2) pancreas immersion in Iodin Polyvidon before and after storage 3) antibiotics in isolation solutions, 4) prophylactic antibiotic therapy in the recipient. Indepedent bacteriological analysis were performed in storage solution, pancreas, unpurified preparation, purified preparation, and final product. The final product was also analyzed for fungi and endotoxins (LAL).

Results: 64 pancreas were processed and 30 (47%) preparations (358±181±98016 IEQ) were transplanted in diabetic patients. Bacterial contamination (staphylococcus epidermidis, bacteroides species) was observed in 4 (6,2%) pancreata, 1 (1,6%) cold storage solution, but none in the following steps. Fungi (candida glabrata, candida albicans, lactobacillus ramosus) were observed in 4 (6,2%) cases. Endotoxin was superior to 0,25 EU/mL in 5 cases (8%) but always inferior to 5 EU/kg of recipient. Two recipients presented hyperthermia within 7 days after Tx, but no infection could be documented.

Conclusion: Despite frequent initial pancreas contamination, stringent procedures and quality management allowed us to control microbiological ecology of human islet preparation and avoid clinical contamination.
PO-020 ISOLATION AND IN VITRO EXPANSION OF MULTIPOTENT COMMESENCHYMAL STEM CELLS FROM SEVERAL HUMAN TISSUES (BONE MARROW, LIVER AND HEART)

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It has been demonstrated the persistence in adult murine bone marrow, skeletal muscle and brain of a subpopulation of mesenchymal stem cells with a very wide multipotentiality. Similar cells have not yet been isolated from human tissues other than bone marrow. The purpose of our study was to isolate, select, in vitro grow and characterize multipotent adult cell lines from human bone marrow, peripheral blood, liver and heart.

**Materials, Methods:** The immunophenotype of the cell lines was investigated by flow cytometry and RT-PCR (n=12). The telomerase activity of selected cell lines was evaluated by TRAP assay (n=9). The multipotency (osteoblastic, adipogenic, endothelial and muscular differentiation), of the cell lines (n=9) was investigated exposing the cell cultures to well known differentiation inducers and testing the differentiation by immunohistochemistry and immunofluorescence.

**Results:** Cell lines with an immunophenotype (CD45-/CD34-/CD38-/CD117-; CD133-+HLA-DR-+CD235a+/KDR+/CD90+/CD133+/CD49b+), a telomerase activity and a differentiation potential similar to that of multipotent adult progenitor cells were obtained from human hearts (n=35), livers (n=12) and bone marrows (n=16). Interestingly all the cells isolated from peripheral blood (n=6) failed to grow.

**Conclusion:** Our findings support the hypothesis that multipotent cells reside in many human tissues and could account for the experimentally observed non-orthodox differentiation of numerous classes of adult stem cells along unrelated cell lineages. Moreover, we found that, under our experimental conditions, resident stem cells are more responsive to growth factor stimulation than circulating stem cells, suggesting that these latter are in a more quiescent state.

PO-021 COMPOSITE TISSUE ALLOGRAFTS MODELS ON THE RAT

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The aim of this work was primary to familiarize with some experimental animal models used in the research field of Composite Tissue Allografts (CTAs) and secondary to develop advanced microsurgical skills. All these animal models are vascularized allotransplants from Brown Norway to Lewis rats. A total of 97 procedures were done: orthotopic (n = 60) and heterotopic (n = 5) limb transplantation, femur transplantation (n = 5), limb and contralateral femur transplantation (n = 5), sternum transplantation (n = 2), face transplantation (n = 5), and toe-to-thumb allotransplant (n = 5). All animals received drug therapy (FK506, MMF and Prednisone) for 8 weeks, then treatment was ceased entirely. The average success rate of transplantation was 84.57%. This study demonstrated that the composite tissue transplantation could be a reliable new method to solve the difficult problem of Plastic Surgery – the reconstruction of extensive soft tissue defects or mutilations. In the same time we improved our rate of success performing anastomoses of vessels of less than 0.8 – 0.5 mm in diameter. Clinically such anastomoses are necessary for replantation of the distal digits in adults and whole digits in children, and for the new direction of perforators’ free flaps. With this techniques practiced, there will be more ease, confidence and success when doing small tissue transplantation or replantation in humans, even in infants.

PO-022 SENTINEL SKIN ALLOGRAFT – A RELIABLE MARKER FOR MONITORING OF LIMB TRANSPLANTS REJECTION

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Previous studies led us to the hypothesis that a simultaneous skin graft may act as an effective marker of limb rejection. The aim of this study was to test the predictive value of a sentinel skin graft as a marker of rejection, using a hind limb transplantation model in rats. Lewis rat recipients received a hind limb transplants alone from Brown Norway donor (control, n=15) or combined with a full thickness 15 cm² sentinel skin graft (n=45). All animals received drug therapy (FK506, MMF and Prednisone) for 6 weeks, then treatment was ceased entirely. Rejection of the skin graft and limb skin, was assessed by both visual and histologic grading system. Detectable rejection (grade 1) was observed 1.35 ± 1.5 days earlier in the sentinel skin graft than in the limb skin (p = 0.0005) and clearest rejection (grade 2) appeared 0.91 ± 1.58 days earlier in the sentinel skin graft (p < 0.005). The average histologic grade for early rejection of the skin graft was 1.46 and 1.08 for the limb skin (p < 0.05). These findings confirm a visual and histological delay in rejection of the limb skin compared to a distant sentinel skin graft. Skin grafts transplanted simultaneously with hind limbs can be a useful marker of early rejection.

PO-023 SPLENIC AUTOTRANSPLANTATION COMBINED WITH SPLENECTOMY AND PORTAL – VARICEAL DISCONNECTION IN THE TREATMENT OF PORTAL HYPERTENSION

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In an attempt to preserve splenic function and to prevent complications of splenectomy, such as sepsis, metabolism disturbances and alterations on hematologic series, in 29 patients with portal hypertension submitted to total splenectomy, we implanted 20 fragments of the spleen, measuring 1 to 2 centimeters, on the greater omentum. This procedure was combined with portal-veariceal disconnection, with external ligation of the right gastric vein, the left gastric vein, all posterior gastric and lesser curvature veins as well as external ligation of the abdominal periesophageal veins. Transgastric running suture of the lower esophageal and gastric varices completed this treatment. As result of this operation, there was no complication related to the splenic implants and there was no mortality. Hematological and immunological exams (abnormal circulating particles, red cells, white cells, platelets, IgA, IgM and IgA counts) were normal. Scintigraphy with 99m-technetium sulfur colloid registered images of the splenic autotransplants in all cases. In conclusion, the implantation of splenic fragments on the greater omentum seems to be a safe and probably useful procedure to maintain the splenic function.

PO-024 RENAL TRANSPLANTATION FROM LIVING RELATED VS. UNRELATED KIDNEY DONORS

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Our study population consisted of 402 Living Related Donors (LRD)- of which 344 pairs shared 1 haplotype (Group A) and of 209 Living Unrelated Donors (LURD) (Group B): 173 between spouse pairs (Group C) – 132 from wife to husband (Group C1) and 43 from husband to wife (Group C2) as well as 32 between relatives in law or emotionally related patients and 2 between members of clergy (Group D). 199 pairs showed 3-6 HLA A B Dr mismatches (MM) with the donor and in 10 cases 0-2 MM. Donor and recipient mean age was 49±13.4 and 29±10.3 in Group A and respectively 46±11.2 and 48±9.6 in Group B. The post-transplant immunosuppression therapy was based on Cyclosporin A (CsA). C2 test was used to assess statistical significance.Donor mortality was 0%; perioperative morbidity was 15.2%. Graft function immediately after surgery. The actuarial 1yr, 5yrs, 10yrs and 15yrs graft survival was in Group A: 94%, 86%, 84%, 75% vs. Group B: 89%, 78%, 71%, 70% (NS), Group C1: 90%, 75%, 67%, 69% vs. Group C2: 81%, 74%, 72%, 62% (NS) and Group C: 88%, 78%, 71%, 60% vs. Group D: 91%, 80%, 71%, 61% (NS). There was no statistically significant difference between LURD and LRD as far as graft survival. In conclusion, we certainly agree with the guidelines issued by the International Congress on Ethics in Organ Transplantation (Munich, December 10-13,2002): kidney transplantation from living donors is a safe and effective procedure and should not be discouraged.
The research program "innovative strategies to expand cadaveric donor pool for live liver transplantation" (SITF Project) has been formally approved in 2002 by Italian Ministry of Health (IMh) as a two-years exploratory experimental project. The main goals of the SITF Project are to improve matching criteria for split liver transplantation (SLT) in both pediatric and adult recipients, to promote an increase of the SLT/full-size liver transplantation ratio at the national level, and to establish shared criteria for SLT in two adult recipients. The original executive plan of SITF Project prefigured the participation of both the Italian transplantation Centers with more advanced experience in the field of SLT, and institutional partnerships such as Nord Italia Transplant (NITp) and Italian National Transplant Center. A first Web public area concerning the SITF Project has been activated, as well as a reserved Web area with the aim to share cadaveric donors and patients in the waiting lists between Operative Units involved in the research program. For this objective, a specific Oracle-based database able to perform an automatic matching between a single cadaveric donor and two potential adult recipients has been released in the beta version. The SITF Project represents a new approach in the management of SLT for two adults recipients in Italy, and as a model for a functional network between Italian transplantation Centers.

### Table 1. Reasons for rejection

| Reasons          | Primary factor % | Secondary factor % |
|------------------|------------------|--------------------|
| 1 Abnormal CXR   | 28.1             | 0                  |
| 2 Chest infection| 15.6             | 0                  |
| 3 Smoking        | 31.3             | 21.9               |
| 4 Poor gases     | 6.3              | 3.1                |
| 5 Age            | 6.3              | 12.5               |
| 6 Other          | 12.5             | 15.6               |

**Conclusion**: Expanding the criteria of suitability of donor lungs can increase the donor pool without significantly affecting survival.
AVAILABILITY OF SPLIT LIVERS ACCORDING TO PRIMARY FUNCTION

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The potential liver grafts gained from systematical splitting of optimal organs has been evaluated according to strict theoretical criteria (Transplantation 2006; 81:35/90) were available for splitting for one adult and one child (AC) or two adults (AA). These criteria allowed only an approximation of reality. To better assess the potential impact of split liver transplantation, we investigated the proportion of donors that could be considered for this procedure according to the outcome after transplantation as wholeorgan(WO).

Methods: The records of 90 liver donors harvested from 1.1997 to 12.2000 were analyzed and compared with the primary function (PF) after adult transplantation as WO. Livers with good primary function (GPF) were defined as having <600U/l peak sGPT and <65% factor V on post-op-day 2, allowing the selection of donors, which are easily "splittable." Beside function, weight >45kg and >70kg were considered for AC and AA.

Results: Overall, 68% (51/90) of livers demonstrated a GPF after transplantation as WO. None of the previously studied criteria demonstrated an impact on PF. Similar to the previous study, by applying all criteria on the whole population, 13.3% or 8.8% of livers would be available for splitting for AC or AA in our population. According to primary function and weight, 68% (61/90) on 39% (35/90) were available for AC or AA.

Conclusion: Splitting could increase the number of liver grafts up to 68% and 39% for AC and AA. A wider use of this technique could reduce the patient's time on the waiting list.

Critical Care (CC) staff attitudes to organ donation vary between professional categories, hospitals, and countries depending on cultural and religious beliefs and, hence, may influence donation rates.

Aim: To enter into the DA database to compare staff attitudes towards donation as WO. None of the previously studied criteria demonstrated an impact on PF. Similar to the previous study, by applying all criteria on the whole population, 13.3% or 8.8% of livers would be available for splitting for AC or AA in our population. According to primary function and weight, 68% (61/90) on 39% (35/90) were available for AC or AA.

Conclusion: Splitting could increase the number of liver grafts up to 68% and 39% for AC and AA. A wider use of this technique could reduce the patient's time on the waiting list.

PO-031

CRITICAL CARE STAFF ATTITUDES TOWARDS DONATION: A COMPARISON BETWEEN JAPAN AND EUROPE

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Critical Care (CC) staff attitudes to organ donation vary between professional categories, hospitals, and countries depending on cultural and religious beliefs and, hence, may influence donation rates.

11.911 Donor Action (DA) Hospital Attitude Survey (HAS) questionnaires were entered into the DA database to compare staff attitudes towards donation as well as their knowledge, training needs and comfort level with donation related issues between Europe (n=6,064; 7 countries) and Japan (n=5,527; 9 prefectures).

General support for donation was higher amongst European staff (92%) compared to their Japanese colleagues (69%; p<0.001). Whilst 84.5% of European staff would donate their own organs, only 35% of Japanese would do so (p<0.001). In Europe, 92% of CC staff would donate organs from a relative, versus only 45% in Japan (p<0.001). Confidence levels with referring a potential donor, explaining brain death (BD) or introducing the subject of donation were 65, 62 and 54% respectively amongst European staff, against only 17, 25 and 16% in Japan (p<0.001). BD was accepted as a valid determination of death by 82% of staff in Europe, versus only 38% in Japan (p<0.001). In Europe, 16% of staff on average had received specific training in organ donation related issues, only 3% in Japan (p<0.001). The data presented suggests that Japan's problem with low donation rates already starts at CC staff level: staff's demonstrated lack of specific education may trigger a cascading negative effect, starting with disbelief in the concept of BD and explaining lower attitude and confidence levels with donation related tasks. One cannot expect the general public to support donation when CC staff themselves struggle with fundamental concepts.

PO-032

PO-033

SHORT TERM GRAFT SURVIVAL RATES AFTER LIVER RETRANSPLANTATION, IN THE LAST YEARS

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Aim: Our aim is to verify if in recent years short term graft survival rates after liver retransplantations (RETX) changed, and/or if differences occurred in donor/recipients characteristics or in surgical techniques.

Patients and methods: We time periods were compared: from 1995 through 1999 (time A) and from 2000 through April 2005 (B). In our Unit 135 liver transplantations (TX) including 16 (11.8%) RETX were performed during time A, whereas 168 including 17 RETX (10.1%), during time B. Donor (age), recipient (age, sex, urgency or elective conditions, cause of RETX, MELD, serum Creatinine and Bilirubine, INR, days from previous TX) and surgical (Total ische- mia time, wholeorgan(WO) were analyzed and compared with the primary function (PF) after adult transplantation as WO. None of the previously studied criteria demonstrated an impact on PF.

Conclusions: The data presented suggests that Japan's problem with low donation rates already starts at CC staff level: staff's demonstrated lack of specific education may trigger a cascading negative effect, starting with disbelief in the concept of BD and explaining lower attitude and confidence levels with donation related tasks. One cannot expect the general public to support donation when CC staff themselves struggle with fundamental concepts.

PO-034

INCREASED DONOR AGE IS ASSOCIATED WITH A STRONGER IMMUNE RESPONSE EARLY POST TRANSPLANTATION

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Recently we could show the correlation of donor age, modified immune response and reduced long-term graft survivals. Hence, the role of the use of split grafts and an older recipi- ent population, short term graft survival rates after RETX improved, even without differences with statistical significance.

RETX must be faced when there are no overwhelming risk factors.

PO-035

ATTITUDE TOWARDS RELATED LIVING DONATION OF PATIENTS ON THE WAITING LIST FOR A CAUDACER SOLID ORGAN TRANSPLANT

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Introduction: Spain is the country with the highest rate of cadaveric donation. However, given the deficit in organs, living donation is being encouraged. The objective here is to analyse attitude towards living donation in patients on the waiting list for a transplant.

Materials and Methods: Patients on the waiting list (n=96; 46 kidney and 50 liver) in the last year. The psychosocial survey was carried out in a direct
CONVINCING SKEPTICAL PEOPLE TO INCREASE ORGAN DONATION FOR TRANSPLANTATION IN A NON-HEART-BEATING DONORS: THE FORGOTTEN POOL

The main question of all transplant coordination teams is how to convince skeptical people to accept the idea of donation. As a comparator, probabilities to observe 15, 30 consecutive non-surviving (y) are almost zero. Even using a single probability of non-dying of 50% (the same as tossing a fair coin), the probability to have not observed any non-dying BDP after long time periods is near zero. This rationale could help to convince skepticals to cooperate in achieving brain death. Even if the probability of surviving could be higher than zero, the probability of observation more than 15 consecutive non-surviving BDP is almost zero. This rationale could help to convince skeptics to cooperate in achieving effective donors.

CONVINCING SKEPTICAL PEOPLE TO INCREASE ORGAN DONORS FOR TRANSPLANTATION

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One of the limitations to achieve more donors for transplantation is the belief that miracles could happen and brain death patients (BDP) could survive. Even with full life support, BDP develop cardiac arrest in few days (J-Neurology-Neurosurgery-Psychiatry 1995;58:75-80).

An argument potentially useful to convince skepticals is showing that there is a risk to the family member. Finally, only 6% considered living donation to be their first choice and 42% did not consider it at all. Up to 96% would donate an organ to a family member.

Conclusion: The patients on the waiting list are not very favourable towards living related donation for themselves, although members of their family have proposed it to them. However, the liver patient is more prepared to accept it, possibly because the patient has no other alternative. Even so, they are very favourable towards donating a living organ if a family member were to request one. In general, living donation is not being proposed to these patients as a real option, partly because of their doctors.

DONOR ACTION IN ACTION IN FINLAND

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In the 1990-ies the number of cadaver donors have not increased in Finland (inhab. 5.2 million), but stayed between 20-16 pm. The Donor Action (DA) program was implemented in 2001-2005 in 19/20 regional and university hospitals at a time of severe economic and personnel restriction in the hospitals. The physician and nurse in charge of the local ICU's implemented the DA programs. No reimbursement is performed to donor hospitals.

Results: In 1 year in each hospital Medical Records Review (MRR) was performed in 2374 succumbed patients. 184 potential donors were identified, family was approached in 159 cases and 102 cadavers ended up as organ donors. Thus the gap between potential and actual donors was high, 82 cadavers.

Liver Allocation based on the MELD score does not offer additional advantage over a modified continuous disease severity score in a system characterized by low organ donation rates and long waiting times.

DONOR ACTION IN ACTION IN FINLAND

Federico Oppenheimer2, Lutz Fritsche2, Volker Kliem2, Yvon Lebranchu2, Maurizio Salvadori1, Jeremy Chapman2, Andreas Bock2, Bertrand Dussol2, Lutz Fritsche2, Volker Kliem2, Yvon Lebranchu2, Federico Oppenheimer2, Erich Pohanka2, Gunnar Tuvelius2.

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they received similar immunosuppressive regimen. Their DGF-incidence was higher (40% vs 27% in CAD, p < 0.001), but their GFR at year 1 as well as their GFR-decline from year 1 onwards were unaffected (GFR 56 vs. 59 mL/min at 1 year, GFR-decline -1.3 mL/y). Multifactorial analyses confirmed donor and recipient age and DGF as factors affecting 1-year GFR in NHB donors, but NHBD did not independently affect GFR at 1 year, when donor age and gender, recipient age, DGF, and acute rejection were taken into account.

Conclusion: Receiving a NHBD-graft was associated with a higher rate of DGF, but did not independently affect GFR. Most NHBD-grafts that survive to one year post transplantation maintain encouraging graft function on a CsA-based regimen.

**PO-041 NON-HEART-BEATING (NHB) DONATION IN THE NETHERLANDS: AN IMPROVEMENT OF THE ORGAN SUPPLY?**

Bernadette J. Haase, Karin M. Keizer, Hendrik A. van Leiden. Dutch Transplant Foundation, Leiden, Netherlands.

**Purpose:** In the Netherlands there is a fast increase of NHB donation. In this study the question is raised whether NHB donation contributes to improvement of the organ supply.

**Method:** From 1994-2004 donor data of heart beating (HB) and NHB donors were analyzed.

**Results:** In this 11 year period the total number of used post mortem donors hardly increased (1994:196, 2004:228), while the percentage of NHB donors increased from 5% in 1994 to 41% in 2004. The percentage of NHB donors within the total number of donors reported, increased from 5% in 1994 to 48% in 2004; the average discard rate of HB and NHB donors is 3% and 2% respectively. Although NHB donors are mostly kidney-only donors, the overall percentage of multi organ donors (MOD) did not decrease. NHB donation excluded, the percentage MOD increased from 62% in 1994 to 81% in 2004. The total number of kidney transplantations with post mortem kidneys did increase.

The long term results of transplantation are similar in the HB and NHB group. The estimated NHBD donor potential is at least twice as high as the HB pool.

**Conclusion:** Although the number of NHB donors increased considerably, the total number of post mortem donors did not. The discard rate of NHB donors is higher compared to HB donors. So far, the increase of NHB donors did not decline the number of extra renal transplants, due to a higher efficiency of MOD's. Extra effort should be put to increase the HB donation pool and NHB donation should be further expanded for both renal and non renal organs.

**PO-042 QUALITY OF LIFE AFTER LAPAROSCOPIC V OPEN LIVING DONOR NEPHRECTOMY**

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**Purpose:** We conducted a quality of life assessment on living kidney donors from 1994 to 2003. We aimed to see if there was any significant difference in long term quality of life for the donor between a laparoscopic and open incision. Laparoscopic surgery is known to reduce convalescence and chronic wound pain.

**Materials and Methods:** The subjects were taken from the living donor transplant programme at Guy's Hospital, London. The short form-36, version 2, a standardised measure of health related quality of life was sent to 77 subjects, 37 were laparoscopic donors and 40 were open.

**Results:** The outcome measures were the scores for the eight dimensions of the UK SF36-II. These are physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The mean scores were compared and a paired t-test done for each category. The mean follow up from transplant was 298 days.

**Conclusion:** The survey was completed by 51 (26 lap, 25 open) living kidney donors (66% response rate). For both groups, the quality of life exceeded that of the UK population normative values throughout the categories. For general health, the UK norm was 71.06, the lap group 84.40 and the open group 89.12. A paired t-test for each category showed no significant difference between the groups with a p value greater than 0.05 for each dimension. Mean bodily pain score was 86.36 for lap and 88.36 for open (p = 0.5435).

**PO-043 LIVING KIDNEY DONORS > 60 YEARS OF AGE: IS IT ACCEPTABLE FOR THE DONOR AND THE RECIPIENT?**

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Donors > 60 years are now frequently accepted for living kidney transplantation (LKT). We analyzed outcome of donors and recipients using organs from donors > 60 years. Demographic details of donors and recipients were recorded and long term outcome was analyzed. Results following LKT from donors > 60 years (group A) and from donors < 60 years (group B) were compared. At our centre 34 kidney grafts were obtained from donors > 60 years and 202 from donors < 60 years. In group A 41% and in group B 25% of grafts were from donors > 60 years. Group A and B 98% and 96% for group B. Mean GFR at 1 year was significantly better for recipient of group B (133 and 160 mL/L) compared to group A (176 and 250 mL/L).

**PO-044 EVALUATION OF DISCONTINUED THORACIC DONOR NEPHRECTOMY IN THE CENTRAL REGION OF GERMANY ANALYZING THE PROCEDURE FROM INFORMATION TO TRANSPLANTATION**

Monika Schmid, Dietmar Mauer. Region Mitte, Deutsche Stiftung Organtransplantation, Mainz, Germany.

**Background:** For quality assurance in organ donation and transplantation it is necessary to implement a documentation system, which provides for a complete analysis of all donor related organ data as to estimate transplant results.

**Method:** From 2003 to 2005 each organ donation procedure was evaluated real time and documented if. In which phase of the process a thoracic organ has been omitted from the procedure. Examinations of potential thoracic donors included ECG, thoracic X-rays, echocardiography, bronchoscopy and coronary angiography.

**Results:** In the study period of two years we had 295 donors reported to Eurotransplant, yet only 116 were suitable as heart and 72 as lung donors. Reasons for the comparatively small proportion of heart donors are the missing consent (n = 52), age (n = 61), previous heart diseases (n = 26) or poor quality of left ventricular myocardial function (n = 81). Potentional lung donors were not reported due to three main reasons: missing consent (n = 52), age (n = 54) and infection (n = 81).

During the allocation process we lost 5 hearts and 11 lungs due to age, insufficient function or no recipient.

In the operating theatre 12 hearts were declined due to poor function or coronary sclerosis and 11 lungs were diagnosed as not transplantable due to insufficient function, trauma or aetelactsis.

**Discussion:** Higher donor age (> 40% over 55 years), age related comorbidity, high infection rates and missing consent to thoracic organ donation mainly caused the small number of heart and lung retrievals. These findings enable us to detect and analyze weak points in the organ donation process and to continually improve donor diagnostics, therapy and donation procedure.

**PO-045 LAPAROSCOPIC KIDNEY DONATION IN THE OVER 60’S**

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**Introduction and Methods:** There is evidence that live donors over the age of 60 may be more at risk from cardiac and pulmonary complications during conventional donor nephrectomy. We reviewed our centre’s experience of laparoscopic donor nephrectomy with respect to donor age.

**Results:** 31 laparoscopic nephrectomies for donation were performed between April 2002 and December 2004. Seven (23%) donors were over 60 (range: 63 - 81 yrs) and considered “fit for operation” after appropriate cardio respiratory investigations. The older donors had a lower GFR (mean 88 vs. 102 mL/min, p=0.05, Mest) and gave to older recipients (52 vs. 37 yrs, p=0.03).

There were no significant peri-operative complications in the over 60’s and the mean hospital stay was 4 days (under 60: 3 days, p=0.13). All the grafts derived
from elderly donors functioned immediately, however, the recipient function was slower (see figure).

Conclusions: After careful assessment laparoscopic nephrectomy is an option for healthy, elderly individuals wishing to donate a kidney.

References: 1. Faulchald P. et al. Transpl Int 1991; 4: 51-53.

PO-046 EFFECTS OF A COURSE FOR REQUESTERS IN THE NETHERLANDS

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Purpose: Lack of hospital staffs’ competence leads to higher refusal rates of donation requests. Training to enhance this competence is therefore paramount. For this purpose the Dutch Transplantation Foundation initiated the development of a training course for requesters, based upon sound theory and empirical evidence. The training was developed by the first author.

Methods: All theory and evidence indicate that requesters should be aware of their personal attitudes, knowledgeable about brain death and the donation procedure; they should have a thorough understanding of teamwork and should possess excellent communication skills. In the 8,5-day course, including a follow-up after 6 months, all issues are dealt with. Assessment and feedback procedures are an integral part of the course as these enhance the effectiveness of the learning process. Learning experiences could be put into practice in the 6 months period between the course and the follow-up.

Results: The competence of the participants (skills, knowledge, attitudes and self-efficacy) was measured before and after de course. In reflective journals the participants described their learning experiences in the course and during their practice period as well as the consultations with relatives in practice and the decisions these relatives made about organ donation.

Conclusion: The results show that the requester course is a promising initiative.

Discussion: The studied population was large enough to justify this study, the resulting figures however remained too small to reach statistical conclusive results. Despite this remark, we are faced with an open attitude for further improvement in hospital development, positive aspects of this pilot can be further introduced in the Netherlands.

PO-049 THE ALTERNATIVE TO DESENSITIZATION OF HIGHLY SENSITIZED KIDNEY PATIENTS IS THE ACCEPTABLE MISMATCH PROGRAM SHORT WAITING TIME, REDUCED COSTS, AND EXCELLENT GRAFT OUTCOME

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The almost impossibility to obtain a crossmatch negative offer for highly sensitized patients (HSP) prompts the need of new protocols. Recent reports advocate the removal of donor-specific HLA antibodies before transplantation, including intravenous immunoglobulins, plasmapheresis and immunoglobulins, or immunoabsorption. Ca. 80% of the HSP can be transplanted. The others stop treatment because of side effects. The 1-year graft survival is in the range of 80%. The high immunosuppression for desensitization may have impact on the short and long-term immune surveillance (infections, cancer). Here we advocate, the selection of crossmatch negative donors on the basis of the Acceptable Mismatch Program (AMP) as the first and best option to transplant HSP. The AMP makes use of the holes in the immune repertoire, which depends on the short-antigens. AM can be defined by analysis of the typing of panel donors with negative reactions in the screening or by direct crossmatching of blood donors with 1 HLA mismatch to the HSP. In the period 01.2002-07.2003, 129 patients entered the AM-program and 57 were transplanted (mean waiting time 9.7m, range 0-130m). Graft survival at 2 years was 87% identical to the non-sensitized patients. As the nature of the HLA polymorphism does not allow all patients to profit from this approach removal of circulating HLA antibodies can be considered as a rescue therapy for those patients for whom the AM-program does not give a solution.

PO-050 DOES MACHINE PERFUSION AFFECT ANTIVIMENTIN ANTIBODY LEVELS IN NON-HEART BEATING DONOR KIDNEYS?

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NHBD are a valuable resource though ischaemic damage causes a high incidence of DGF. Ischaemia primarily affects the vascular endothelium increasing the antigenicity and hence production of anti-vimentin antibodies (AVA). The...
PO-051 DOES STREPTOKINASE IN PRE-FLUSH INDUCE ANTI-STREPTOKINASE ANTIBODIES IN NHBDB RECIPIENTS?

Ajay Gupta, Hua Mi, Mohammad Gok, Brian Shenton, Naeem A. Soomro, Brian C. Jacques, David Rix, Derek M. Manas, Ajay Gupta, Hua Mi, Mohammad Gok, Brian Shenton, Naeem A. Soomro, Brian C. Jacques, David Rix, Derek M. Manas. Renal and Liver Transplantation Unit, Freeman Hospital, Newcastle upon Tyne, United Kingdom.

Streptokinase used for preflush in the NHBDB procurement can improve the quality of the kidney retrieved from NHBDBs. Intra-venous and intra-pleural administration of streptokinase is known to cause production of anti-streptokinase antibodies.

**Aim:** The aim of this study was to evaluate whether the use of thrombolytic streptokinase as a preflush during NHBD procurement results in production of anti-streptokinase antibodies in the recipients after renal transplantation.

**Methods:** Between 2000 and 2003, a total of 36 renal transplants from NHBDBs were randomised into 2 groups: streptokinase group (n = 18) who received streptokinase and non-streptokinase group (n = 18) who received a saline placebo as preflush during organ procurement. After routine nephrectomy, kidney samples were taken for post mortem biopsy screening prior to transplantation. Blood samples were drawn from all recipients pre-transplant, 1 and 6 months post-transplant. Anti-streptokinase antibodies were measured using ELISA and results expressed in arbitrary ELISA units.

**Result:** The median anti-streptokinase antibodies level in recipients receiving streptokinase as a preflush in NHBDB procurement was 40, 240 and 40 units respectively at pre transplant, 1 and 6 months post transplant (student-t test, p = NS). In the control group, median anti-streptokinase antibodies level was 120.160 and 120 units respectively at pre transplant, 1 and 6 months post transplant (p = NS). There was no significant different of median anti-streptokinase antibodies level between these two groups (MWU test, p = NS).

**Conclusion:** The use of thrombolytic streptokinase as a preflush in NHBDB procurement does not result in the production of anti-streptokinase antibodies in recipients after renal transplantation. We conclude that the practice is safe and helps improve graft survival.

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**PO-052 EXPERIENCE OF THE HOSPITAL CLINIC DE BARCELONA IN ORGAN AND TISSUE PROCUREMENT FROM NON-HEART-BEATING DONORS (1986-2004)**

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**Objective:** Review the different organ preservation techniques in non-heart-beating donors and describe the procedures, potential donors and organ and tissue generation from these donors throughout 18 years of experience.

**Methods:** Compare the results obtained with the different organ preservation techniques (in situ perfusion, total body cooling and nontherapeutic recirculation). Analyse the potential non-heart-beating donors accepted according to a certain inclusion criteria.

**Results:** Accepting as inclusion criteria: those applied to all donors, age ≤ 65 years, donor donation after cardiac death (DCD) and no specific previous of high ischaemic reperfusion injury (IRI) (≤ 30 minutes), 122 potential donors were considered. From these, 59 became organ donors (49 also tissue donors) and 25 tissue donors. The procedure for organ recovery was aborted in 40 cases for one or more clinical contraindications. In 17 cases due to IRI, 1 case due to refusal and 6 cases due to 60% of organ recovery was performed and 116 kidneys were procured (92 transplanted) and 23 livers were procured (7 transplanted). In addition to that, 124 corneas, 29 hearts for valves, 17 blood vessels, 39 musculoskeletal and 6 skin donations were obtained.

**Conclusions:** The non-heart-beating organ donor program has been useful in increasing the number and quality of organs and tissues for transplant, as a successful complement of a brain death donation program. The review of this activity shows similar results as those from brain death donors procurement, regarding graft survival and tissue viability.

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**PO-053 CHARACTERISTICS OF HIGHLY SENSITISED PATIENTS ON THE RENAL TRANSPLANT WAITING LIST: A SINGLE CENTRE UK STUDY**

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**Purpose:** The first aim of this study is to establish whether highly sensitised patients have to wait longer for renal transplantation than other patients on the waiting list. The second aim is to identify characteristics of this group that may be associated with the long waiting time.

**Methods:** Data, collected prospectively on all patients awaiting renal transplant in the South East of England, were analysed. Highly-sensitised patients were identified and compared with the rest of the patients on the waiting list. Results: Some 409 patients awaiting renal transplantation were identified. 48 (11.7%) were highly sensitised patients. The mean waiting time for transplantation in this group was 1722 days with a maximum waiting time of 6851 days. By contrast, the mean waiting time for the unsensitised group was just 570 days. This difference between the two groups was significant (p=0.001).

**Table 1** shows the characteristics of highly-sensitised versus unsensitised patients.

| Characteristic | Highly-sensitised | Un sensitised | Significance |
|----------------|------------------|---------------|--------------|
| Gender         | Male 19, Female 29 | Male 204, Female 157 | p=0.040 |
| Age            | Mean 47.7 | Mean 48.1 | p=0.598 |
| Ethnic group   | 29 White, 13 Black, 4 Asian, 2 Other | 233 White, 71 Black, 38 Asian, 19 Other | p=0.522 |
| Matchability points | Mean 8.83 | Mean 5.68 | p=0.001 |

**Conclusions:** Highly-sensitised patients wait longer than unsensitised patients to be transplanted in the South East. There was a significantly higher proportion of females in the highly sensitised group, whereas ethnic group did not reach significance. One way of dealing with this problem is for the allocation scheme to be changed to take more consideration of those characteristics found to be significantly associated with sensitisation. Alternative approaches are the use of desensitisation regimes or changes in the system to allow for more cadaveric donations.

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**PO-054 SIROLIMUS IN KIDNEY TRANSPLANTATION FROM ELDERLY DONORS**

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**Nephrotoxicity caused by calcineurin inhibitor can lead either to delayed graft function either to long term decline of renal function after kidney transplantation.** Renal transplant recipients from marginal donors require nonnephrotoxic immunosuppression.

Twelve patients underwent kidney transplantation from marginal donors (age≥ 55 years, mean age 63.4 years, 34.3 years, 6 patients were treated with sirolimus regimen calcineurin inhibitor free, based on basiliximab, micophenolate mofetil (MMF), steroids and sirolimus. Mean follow up was 24.9 months. We report immediate renal function in 6 patients and delayed graft function (DGF) in 6 patients. All the patients had a good recovery after DGF with a mean creatinine of 1.8 mg/dl (±0.8) after 1 month from transplantation. Hypercholesterolemia and hypertiglyceridemia were the most common adverse effects (n=11), associated to arthralgia (n=1) and thrombocytopenia (n=2). Three patients underwent switch to tacrolimus, due to sirolimus induced side effects.

Immunosuppression without the use of calcineurin inhibitors is a safe and effective regimen in kidney transplantation, although sirolimus related side effects still represent a morbidity factors in these patients.
ARE BRAZILIAN OPOs EFFECTIVE?: ANALYSIS OF 7 YEARS OF ACTIVITIES OF A BRAZILIAN OPO

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Aiming to increase organs supply the Brazilian government introduced the Organ Procurement Organisations (OPOs). However, there were few reports on the effectiveness of these OPOs. To analyse the Regional OPO (OPOSJRJP) effectiveness during the period of 7 years of its activities, we retrospectively analysed data of 1780 notifications of potential donors (PD) of corneas (C) (n = 12303) and multiples organs (MO) (n = 458), number of effective donations (ED) and the reasons of refusal to donate. It was observed that, despite a reduction of 25% in the notification of PD, the number of ED-MO and ED-C increased 280% and 78% respectively. The most important reasons for non donation of were family refusal (FR) and medical contraindication (MCI). Comparisons of these data with those from other São Paulo OPOs demonstrated that the OPOSJRJP have the highest notification (34 ppm) and donation rates (12 ppm), as well as the smallest FR rate. However, and elevated rate of MCI was observed. The increment observed in the effective donations may be due to acquisition of more experience by the OPOSJRJP with the process of family approach while the high rate of MCI could be consequence of lack of training in the maintenance of the PD. CONCL. The OPOSJRJP increased significantly the number of ED-MO and ED-C donations as well as the deceased donor rates ppm/year, we suggest that efforts must be directed to also improve these national rate in order to increase organ transplantation in Brazil.

Results: Findings revealed that 49.3% of employees had knowledge about organ donation. The most common resource for acquiring knowledge was group media (33%) and the least common resource was medical personnel (3.3%). There is significant difference between employees’ attitude and their relative’s attitude about organ donation (p<0.001). There is significant difference between attitudes of employee’s relatives and employees according to organ transplantation, knowledge of organ donation and tendency to have donation card.

Conclusion: According to undesirable results about attitude of employees in organ donation, it is necessary that medical personnel must accompany in community education and motivate them about organ donation.

RETROSPECTIVE ANALYSIS OF THE CAUSES OF REJECTION OF POTENTIAL DONORS FOR LIVING RELATED LIVER TRANSPLANTATION

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Background: A major prerequisite for living related liver transplantation (LRLT) is to ensure both donor safety and optimal graft quality. Therefore, excluding unsuitable donor candidates should be an important priority of the transplant team.

Purpose: is to analyze the criteria for exclusion of potential living related donor.

Patients and Methods: From November 2000 to March 2005, 327 potential living related donors for 136 potential recipients for liver transplantation were screened and worked up at the Liver Transplant Center, King Abdul Aziz Medical City. They were evaluated in a stepwise manner including medical, physical, laboratory, psychosocial, and imaging assessment. Data regarding potential donors was retrospectively reviewed. Reasons for rejection of disqualified donors were analyzed.

Results: Out of the 327 potential donors, 223 (68.2%) were rejected at an early stage. One hundred and four cases (31.8%) had CT- volumetry and/or MRCP. While 44 (42.3%), of those who had CT- volumetry and/or MRCP had their work up completed, 24 (23%) went for surgery. Causes for donor rejection were classified as donor related factors (inadequate volume, unsalvage anatomy, abnormal liver function tests, medical/psychiatric, fatty liver, etc.), n = 191 and recipient related factors (too ill, died, received cadaveric transplant, etc.), n = 112.

Conclusion: In our as well as in most other centers’ experience, small proportion of potential donors prove to be satisfactory candidates. Therefore, strict attention to a stepwise evaluation process is of utmost importance to disqualify unsuitable potential donors as early as possible during work up.

PO-056 ATTITUDE OF GOVERNMENT EMPLOYEES AND THEIR RELATIVE ABOUT ORGAN DONATION AFTER BRAIN DEATH

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Introduction and aims: The need for organ donation has increased 200% over the past decade, while the number of organ donors has remained relatively constant. The individual’s knowledge declined from concepts of brain death and transplantation of major organs has been hindered them attitudes about organ donation. The purpose of this descriptive study was to determine government employees and their relatives about organ donation after brain death.

Material and methods: The sample was 400 persons that they are selected with clustering randomized sampling method. Data collection tool was questionnaire. For the analysis, Descriptive statistic, T test and T- paired test, Kruskal walls and ANOVA tests were used.

PO-057 HYPALBUMINEMIA IN BRAINDEAD ORGAN DONORS

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Hypoalbuminemia is documented to be associated with severe head-injury and attributed to hypermetabolism/hypercatabolism seen in these patients. However, no known study on the albumin status in brain-dead organ donors has been documented. To determine the albumin status in brain-dead organ donors seen at the Transplant Unit. Thirty-seven brain-dead organ donors seen at GSH Transplant Unit between Jan. 2001 and Dec. 2002, were retrospectively assessed for age distribution, biochemical parameters (Serum electrolytes, urea, creatine, liver function test (AST, GGT, LDH, total protein and albumin), and hemograms (Hemoglobin and platelets), time of injury, item certified brain dead, and biodata (weight and height). The results were then statistically analysed.

The mean age of 37 brain dead organ donors seen over two years was 27.6 years (±SD 10.70). The male-female ration was 3:1 (n=28: n=9). About 51% (n=19) of the brain-dead organ donors were white, while the remaining races together constitute about 49% (n=18). The cause of death in the majority of the subjects (n=26, 70.3%) was trauma related (Assault, MVA, GSW, Fall). The average time interval between being certified brain dead and harvesting of the organ is 11 hours (±SD 6.2). The mean height recorded in 27 subjects was 1.72m (±SD 0.11), and the average weight recorded in all patients was 69.6kg (±SD 19.0). The average total albumin recorded in 33 subjects was 49.4g/dL (±21.05D), while the meanalbumin level was 23.2g/dL (±7.4SD). Other electrolytes and liver function test parameter were normal.

This study demonstrated significant hypoalbuminemia and hypoalbuminemia in brain dead organ donors seen at the Transplant Unit of GSH. A further controlled prospective study is needed to validate this finding.

PO-058 HOW COULD WE AVOID TRANSFERRING RARE INCURABLE INFECTIOUS DISEASES

Danica Avsec Letonja, Slovenija-Transplant, Institute of the R of Slovenia for Transplantation of Organs and Tissues, Ljubljana, Slovenia.

Patients with organ failure are in life threatening situation and every additional disease after transplantation could be fatal. We have to exclude the transfer of incurable infectious and malignant diseases with transplantation.

To exclude the malignant and incurable infectious diseases at the procurement of organs and tissues for transplantation we use the following methods:

– Checking the present and past history
– Different biological tests
– Additional findings

In the Guide to safety and quality assurance for organs, tissues and cells published by Council of Europe are stated methods of screening packet, which should be performed in every deceased donor. If there is a suspicion for some additional infectious or malignant disease in the history of the deceased we should do further investigation. Consequently we notice that heteroanamneses is a very essential part, it is obtained in the family interview and serves also for collecting data needed as exclusion criteria for exploitation of organs and tissues.

The article shall present the scheme of all possible infections, which could appear in the European place and consequently collect the questions to be asked to minimise the possibility of transferring very rare incurable infectious diseases.

We should be aware, that some incurable infectious diseases, even appearing very rare, could cause disastrous consequences not only for the recipient but also for the entire transplant medicine. We all know about the transfer of rabies from the donor to the recipients and the alarm regarding the unfortunate accident. It is our duty to prepare all the necessary measures to avoid or at least minimise such type of events.
THE HEMODYNAMICALLY INSTABLE LUNG DONOR: A CASE FOR NON-HEART-BEATING DONATION

György Lang1, Gabriel M. Marta2, Clemens Aigner3, Shahrokh Taghavi2, Wilfried Wisser2, Walter Klempko2, 1 Thoracic Surgery, Karolinska National Institute for Pulmonology, Budapest, Hungary; 2 Cardiothoracic Department, Medical University Vienna, Vienna, Austria.

Objective: Initial experience with non-heart-beating donation has demonstrated the feasibility of the method. The same principle could be applied for management of hemodynamically unstable donors, who in the past were excluded from lung donation.

Methods: A 47 years old female donor was referred from a remote country hospital. Functional parameters of the lungs were excellent, with a PaO2 of 555 mmHg at FiO2=1.0 and a clear chest X-Ray. Prior to organ harvesting circulatory arrest occurred and the donor was resuscitated for 15 minutes, resulting in regain of a spontaneous heart activity. Attempts to transfer the donor to the operating theatre were made. On the way to the OR the donor heart arrested again and resuscitation was restarted, however being ineffective this time. Since the lung harvesting team was not yet on the site the abdominal team was asked to perform topical cooling of the lungs with cold saline solution. After 20 minutes of warm and 60 minutes of cold ischemia, the lung team arrived and harvested the lungs. Bilateral lobar transplantation was performed in a 28-year-old recipient suffering from CF.

Results: PaO2 sample, taken from the pulmonary vein prior to perfusion, was 445 mmHg, indicating excellent allograft function until cardiac arrest 80 minutes earlier. The cold ischemic time was 275 and 350 minutes for the right and left side, respectively. The allograft showed excellent oxygenation and the patient was weaned from the respirator within 7 days, and left the hospital after 22 days.

PO-061 ETHICAL CONSIDERATIONS ON KIDNEY TRANSPLANTATION FROM LIVING DONORS
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Kidney transplantation from living donors is performed all over the world. Living nephrectomy for transplantation has no direct advantages for the donor other than an increased self-esteem, but remains an extremely safe procedure, with a worldwide overall mortality of 0.03%. This theoretical risk for the donor seems to be justified by the socioeconomic advantages and increased quality of life of the recipient, especially in selected cases, such as pediatric patients, when living donor kidney transplantation can be performed in an unequivocal phase, avoiding the psychological and physical stress of dialysis, which in children is not well tolerated and cannot prevent the retarded growth. Some forms of psychological conditioning are difficult to be recognised in a family setting, while economic dealings may be on purpose concealed even by the donor. According to the Ethical Council of the Transplantation Society, conditioned altruism must be effectively prevented, not only for ethical but also medical reasons. The risks are too high not only for the donors, but also for the recipients, as a consequence of poor donor screening and evaluation with consequent transmission of HIV or other infective agents, as well as of inappropriate medical and surgical management of donors and also of recipients, who are often discharged too early. Most public or private insurance companies are considering kidney donation a safe procedure without long-term impairment and therefore do not increase the premium, while recipients' insurance of course should cover hospital fees for the donors. "Rewarded gift" or other financial incentives to compensate for the inconvenience and loss of income related to the donation are not advisable, at least in our opinion. We do not perform anonymous living organ donation or "cross-over" transplantation.

PO-062 ABSTRACT WITHDRAWN

PO-063 EXPERIENCE WITH ALTRUISRIC LIVING KIDNEY DONATION
Wilij Zuidema1, Leonieke Kraanenburg2, Medard Hilhorst3, Jan Uzermans4, Willem Weimar1, 1 Internal Medicine, Section Transplantation, Erasmus MC; 2 Medical Psychology; 3 Medical Ethics; 4 General Surgery, Erasmus MC, Rotterdam, Netherlands.

Research into altruistic living kidney donation to complete strangers or remote acquaintances is gaining increasing attention. Surveys have indicated that a significant number of individuals are willing to donate altruistic kidneys. Studies on legal and ethical aspects of altruistic kidney donation found their way into professional and public debate. However, information on the actual number of altruistic donations performed is scarce.

Results: During the last 5 years 19 individuals approached our clinic, regarding altruistic kidney donation, after they were informed by telephone and booklet about the procedures. Eight of them reconsidered their offer after the first visit. After obtaining consent we embarked on the medical and psychosocial work-up with the remaining 11 individuals. During the assessment one donor proved to have somatic contra indications, three others were declined on psychological grounds and one woman withdrew consent after strong negative advice from her monastic community. Six individuals, median age 59.5 (range 38-76) years, 3 women and 3 men underwent nephrectomy. Two donated anonymously to the pool according to the allocation criteria for deceased donor kidneys. Donation was evaluated anonymously to the pool according to the allocation criteria for deceased donor kidneys. Donation was evaluated anonymously to the pool according to the allocation criteria for deceased donor kidneys. Four donated to remote acquaintances in the absence of an emotional or commercial relationship. Median follow-up is 21 (range 4-50) months. All donors and partners of some of the donors ever regretted the donation or ever had second thoughts.

Conclusion: Altruistic kidney donation is a realistic option to expand the living donor pool. Explicit publicity to motivate the general public and efforts to modify transplant laws should be considered.

PO-064 RELATED LIVING DONOR (RLD) IN RENAL TRANSPLANTATION (RT): PSYCHOLOGICAL IMPACT
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Objective: To assess the psychological impact of donation on the RLD in RT. Methods: Retrospective structured phone survey, consisting of 12 questions. Bond, physical aspects and daily, family and work life were evaluated.

Results: 16 donors (D) were evaluated, 12 women and 4 men, the average age being 51.8. Relationship between D and recipient: 4 brothers and sisters (25%), 10 mothers (62.5%) and 2 fathers (12.5%). Own-volition donation was observed in 15D (94%). The D/R bond before and after the RT was maintained or improved in 13D (81%) and worsened in 3D (19%). As for physical health and body image, some alterations were shown in 3D (19%) and self-care increased in 7D (44%). Regarding the mood, 7D (44%) expressed an improvement and 9D (56%) did not indicate any changes. The daily life of 2D (12.5%) and the work situation of 1D (6%) were modified. 3D (19%) mentioned some changes in the family or couple relation and some concerns about the organ functioning. 1D (100%) well expressed that they would donate again.

Conclusions: The bond between D and R has improved since the donation. No significant modifications are observed in the daily life, and in the physical, family and work areas. A positive donation assessment is observed.

PO-065 ATTITUDE OF NON-HEALTH PERSONNEL TOWARDS CADAVERIC ORGAN DONATION IN PRIMARY CARE CENTRES AND HOSPITALS
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Objective: To analyse the attitude towards cadaveric donation of non-health professionals in Primary Care (PC) centres and in Hospitals and to determine the psychosocial factors which determine this attitude.

Materials and Methods: The study was carried out in 32 PC health centres and in a third level hospital with an ongoing programme of solid organ transplantation. A random sample was obtained and stratified for sex and health area (n=120 in PC, n=277 in hospitals). Attitude was evaluated using a validated questionnaire on psychosocial attitude, which was completed anonymously, self-administered.

Results: 67% in PC centres and 64% (p<0.05) have a favourable attitude towards donation. No relationship has been found between attitude towards donation and any of the psychosocial variables, except in two: understand the concept of Brain Death (p=0.004) and possible mutilation after extraction (p<0.0005).

Conclusions: Attitude towards cadaveric organ donation among non-health personnel is similar in both subgroups and is similar to that found in population studies. Lack of understanding of Brain Death and fear to mutilation are the main psychosocial factors involved in making such a decision.
PO-066 LIVER TRANSPLANT ON THE WORLD WIDE WEB
Faisal Hanif, Andrew Butler, Rajesh Sivaprakasam, Emmanuel Huguet, Gavin J. Pettigrew, Raaj K. Praseedom, Chris J. Watson, Paul Gibbs, Neville V. Jamieson, Andrew Bradley, Transplant Unit, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom.

Introduction: Orthotopic liver transplant (OLTx) has evolved to a successful surgical management for end-stage liver diseases. Awareness and information about OLTx is an important tool in assisting OLTx recipients and people supporting them, including non-transplant clinicians. The study aimed to investigate the nature and quality of liver transplant-related patient information on the World Wide Web.

Methods: Four common search engines were used to explore the Internet by using key words "Liver transplant". Each website was assessed on the following criteria: website age, authorship, content and quality. A weighted Information Score (IS) was created to assess the quality of clinical and educational value of each website and was scored independently by three transplant clinicians.

Results: A total of 58 websites were assessed. The overall median weighted IS was 22 (IQR 1-42). Median weighted IS of publications originating from Europe and U.S.A. was 40 (IQR=22-60) and 23 (IQR= 6-38) respectively. Websites belonging to the academic institutions and the professional organizations scored significantly higher with a median weighted IS of 28 (IQR= 16-44) and 24(12-35) respectively as compared to the commercial websites (median=6 with IQR of 0-14, p = .001). There was an Intraclass Correlation Coefficient (ICC) of 0.89 and an associated 95% CI (0.83, 0.93) for the three observers on the 58 websites.

Conclusion: This study identifies the difference between academic institutions and commercial institutions. In addition, it also highlights the need for improvement in the information available on the World Wide Web about OLTx.

PO-067 MEDIA COVERAGE OF ORGAN DONATION IN SWITZERLAND 1999-2003
Joachim Haes 1, Peter J. Schütz 1, Angelo Tomada 1, Roberto Malacrida 2, 1Health Care Communication Laboratory, USI University of Lugano, Switzerland; 2Ospedale Regionale di Lugano, Switzerland.

Information about organ donation reaches the public through media long before people feel the need to talk to friends, relatives or their doctors about the topic. Concerning donation, it is necessary to make organ donors more than three times as many organs relative to their population as German and French speaking Swiss, we wanted to find out, if there are significant differences in the newspaper coverage of organ donation and how this might influence attitude and behavior. We performed a content analysis of 15 newspapers through the years 1999-2003. Finding 500 German, 303 French and 164 Italian articles, we analyzed statements like "There is a great need for organ donors." and "You can become an organ donor by signing an organ donor card" and misconceptions like "Before signing an organ donor card, you have to stand a medical examination". To evaluate the media's influence, we conducted a national survey of high school students of the last two classes of high school had a lesson based on a standard CD-ROM-support. Afterwards they were asked to fill in a questionnaire. Some weeks later they participated at an interactive conference given by a same transplant surgeon and successfully transplanted patients.

Results: The analysis relates to 2793 questionnaires returned by 49% males and 51% females; 69.4% were catholic, 23.4% liberal and 7.2% moslim. See table 1.

Conclusions: Organ donation and transplantation is known, but there is still a major lack of information in relation to brain death and organ donation. Specific sensitisation actions for adolescents are therefore utmost important in order to improve organ donation in the future.

PO-068 ADOLESCENTS' OPINION ON ORGAN DONATION IN BELGIUM
Francine M. Roggen, Jules A. Mathys, Chantal C. De Reyck, Jan P. Lerut, Liver Transplant Unit, Univ Hosp St-Luc, Brussels, Belgium.

Information and promotion of organ donation and transplantation remains a necessity; adolescents are not well informed in relation to these subjects.

Methods: After a meeting with directors, students of the two last classes of high school had a lesson based on a standard CD-ROM-support. Afterwards they were asked to fill in a questionnaire. Some weeks later they participated at an interactive conference given by a same transplant surgeon and successfully transplanted patients.

Results: The analysis relates to 2793 questionnaires returned by 49% males and 51% females; 69.4% were catholic, 23.4% liberal and 7.2% moslim. See table 1.

Conclusions: Organ donation and transplantation is known, but there is still a major lack of information in relation to brain death and organ donation. Specific sensitisation actions for adolescents are therefore utmost important in order to improve organ donation in the future.

PO-069 ECONOMIC EVALUATION OF KIDNEY TRANSPLANTATION VERSUS DIALYSIS IN ARGENTINA
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Aims: The economic impact of transplantation has been studied in several countries. We aim to determine the cost-effectiveness of transplantation versus dialysis in Argentina.

Methods: A predictive Markov model was used predict costs and outcomes associated with transplantation and dialysis. Two hypothetical cohorts (transplanted or dialyzed) were followed for 20 years. Patient, graft survival and health utilities were derived from Canada. The model was adapted to Argentina through local protocols and expert opinions; costs were valued in Argentine pesos and converted to US dollars. A microemulsion CsA, steroids, mycophenolic acid and induction protocol was assumed. The analysis used a health care payer perspective and a 5% discount rate was applied for cost and effects.

Results: Per patient quality adjusted life years (QALY) was predicted to be 6.65 with transplant and 4.67 with dialysis, thus transplant provided 1.99 extra QALY. First-year per patient cost were $17,784 for transplant and $9,441 for dialysis. This difference was offset by savings in the follow up transplant years: 10-year cumulative cost were $59,613 for transplant and $60,090 for dialysis, 20-year cumulative cost were $81,137 for transplant and $79,750 for dialysis. The incremental cost-effectiveness ratio (ICER) of transplant was $698/QALY. At a threshold of $4,130/QALY (2005 projected GDP per capita), transplantation is cost-effective.

Conclusions: Transplantation may provide a 42% increase in QALY with similar costs relative to dialysis. This projection uses international clinical data and local cost and thus provides a preliminary assessment of the economic impact of kidney transplantation in Argentina.

PO-070 ECONOMIC ANALYSIS OF MMF DOSE MODIFICATION FOLLOWING GASTROINTESTINAL COMPLICATIONS IN RENAL TRANSPLANTATION
Gerardo Machniccki 1, Mark Schnitzler 2, Jean-Francois Ricci 1, 1Health Economics, Novartis Pharma AG, Basel, Switzerland; 2Department of Medicine, St. Louis University, St. Louis, USA.

Aims: Minimization of MMF coverage is commonly used to alleviate post-transplant gastrointestinal complications (GI), but has been associated with impaired graft outcomes. We investigated the economic impact of MMF dose modifications following GI.

Methods: Adult renal transplant recipients with a Medicare covered MMF pre-
Heart

**PO-071** SPECIAL AUTHORIZATION AND ADDITIONAL FINANCIAL SUPPORT TO ACT AS TRANSPLANT CENTRES – A NECESSARY QUALITY PARAMETER TO ENSURE AND ENLARGE ORGAN TRANSPLANTATION RESULTS?

Elke Rampf-Platte, Lawyer, ETCO Co Chair Legal & Ethical Committee, Munich, Germany.

Organ shortage urges to use the available organs in the most effective and efficient way. Allocation rules and medical guidelines and procedures to optimize both of them as well as the increasing number of living donated organ transplantation are not sufficient enough to face organ shortage. Procedure rules are corresponding to cooperation structures and control mechanism to develop instruments to optimize quantity and quality of organs and transplantation results.

Transplant centres and ICUs are essential focus and gatekeeper concerning detection of donors, enlargening the donor pool and optimizing organ quality. Since 1.1.2004 numerous legal rules have been added to complete

1. organspecific conditions
2. personal skill and conditions
3. structural conditions
4. financial rules for transplant centres and ICUs to fulfill the conditions for financial support in case of detecting potential donors and exploitation. These additions will be presented in an overview including the quality and quantity parameter of experience as condition for authorization to act as transplant centre and to be kept in mind and organisation of ICUs

The report will show, if the methods are available to examine these conditions and their effects and give a glance to the sanctions in case of disregarding the conditions for the concerned parties.

**PO-072** IMPACT OF DONOR HYPERNATREMIA AT EARLY OUTCOME AFTER HEART TRANSPLANTATION (HTx)

Helena Bedanova, Erik Petrikovits, Josef Necas, Pavel Studenik, Jan Cerny. Transplantation, Center of Cardiovascular and Transplant Surgery, Brno, Czech Republic.

**Introduction:** Because sodium plays an important role in repuferation injury, donor hypernatremia is generally believed to produce myocardial stunning, causing a higher incidence of primary graft failure after HTx. We evaluated the effect of graft-donor hypernatremia on early postoperative period.

**Methods:** We analyzed 159 pts (130 men), who underwent HTx at our institution during 1995-2003. These pts were divided into 3 groups according to graft-donor serum sodium levels. Group A, with normonatremia (131-145mmol/l), included 61 pts (50 men), group B, with mild hypernatremia (146-155mmol/l), 50pts (43 men) and group C, with severe hypernatremia (>156mmol/l), 48pts (37 men).

We focused on: primary graft failure, mortality, IABP support, higher doses of catecholamines, frequency and severity of rejection episodes during early postoperative period and within 6 months after HTx.

**Results:** Primary graft failure occurred in 9 of 159 pts (5.7%), three cases in each group. Early-graft-recipent mortality was 5, 3 and 3 pts in groups A,B, and C, respectively. Higher catecholamine support or IABP was necessary in 13 pts from group A and 9 in groups B and C respectively. During the first post-HTx month 70% of specimens from groups A and C and 80% from group B were in rejection episode, documented in 25% of both A and 34% in groups A and C and 1% in group B. Differences in rejection rate between groups were not significant.

**Conclusion:** No impact of graft-donor natrium serum level on short-term outcome after HTx was proved. Grafts from donors with hypernatremia should not be considered inappropriate for HTx.

**PO-073** FIBROGEN IS AN INDEPENDENT RISK FACTOR FOR MAJOR ADVERSE CARDIAC EVENT IN CARDIAC TRANSPLANT PATIENTS WITH ALLOGRAFT VASCULOPATHY

Jean Pierre Villerot1, Richard Dorent2, Isabelle Bourdais3, Gerard Drobnis3, Vanessa Villami1, 1Cardiac Surgery, Bribals Hospital, Nancy, France; 2Cardiac Surgery, Hopital de La Pile-Salpietre, Paris, France; 3Biostatistics, Novartis Pharmaceuticals, Rueil, France;Cardiology, Hopital de La Pile-Salpietre, Paris, France; 3BU Tx, Novartis Pharmaceuticals, Basel, Switzerland.

**Purpose:** Cardiac Allograft Vasculopathy (CAV) is the result of immunologic and nonimmunologic endothelium injury. In the non-transplanted population markers of inflammation are associated with cardiovascular events. The aim of this study was to identify risk factors for Major Adverse Cardiac Events (MACE) in cardiac transplant (CT) recipients with CAV included in a 2-year, multicenter, randomized, double-blind, placebo-controlled fluvastatin study.

**Methods:** 85 CT patients (75 males, 10 females, 55±10 years) were randomly assigned 76±37 months after transplantation to fluvastatin (n=43) or placebo (n=42). MACE were defined as cardiac death, non-fatal myocardial infarction (MI), heart failure or need for revascularization or for retransplantation. Eight potential risk factors including age of recipient, BMI, baseline LDL cholesterol, triglycerides, fibrinogen, daily dose of Neoral, pretransplant coronary disease and time from transplantation were related to risk of MACE using a Cox model.

**Results:** Of the 85 patients 25 suffered one or more MACE. Need for angioplasty (14/25), heart failure (8/25), cardiac death (2/25) and MI (1/25) represented the events. In multivariate analysis baseline fibrinogen (p=0.0365, risk ratio=2.624 and triglycerides (p=0.0087, risk ratio=2.588) were associated with a higher risk of MACE whereas age (p=0.0930, risk ratio=0.910) was a protective factor.

**Conclusion:** Levels of fibrinogen and triglycerides can be used to identify CT patients with CAV at higher risk of MACE. Further studies are needed to evaluate whether specific therapies provide additional benefit to the patients.

**PO-074** SOLUBLE APOPTOTIC MARKERS IN STABLE HEART TRANSPLANT RECIPIENTS TREATED WITH NEORAL VS. TACROLIMUS

Jan Hlok, Jan Cerny, Jiri Ondrasek, Helena Bedanova, Marie Osmerova. Centre of Cardiovascular and Transplant Surgery, Centre of Cardiovascular and Transplant Surgery, Brno, Moravia, Czech Republic.

**Introduction:** The antiapoptotic soluble form of the fas-receptor (sFas) and the soluble proapoptotic fas-ligand (sFasl) were investigated in the plasma of stable heart transplant (HTx) recipients administered either Neoral or Tacrolimus.

**Patients and methods:** Eighteen adult heart transplant recipients, nine treated with Neoral and nine with Tacrolimus (including concomitant therapy), followed up for 18 months. All patients were free from infection and acute rejection episodes (<1A grade). Healthy adult volunteers (n=18) served as controls. Plasma levels of sFas (pg/ml) and sFasl (pg/ml) were determined by a commercial sandwich ELISA kit. Samples were collected before and at 6, 12 and 18 months after transplantation.

**Results:** In the patients before HTx, the mean sFas was 48.8±15.5 pg/ml (S.D.), as compared with 36.5±10.0 pg/ml in the controls (p<0.01). In the recipients after HTx (both Neoral and Tacrolimus groups followed up for 18 months), the level was 80.3±17.7 pg/ml (p<0.001, as against the controls and patients before HTx). The mean sFasl levels increased slightly (controls 0.43±0.29 ng/ml; patients before HTx 0.47±0.28 ng/ml; HTx recipients 0.57±0.32 ng/ml) with no significant differences between the groups. The two HTx recipient groups showed no significant differences in either sFas levels (Neoral 79.3±17.3 pg/ml vs. Tacrolimus 81.3±19.3 pg/ml) or sFasl (Neoral 0.57±0.35 ng/ml vs. Tacrolimus 0.57±0.32 ng/ml).

**Conclusions:** In stable heart transplant recipients, immunosuppressive treatment with either Neoral or Tacrolimus resulted in no significant differences between plasma values of soluble Fas and soluble Fasl. An increase in soluble Fas levels after transplantation, as against controls (p<0.001) and patients before transplantation (p<0.001), occurred in both recipient groups.

**PO-075** EVEROLIMUS IN CARDIAC TRANSPLANT RECIPIENTS

Martin Schweiger, Andre Wasler, Guenter Prenner, KarlHeinz Tschieliesing, Medical University Graz, Dep. Transplantation.

**Background:** Some recent studies have shown the value and safety of
ONE YEAR EXPERIENCE WITH TWO-DOSES OF DACLIZUMAB AS INDUCTION THERAPY IN DE NOVO HEART TRANSPLANT PATIENTS

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Purpose: Daclizumab is used as induction therapy in heart transplantation (HTx) with repeated administrations over several weeks. Based on its half-life we used two doses, with mycophenolate mofetil (MMF), tacrolimus and rapid ACTH bolus. Daclizumab is used as induction therapy in heart transplantation (HTx) with repeated administrations over several weeks. Based on its half-life we used two doses, with mycophenolate mofetil (MMF), tacrolimus and rapid ACTH bolus.

Methods: Forty-nonsensitized patients undergoing a first HTx received daclizumab (1 mg/kg) intravenously 6 hours after surgery and on day 14th, with MMF, tacrolimus and low dose of prednisone. Primary end points were rejection incidence and severity.

Results: Thirty-five men and five women (mean age 55.8 years) were folowed. Seven patients withdrawn the study and 3 died (septic shock, primary graft failure and cardiac tamponade secondary to pacemakerinsertion) being 1 year survival 92.5%. Two hundred and ninety biopsies were perfoimed according protocol and 9.3% of them were >3A ISHLT grade. Two rejection cases (0.7%) were symptomatic, being the rest found in the protocol biopsies. One rejection of maximum ISHLT grade 1A.

Conclusions: Induction with two-doses of daclizumab with MMF, tacrolimus and low dose of steroid is safe, well tolerated and effective to prevent acute rejection. It is a valid immunosuppressive regimen in de novo HTx recipients.

SUCCESSFUL POSTOPERATIVE MANAGEMENT OF BLEEDINGS AFTER CARDIAC TRANSPLANTATION IN A PATIENT WITH HEPARIN-INDUCED THROMBOCYTOPENIA

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Introduction: Heparin-induced thrombocytopения might be more common than expected. Thrombotic complications and life-threatening postoperative haemorrhage in these patients are frequent problems.

Case report: Patient with known dilatative cardiomyopathie, already listed for cardiac transplantation, was admitted to hospital because of cardiac decompensation.

At stabilizing the patient with catecholamines and an intratraic balloonptom he was transfened to our center. Weaning of IABG and catecholamines failed. The patient was put on high urgent status for heart transplantation. Suddenly declining platelets were noticed. 14 days after admission multiple thrombosis occurred. A PFO/heparin immunoassay, performed as heparin induced type II thrombocytopenia was suspected, subsequently confirmed the diagnosis.

Heparin was replaced by Lipirudin. Because of the thrombosis a systemic heparin was done without any further complications. 10 days later cardiac transplantaion was performed.

His postoperative course was stormy with excessive bleeding through the chest-tube drains beginning immediately postoperatively. The patient was retured two times to the operation theater but no specific bleeding site was identified. As brisk bleeding continued decision was made to treat the patient with recombinant factor VIIa.

Bleedings stopped within a few hours and patient stayed stable the next days. Without any further complications the patient was transferred to normal station and is now at home in good shape and anticoagulated.

Conclusions: No thrombotic complications occurred after application of recombinant factor VIIa, the patient stayed stable and bleeding stopped. We suggest that recombinant factor VIIa was save and effective.

SINGLE-CENTRE FIRST EXPERIENCE WITH EVEROLIMUS AND CSA FOR DE NOVO HEART TRANSPLANT RECIPIENTS

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Purpose: Everolimus is a proliferation signal inhibitor that allows for cy- clocsporin (CsA) dose reduction in heart transplantation (HTx) patients. It may therefore be beneficial for patients with anticipated renal problems. We report the results of a single-centre experience with 20 de novo HTx patients treated with oral everolimus and CsA.

Methods/Materials: Each patient received everolimus 0.75 mg b.i.d. with weekly monitoring to ensure blood levels of 3–8ng/mL and concomitant CsA with C2 target levels of 200–250ng/mL (1 month), 175–200ng/mL (2–3 months) and 135–150ng/mL (4–6 months).

Results: Mean CsA levels were 217ng/mL (range: 194–368ng/mL) at 2 weeks after HTx. These were reduced at 4 weeks to a mean level of 185ng/mL (range: 170–262ng/mL) and further reduced at 3 months to a mean level of 172ng/mL (range: 114–225ng/mL). Post-transplant everolimus troughs were 7.2ng/mL (range: 3.5–13.1ng/mL) at 2 weeks, 6.8ng/mL (range: 3.2–12.1ng/mL) at 4 weeks and 5.9ng/mL (range: 3.0–9.4ng/mL) at 3 months. Mean creatinine levels were 1.6mg/dL (range: 0.6–2.5mg/dL) prior to HTX.

Post-transplant, creatinine levels were 2.2mg/dL (range: 1.0–3.9mg/dL) at 2 weeks, 2.0mg/dL (range: 0.9–3.2mg/dL) at 4 weeks and 1.6mg/dL (range 0.6–2.4mg/dL) at 3 months.

Non-invasive rejection monitoring using echocardiography and intramyocar- dial electrocardiography revealed that 28.5% of patients experienced rejection. Routine 4–6 weeks biopsy showed that 5/20 patients (25%) experienced acute rejection of maximum ISHLT grade 1A.

Conclusion: Everolimus troughs were maintained within a range of 3–8ng/mL soon after the transplant with high patient compliance. CsA dose was reduced, which did not lead to an increase in the number of rejections. All rejections observed were mild and none of the patients were haemodynamically compro- mised.

SUCCESSFUL POSTOPERATIVE MANAGEMENT OF BLEEDINGS AFTER CARDIAC TRANSPLANTATION IN A PATIENT WITH HEPARIN-INDUCED THROMBOCYTOPENIA

PO-077

THE IMPORTANT QUALITY OF LIFE DIMENSION

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Background: The quality of life (QOL) late after heart transplantation (HTX) is reported to be comparable with general population. A good QOL is associated with positive perception of health status, emotional stability, social support and good physical fitness and sexual activity. Sexual functioning after HTX is as- sociated with body perception, self-assessment, social changes and effect of medications.

Methods: 58 heart transplant recipients (49 male, 9 female), mean age 48.6 years, 12 to 166 months after HTx, were included in the study. Data were collected from the following tools: STA1 (Spielberger’s Questionnaire of Anxi- oty), BDI II (Beck Depressive Inventory), QOLq (Quality of Life Questionnaire according to Oldridge adapted by Lim), SI (Structured Interview) and Visual Analogue Scale.

Results: 60% of patients evaluated QOL as very good, 33% as good and 7% as satisfying. 64% of patients were satisfied with their sexual life. 70% of unsat- isfied patients were anxious or depressed. Depressive symptoms were present in 13% of patients (BDI score >10), 24% of patients presented increasing levels of anxiety (STA1 score >45). QOL score correlated with lower age (r=0.3, p<0.05), NYHA I functional class (r=0.37, p<0.005), lower depression (r=-0.6, p<0.01) and subjective life satisfaction (r=0.5, p<0.01). The good QOL was associated with lower anxiety (p<0.01), rich hobbies activity (p<0.05) and with sexual activity (p<0.05).

Conclusions: The good QOL after HTx is related to younger patients, without...
SIROLIMUS – ALTERNATIVE IMMUNOSUPPRESSION IN HEART TRANSPLANT RECIPIENTS WITH RENAL DYSFUNCTION

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Background: Chronic renal dysfunction due to calcineurin inhibitors (CNI) is a common problem after heart transplantation (HTx). Sirolimus (SRL) is a potent immunosuppressive drug (TOR-inhibitor) which represents potential alternative of CNI in posttransplant immunosuppressive regimens.

Methods: Eight heart transplant recipients (males; 4.5 to 9.5 years after HTx) with chronic renal dysfunction (serum-creatinin level >180 umol/l) were converted from cyclosporine (CSA) - based immunosuppression to SRL. Initial dose of SRL was 6 mg, continued with 2 mg and adjusted according to drug level monitoring. Target trough levels for SRL were 8-14 ng/ml. CSA was tapered down and finally stopped after six weeks. Other immunosuppressive drugs (mycophenolate mofetil, prednisone) continued. Clinical follow-up included endomyocardial biopsies (EMB), ECG, echocardiography and laboratory tests.

Results: Mean serum creatinin level before conversion was 303 ± 165 umol/l (180 to 706 umol/l, one patient was on hemodialysis). 6, 12 and 18 months after conversion mean decrease of creatinin levels was -52 ± 25, -19 ± 24 and -60 ± 19 mmol/l respectively. One year after conversion mean increase of serum cholesterol level was 0.5 ± 1.3 mmol/l. Mean level of triglycerids has not increased. Graft function was normal before and after conversion. One episode of acute rejection 3A occurred in EMB with complete resolution after steroid therapy. SRL was withdrawn in patient on hemodialysis because of severe anemia and minimal influence on glomerular filtration rate.

Conclusion: Conversion from CSA to SRL in heart transplant recipients with CSA-nephropathy improves renal function, especially in early stage of renal insufficiency. SRL seems to be effective and safe alternative of CNI after HTx.

HEART TRANSPLANTATION OUTCOME IN SAUDI ARABIA

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Introduction: The first heart transplantation in Saudi Arabia was performed in 1986. At the end of 2004 there were 101 whole hearts transplanted and 318 used as heart for valves.

Aims: To evaluate the practice of heart retrieval and transplant as well as the survival rate of 17 recipients covering a five year period.

Method: A retrospective study was conducted by the Saudi Center for Organ Transplantation (SCOT) for all heart transplant patients (2000-2004). Data about the Donor's Age, Cause of B&D & ICU Stay were considered to correlate with the outcome of transplantation.

Results: There were 920 documented B&D cases in which families were approached for organ donation during the study period, and consent was obtained in 206 (22.4%). Out of these,17 heart transplants has been done. Donor's/Recipient mean age was 32.39 yrs respectively. The outcome of heart transplantation reveals that 76.5% (13 out of 17) of them are still active, 3 died and one lost follow up. Evaluation of the 13 active cases indicates that 11 of them are in "excellent" condition and 2 in "good" condition. The mean follow up post transplant period was 18 months. Survival rate in the 1st year was 79% and it is expected to be 74%, 66% and 52% for the second, third and fourth years respectively.

Conclusion: The heart transplantation outcome in K.S.A was satisfactory which is comparable to international data; however more efforts are needed to increase the acceptance rate of heart retrieval and transplantation.

CUTANEOUS COMPLICATIONS IN HEART TRANSPLANT RECIPIENTS, OUR EXPERIENCE

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Background: Skin problems in organ recipients result mainly from the induced immunosuppression, but also from specific adverse effects to immunosuppressive drugs.

Methods: Patients who received heart allograft, at the University of Siena Hospital (Division of Thoracic and Cardiovascular Surgery) were examined at our Institution from 1994 to 2004 and included in a retrospective study to evaluate to analyze the type, incidence, predisposing factors and prognosis of cuta-neous complications (CC). This study was carried out among 155 heart transplant recipients. All these patients who had been evaluated before surgery and did not show any pre-existent dermatological disease, were then re-evaluated when they developed CC. The following variables were recorded: age, sex, phenotype, post-transplant immunosuppressive therapy and CC.

Results: One hundred and forty CC were diagnosed in eighty five patients. As in other similar studies (1, 2) the major types were infections (viral and fungal) and tumors. None of the CC caused mortality.

Conclusions: Our study demonstrates the importance of dermatologic follow-up after heart allograft for early, sensitive diagnosis, effective treatment, and improved prognosis.

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CONVERSION OF STABLE HEART TRANSPLANT RECIPIENTS FROM TWICE DAILY PROGRAF TO ONCE DAILY MODIFIED RELEASE TACROLIMUS

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Prograf® (tacrolimus) is a twice daily (BID) formulation. A modified release formulation (MR) of tacrolimus was developed to enable once daily (QD) dosing, to potentially improve compliance. The purpose of this pharmacokinetic study was to evaluate tacrolimus pharmacokinetics in stable heart transplant recipients converted from Prograf to MR.

Eligible patients (18 to 65 years), received a heart transplant >6 months prior to enrolment, and received stable doses of Prograf for ~2 weeks prior to enrolment. Any patients with a rejection episode in the previous 3 months or with a left ventricular ejection fraction <30% were excluded. Patients received Prograf BID once Days 1 to 7, were converted to the same total daily dose of MR QD_on Day 8, and remained on the same dose throughout the study. Pharmacokinetic profiles (24-hour) were obtained on Days 1, 7, 8, 14 and 21. Laboratory and safety parameters were evaluated.

Pharmacokinetic data were evaluated in 46 patients. The mean AUC0-24 of tacrolimus for Prograf (Days 1 and 7) and MR (Days 14 and 21) were comparable and within the equivalence range of 80% to 125%, as were the 90% CI for the comparison. There was good correlation between AUC0-24 and C24h for Prograf and MR, and similar trough levels were observed for the two formulations. MR was well tolerated, with a comparable safety profile to Prograf and no acute rejection episodes occurred.

Steady-state tacrolimus exposure of MR is equivalent to Prograf after a 1:1 conversion in stable heart transplant recipients.

PHARMACOKINETIC PROFILING AND C2 MONITORING OF CYCLOSPORINE IMPROVES OUTCOMES FOLLOWING HEART TRANSPLANTATION

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Cyclosporine (CsA) profiling and C2 monitoring have been shown to provide clinical benefits in renal and liver transplantation but evidence in de novo heart transplant patients is lacking.

Methods: Single CsA profiles were obtained during the first 6 weeks post-transplant in 28 de novo heart transplant patients (venous blood samples taken at 0, 0.5, 1, 1.5, 2, 3, 4, 5 and 6 hours after morning dose) (Group 1). Outcomes were compared retrospectively with the preceding 28 patients in whom CsA profiling was not undertaken (Group 2). CsA dose changes were made according to regular C2 and C4 monitoring in Group 1 but on CsA alone in Group 2. All patients received antithymocyte globulin induction and most received maintenance azathioprine and steroids. Clinical and pharmacokinetic parameters were compared at 3 and 12 months.

Results: Demographics were similar between groups. Patients in Group 1 had a significantly lower incidence of grade 3 biopsy-proven rejection than Group 2 at 3 months (6/98 biopsies versus 19/122 biopsies, p<0.001) and 12 months (11/220 biopsies versus 31/284 biopsies, p<0.002). Mean C2 in Group 1 was 1248±328ng/mL and 1039±362ng/mL at 3 and 12 months post...
transplant, respectively. Mean CsA $C_{\text{av}}$ in Group 1 and Group 2 at 12 months was 252.9±90ng/mL and 239.2±85ng/mL, respectively (n.s). One patient in Group 1 and seven in group 2 developed CsA due to $\geq 2$ episodes of rejection or neurotoxicity.

**Conclusion:** CsA profiling with regular monitoring of $C_{\text{av}}$ and $C_{\text{av}}$ results in improved outcomes following OHTx and potentially this could be augmented in patients who undergo OHTx at risk of sepsis.

**PO-085 ORTHOTROPIC HEART TRANSPLANTATION FOR PATIENTS AT RISK OF SEPSIS: A 15 YEARS EXPERIENCE**

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Pre-operative patient status influences the early and long-term outcome following OHTx and potentially this could be augmented in patients who undergo OHTx at risk of sepsis. We studied such group of patients and the outcome following OHTx.

**Methods:** 500 patients underwent OHTx for ischemic heart disease (IHD) and dilated cardiomyopathy (CM) between 1987 and 2002 at a single centre. Donor demographics, body mass index (BMI), cause of death were collected. Recipient demographics, preoperative haemodynamics, perioperative/postoperative characteristics, incidence of infections, a median follow-up of 15 years, and cause of death were collected. Patients with cardiac pathologies other than IHD and CM were excluded in order to obtain an unbiased representation. On the basis of severity of the organ failure and the risk of sepsis, the patients were classified to three sub-groups (SG).

1. Out-patient 2. Inpatient + single organ failure 3. SG-2 + documented sepsis

The data was analysed using SPSS.

**Results:** There was a notable increase in the mean ischemic time (191±28 minutes), stay in the intensive care unit (ICU) (10.1±11 days) in the CM group of patients. But in the IHD group, the total hospital stay was prolonged and notable decrease in the medium and long term actuarial survival in the IHD in all three sub-groups. The cumulative cause of death due to sepsis was 7.1% with no difference between the sub-groups.

**Actuarial Survival - 1, 6 & 12 years**

|     | SG-1 | SG-2 | SG-3 |
|-----|------|------|------|
| Cardiomyopathy (%) | 87, 72, 60 | 85, 70, 58 | 80, 70, na |
| Ischemic heart disease(%) | 80, 58, 47 | 76, 54, 36 | 74, 44, 32 |
| na-not available |       |      |      |

**Conclusion:** OHTx is still a valuable treatment option for end-stage cardiac pathologies in patients at risk of sepsis.

**PO-086 MULTIPLE AORTIC ANEURYSMS SEVEN YEARS AFTER CARDIAC TRANSPLANTATION**

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Solid organ transplantation requires life-long immunosuppression, thus rendering the patients susceptible to opportunistic infections. A 61 year old male patient underwent orthotopic heart transplantation (HTX) in October 1997. Long-term follow-up after HTX was completely uneventful. In Mai 2004 an aneurysm of the ascending aorta was suspected after a routine chest X-ray examination. Additionally the patient described dyspnoea and recurrent moderate pulmonary infections. CT-examination revealed aneurysmatic bulgings of the ascending (6 cm) as well as the descending thoracic aorta (6.6 cm) and ectasy of the infrarenal abdominal aorta (3.4 cm).

Quarterly laboratory examinations showed no abnormalities. During 2004 the patient demonstrated increased infection parameters and a rise in Chlamydia pneumoniae (CP) antibody titters indicating a recent infection. Clarithromycin and doxycycline was applied for three months.

On August 16th 2004 the aneurysmatic ascending aorta was replaced with a Goretex graft. Two Goretex stents were positioned and deployed. The patient demonstrated increased infection parameters and a rise in Chlamydia pneumoniae (CP) antibody titters indicating a recent infection. Clarithromycin and doxycycline was applied for three months.

Detection of CP in abdominal and thoracic aortic aneurysms has been described before. The association of CP infection with development of aneurysms is still unclear. Our patient has developed aneurysms relatively short after CP infection. The lack of detectability of CP probably relates to the antibiotic treatment before surgery. Furthermore, CP antibody titters are not associated with the presence of CP in the aortic wall.

**PO-087 ADRENERGIC ACTIVATION IN LONG-TERM HTX PATIENTS WITH INCREASING PLASMA LEVELS OF TNF-α**

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**Background:** Normalization of the LV-function by HTx is known not to lead to the expected consecutive decrease of the activated neurohumoral system. Follow-up of the adrenergic system and possible influence of the inflammatory marker TNF-α were investigated in a clinical long-term study.

**Methods and Results:** Routine follow-up after HTx, 37 patients (30 males, 7 females, 53,66y), central- venous plasma levels: TNF-α (ELISA), adrenaline (A) and noradrenaline (NA) (radiochemical method).

| Control | 1) 46 days | 2) 1.7 months | 3) 6.6 years |
|---------|------------|---------------|-------------|
| Noradrenaline (pg/ml) | 326.62 (148.35) | 387.27 (163.90) | 620.36 (325.76) |
| TNF-α (pg/ml) | 61.95 (126.64) | 71.45 (151.38) | 175.08 (241.97) |

*p ≤0.05 **p ≤0.01

Significant correlation of A and NA during follow-up.

**Conclusions:** Despite persisting normal systolic and only slightly compromised diastolic LV-function during follow-up remarkable changes of neurohumoral markers and TNF-α were observed and additionally a continuous further increase of NA and A during late follow-up.

2. The experimentally known influence of inflammatory mediators as TNF-α on the adrenergic system can thus be discussed to be important under clinical conditions.

**PO-088 DIVERGENT CHANGES OF ANP, BNP AND THE INFLAMMATORY MEDIATOR TNF-α IN LONG-TERM HTX PATIENTS**

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**Background:** Vasoactive peptides are well-known regulators of the vascular system dependent on cardiac function. An interaction with inflammatory transmitters could be shown under experimental conditions.

**Methods and Results:** This context was examined in 40 patients after HTx (7 males, 33 females, mean age 53.72 ± 8.71y) during long-term follow-up: Normal LV-function, rejection excluded histologically at controls. Control intervals after HTx: 1.49 ± 1.09 (1), 1.05 ± 0.23y (2) and 3.67 ± 2.05y (3). Central venous plasma levels of ANP, BNP (RIA) and TNF-α (ELISA).

| ANP (pg/ml) | BNP (pg/ml) | TNF-α (pg/ml) |
|------------|------------|---------------|
| (I) | 343.15 (± 154.45) | 224.76 (± 172.97) | 62.19 (± 122.26) |
| (II) | 291.36 (± 111.77) | 54.49 (± 31.88) | 66.84 (± 146.49) |
| (III) | 270.82 (± 141.12) | 121.64 (± 171.51) | 165.52 (± 235.21) |

*p ≤0.05 **p ≤0.01

**Conclusions:** 1. Despite normal systolic and only slightly compromised diastolic LV-function no normalization and different changes of ANP and BNP central venous plasma levels were observed.

2. For the first time the experimentally known relation between TNF-α and BNP can be discussed.

3. This is the first study showing a clinical relevance of this experimentally known context.
PO-089 ELECTROMECHANICAL SYNCHRONIZATION OF THE HETEROTOPIC AND NATIVE HEART BY BIATRIAL STIMULATION FOLLOWING HEART TRANSPLANTATION

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Patients requiring heart transplantation normally are transplanted with the donor organ in orthotopic position. A specific subset, most of them suffering from fixed pulmonary hypertension, need heterotopic heart transplantation (HHTX) with the donor heart in abnormal anatomical position. This should result in two hearts acting in parallel, each contributing to antegrade flow. After HHTX a 59 year-old woman presented with remarkable symptoms of breathlessness and fatigue despite uneventful postoperative course and excellent donor heart function. The main reason was hemodynamic instability because of asynchrony of both hearts. 23 months after HHTX a biatrial pacemaker system was implanted with screw-in leads in both right atria of the native as well as the heterotopic heart. Biatrial pacemaker implantation lead to linkage and synchronized atrial and ventricular contraction in both, the donor and native heart with the faster organ executing the synchronization. Immediately after pacemaker implantation a distinct harmonization of the invasive measured aortic blood pressure curve was observed. Also the cardiac output increased. Clinical condition improved during the first postoperative days resulting in enhanced physical capacity without adjustment of medication. The patients walking distance with the 6 minute walk-test increased about 41%. 3 floors could be overcome without shortness of breath. This case demonstrates the feasibility of true simultaneous biatrial stimulation using advanced pacemaker technology: linkage of both hearts, substantial AV sequential contraction in the donor and native heart and bidirectional electromechanical coupling with the faster organ executing the synchronization. The remarkable relief of symptoms is more than one year after the procedure still evident.

PO-090 POST TRANSPLANT LYMPHOPROLIFERATIVE DISORDER FOLLOWING HEART TRANSPLANTATION

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Background: Post-transplant lymphoproliferative disorder (PTLD) has a hazardous impact on post transplant survival in solid organ recipients. The aim of the current study was to investigate the impact of several risk factors on PTLD.

Results: 8 patients have been identified with PTLD, all cases occurring during the last decade. Mean age at PTLD onset was 46.4±20.0 years and time between transplant and development of PTLD was 26.4±30.4 months. There were 5 EBV-associated PTLDs, 2 non-EBV-associated, C2D0-negative B-cell lymphomas and 1 T-cell lymphoma. Immunosuppression at PTLD onset consisted of a Calcineurin inhibitor based (Cyclosporine A: 5 patients, Tacrolimus: 3 patients). Initial immunosuppression included ATG induction. Six patients received perioperative antiviral prophylaxis with either val-ganciclovir (=4) or acyclovir (n=2) in combination with anti CMV hyperimmunoglobulin (n=1). Two patients experienced a total of five episodes of acute rejection (ISHLT II 1), all were treated with bolused steroids. Four patients are still alive (50%), three of them in current remission of PTLD, one patient is under therapy recently. Median survival was 27 months in survivors and 3.4 months in non-survivors.

Conclusion: These data show, that PTLD is associated with a high mortality rate. The majority of PTLDs are EBV-associated. Therefore, screening for EBV-infection and prophylactic treatment may help to prevent a potentially fatal consequence of heart transplantation.

PO-091 MALIGNANCIES AFTER CARDIAC TRANSPLANTATION – THE INNSBRUCK EXPERIENCE

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Malignancies occur more frequently after cardiac transplantation (HTX) as compared to the general population. The aim of our study was to determine incidence, type and outcome of patients after HTX suffering from malignancies. Since 1983, 250 patients underwent HTX at our institution. Median survival is 167 months, one-year-survival 86.5%, five-year-survival 78.0% and ten-year-survival 65.9%. A malignancy has been detected in 25 patients after HTX. Six patients died due to malignancy (24%). This accounts for 11% of total mortality after HTX. Malignancy was diagnosed 44 months after transplantation in median. As compared to men (13.4%), women suffer less frequently from malignancies (2.5%, p=0.034). No difference could be found concerning the patients age (Malignancy: 53.3±12.5yrs vs. no malignancy 51.6±13.6yrs; p=0.49). Nine of the 26 malignantly deceased patients were cutaneous malignancies, two malignant melanomas and seven squamous cell carcinomas of the face or head. Mean age at transplantation was 60.4±6.7yrs. Two patients died due to cutaneous malignoma (22.2%). Further eight patients developed a malignant lymphoma after transplantation. These patients appear to be younger (46.6yrs), due to the large standard deviation of 20.3 years, however, this difference is not significant. Mortality of patients, suffering from lymphoma is 50%. Further malignancies are renal carcinoma (3.8%), Kaposi's sarcoma (3.8%) and pharyngeal carcinoma (3.8%).

Our data show, that malignancies have a significant influence on morbidity and mortality after HTX. For risk factor the development of a malignant disease. Most frequently, cutaneous malignoma and lymphoma occur. Cutaneous malignancies appear to develop predominantly in older patients, whereas lymphoma develop in younger patients.

PO-092 PRIMARY TRANSPLANT HEART FAILURE SUCCESSFULLY TREATED WITH IMPELLA PUMPS

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Purpose: We describe our case of primary heart graft failure mechanically assisted with the Impella Recover miniaturized axial pumps. (Impella Cardiotechnik AG, Aachen, Germany).

Methods and Materials: A sixty year old man with end-stage dilating cardiomyopathy underwent orthotopic heart transplantation. The donor heart function was initially compromised. After stabilization, tachycardia and anuria persisted, but echocardiography was normal. Bivacual implantation technique was used without any technical difficulties. Ischemia time was 3.5 hours. Patient was weaned from cardiopulmonary bypass (CPB), but despite high doses of inotropics, nitric oxide and intra-aortic balloon pump, and CPB had to be re-instituted. Right and left ventricular assist devices, Impella RV and LD, were implanted and the patient was weaned from CPB with adequate hemodynamics.

Results: Anticoagulation was withheld for two days. Heparin was then infused for Ming the pumps and hemofiltration. Echocardiology was used to check pump position and to assess cardiac function. Impella pumps were explanted and the sternum closed five days after transplantation. Severe thrombocytopenia developed, and an antibody assay supported the clinical diagnosis of heparin induced thrombocytopenia. Heparin was substituted with dana-paroid. 12 days post operation patient died unexpectedly because of massive cerebral haemorrhage.

Conclusion: Impella miniaturized axial pumps provided hemodynamic support with full recovery of the graft in five days. There were no signs of clinically significant hemolysis, thromboembolism or infection. The small size, ease of implantation and explanation, low anticoagulation requirements favor the use of Impella pumps.

PO-093 PANEL REACTIVE ANTIBODIES (PRA) IN PATIENTS UNDERGOING ELECTIVE CARDIAC SURGERY – INFLUENCE OF PRA ON PERIOPERATIVE COURSE, AND IMPACT OF THESE PROCEDURES ON PRA OCCURRENCE

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Background: Cardiac surgery is supposed to be a risk factor of PRA formation, however the role of PRA presence in non-transplant subjects is not known.

Aim of the study: was to assess PRA occurrence in patients undergoing elective cardiac surgery procedures, and to evaluate its influence on perioperative course.

Material and methods: Blood samples were obtained before operation in 44 subjects (36M/8F; 55.9±8.1y/o), undergoing primary elective cardiac surgery procedure – CABG (n=30), CABG + valve (n=2) or valve procedure (n=12). PRA results were obtained after the discharge, and pts. were retrospectively divided into: Group A (n=18) without any PRA, and Group II (n=26) with PRA. Comparison of Groups A and B was performed. PRA screening was repeated 3 months after the procedure in 41 pts. They were divided into Group I (n=13) with PRA-1%, and Group II (n=28) with PRA >1%. Comparison of Groups I and II was performed.

Results: Differences in pre-operative characteristics and procedure type distribution were insignificant. Post-operative complications were more frequent in Groups A and I (pulmonary hypertension in Group I vs.II: 38 vs.4%; p=0.01). Duration of post-op ICU stay was longer in Group vs.B (2.9 vs.1.9; p=0.01). Overall hospital stay was longer in Group A vs.B (10.1 vs.7.8y/o).

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THE ROLE OF EVEROLIMUS IN THE IMPROVEMENT OF RENAL FUNCTION IN HEART TRANSPLANT RECIPIENTS

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Purpose: Everolimus a novel proliferation signal inhibitor and immunosuppressive agent, may suppress cardiac allograft vasculopathy. Another advantage of this new immunosuppressant may be the improvement of renal function in heart transplant recipients. Everolimus is currently approved in Austria and Germany.

The aim of the study was to examine renal function and adverse events in heart transplant recipients with chronic renal failure due to the nephrotoxicity of calcineurin inhibitors. Cyclosporin A, Tacrolimus) after conversion to everolimus.

Methods/Materials: Since January 1, 2004 a total of 100 patients converted to everolimus due to nephrotoxicity of calcineurin inhibitors have been retrospectively analysed. The initial dose of everolimus was 1.5 mg/dl twice a day. Dosages of calcineurin inhibitors were reduced to 0% of initial dosage. Creatinine, BUN, creatinine-clearance, thrombocytes, erythrocytes and leukocytes were evaluated monthly. Serum cholesterol levels were evaluated before and after conversion to everolimus. Furthermore, all adverse events were documented after initiation of everolimus therapy.

Results: Statistical analysis and data evaluation are still ongoing. The following adverse effects have been seen up to now: longual oedema (5%), erythrocytosis (6%), leukocytosis (1%), dermatological complications (10%) and varicose (2%).

Conclusions: We assume that kidney function will improve after conversion to everolimus in heart transplant recipients with chronic renal failure due to nephrotoxicity of calcineurin-inhibitors.

PO-095 MYCOPHENOLATE MOFETIL COMPARED WITH AZATHIOPRINE ALLOWS LOWER CYCLOSPORINE LEVELS WHILE ACHIEVING BETTER CONTROL OF REJECTION WITH IMPROVED RENAL FUNCTION AND INCREASED STEROID WEANING AFTER HEART TRANSPLANTATION

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Two-hundred and forty-four cardiac transplant patients (190 male; mean age 47 [range 18-67] years) were treated with either mycophenolate mofetil (MMF) or azathioprine (AZA) in combination with Neoral (Csa) and corticosteroids after Rabbit Antithymocyte Globulin induction; N=120 AZA (August 1997-2000) and N=124 MMF (June 2000-August 2004). By protocol, lower cyclosporine levels (parent compound in whole blood by HPLC mass spectrometry) were targeted in the MMF group: at 3 months Csa levels were MMF 233±7 SEM % vs. AZA 262±7 mg/ml p= 0.005 and Csa doses were 3.6±0.1 vs. 4.3±0.2 mg/kg respectively p= 0.05. Patient survival at 1-year was similar: 81% vs.80% p = 0.87. In patients followed up for at least 1 year (n=184), there was less biopsy-proven ISHLT >3A acute rejection (BPAR) in the MMF group at 3 months (0.18±0.05 episodes per patient vs. 0.39±0.07, p=0.01) with a trend for fewer BPAR episodes at 1 year (0.4±0.08 vs.0.5±0.09, p=0.36). There were fewer treated rejection episodes by 1-year (0.75±0.11 vs.1.15±0.10, p= 0.009) and less need for cytolytic therapy in the MMF group (4.5% vs. 13.5%, P=0.04). Creatinine clearance at one year (Cockcroft and Gault) was greater in the MMF group (67.3±3 vs.59.3±3 ml/min, p=0.05). Ejection fractions were similar at 1-year (75±1% vs.74±1%, p=0.24 respectively). Fewer MMF patients were receiving corticosteroids at one year (39% vs.59%, p=0.007). MMF used in combination with lower Csa levels resulted in better control of rejection as well as improved renal function and increased steroid weaning at 1-year.

PO-096 ECONOMIC EVALUATION OF EVEROLIMUS AND MYCOPHENOLE 或 MOFETIL (MMF) vs AZATHIOPRINE (Aza) IN DE NOVO HEART TRANSPLANTATION

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Everolimus (1.5mg/day) has shown superior efficacy vs. Aza in de novo heart transplant patients. Trial results for MMF (3g/day) vs. Aza in comparable de novo heart transplant patients were also published. This study assesses cost-effectiveness of everolimus and MMF vs. Aza.

Methods: The evaluation was performed from the German health insurance payer perspective, using drug public prices and a 6-month post-transplant timeframe. The composite efficacy endpoint in the everolimus trial comprised death, graft loss, retransplant, loss to follow-up, biopsy-proven acute rejection (BPAR) = grade 3A or 4B rejection with hemodynamic compromise (HDC). The composite efficacy endpoint in the MMF trial did not contain BPAR = grade 3A nor lost to follow up. To mimic the same endpoint as in the everolimus trial, two mapping scenarios were developed to avoid double counting of event. The result of the indirect comparison of everolimus vs. MMF in Scenarios 1 and 2, respectively.

Conclusion: Cost-effectiveness in favor of everolimus compared to MMF in the management of de novo heart transplant patients. Everolimus may achieve a higher efficacy gain vs. Aza than MMF and has lower incremental drug cost vs. Aza than MMF.

PO-097 NEORAL AND CERTICAN CAN SAFELY BE COMBINED IN STABLE CARDIAC TRANSPLANT RECIPIENTS: SIX WEEK INTERIM ANALYSIS OF A CANADIAN PILOT STUDY

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The proliferation inhibitor everolimus (EVL) enhances CNI-related nephrotoxicity.

Objectives: to determine 1) the extent of Neoral dose reduction required to maintain GFR after conversion to EVL; 2) the incidence of ACR after conversion; 3) the daily EVL dose required to achieve a target C0 level of 5-10 ng/ml.

Study design: MMF or AZA were replaced with EVL 0.75 mg b.i.d. Neoral was reduced by 25% at time of EVL conversion. After 6-8 days, EVL was adjusted to a C0 level of 5-10 ng/mL. C0 was found reduced each time cGFR was below 75% of baseline. Six week interim analysis: 25 maintenance heart transplant patients, aged 58.7±8.2 years, were included. Data are presented as median (range). At 6 weeks the daily EVL dose was 1.5 (0.5-3.0) mg/d with a mean blood C0 level of 7.0 (3.8-10.6) ng/ml. 17 patients (68%) were in the targeted range. The Neoral dose was reduced from 1.9 (1.2-3.6) mg/kg/d to 1.4 (0.7-2.6) mg/kg/d. Neoral C0 levels remained unchanged [432 (202-866) mg/ml and 434 (197-1038) mg/ml]. The cGFR (Nankivell) at baseline and week 6 were 67 (41-100) ml/min and 65 (45-104) ml/min, respectively. All differences were ns. 15 AEs (1 SAE) were reported of which 9 were of GI nature (aphthous stomatitis, diarrhea). No acute rejection episode occurred.

Conclusion: with appropriate reduction in Neoral dosing, everolimus can be safely introduced without worsening in attendant renal function.

PO-098 INITIAL EXPERIENCE WITH EC-MPA (MYFORTIC) IN PATIENTS WITH GASTROINTESTINAL TOLERANCE TO MYCOPHENOLE OR MOFETIL (MMF)

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Objective: We analyzed the safety, tolerability and efficacy of enteric coated mycophenolic acid post heart transplantation in patients that did not tolerate mycophenolate (CellCept) due to gastrointestinal complications.

Methods: Between 8/2003 and 9/2004 15 patients transplanted between 1997 and 2004 had to stop MMF due to gastrointestinal complications 34.8 ± 28 post transplantation. All of those were started on EC-MPA after discontinuation of MMF and cessation of symptoms (14-21 days). Starting dose was 720 mg BID. Daily doses were adapted to achieve a target fasting level of 2-4 mg/l. Concomitant immunosuppression was neoral (n = 9), tacrolimus (n = 6) and 9/15 are off steroids.

Results: Average follow-up of EC-MPA intake is 13.1±3.5 months. Only 4 patients showed again gastrointestinal symptoms after 1 week and 2 months requiring to stop medication. Average daily dose to achieve target levels was 19.1 ± 589 mg on EC-MPA compared to 44.4 ± 530 mg on MMF normalized to dose equivalent 3.21 ± 1.6 tabs vs. 3.88 ± 1.1 tabs, respectively (p-n.s.). No acute rejection requiring treatment (ISHLT grade >2BPAR) nor relevant infections were diagnosed in any patient after switch to EC-MPA.
Conclusion: In this study cohort 73.4% of patients tolerated treatment with EC-MPA after a mid-term follow-up after previous intolerance of MMF. There were no significant differences in dosing necessities to achieve comparable target levels. We conclude that switch from MMF to EC-MPA in case of gastrointestinal intolerance is a worthwhile strategy.

PO-099 POST-STERNOTOMY MEDIASTINITIS AFTER HEART TRANSPLANTATION. A CASE SUCCESSFULLY TREATED WITH THE USE OF VACUUM ASSISTED CLOSURE SYSTEM AND PECTORALIS FLAP
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Purpose: Post-sternotomy mediastinitis remains a serious cause of postoperative morbidity and mortality and is always lethal in heart transplant recipients. We report on a successfully treated severe methicillin-resistant staphylococcus aureus mediastinal (MRSA) infection after heart transplantation.

Materials: A 34-year old patient with dilative cardiomyopathy underwent orthotopic heart transplantation. In-hospital postoperative period was uneventful. On the 31th postoperative day, the patient was admitted because of sternotomy wound infection, sternal instability and high fever (39.2°C).

Results: Surgery revealed sternal dehiscence with supplicative mediastinal infection. Surgical debridement was performed and use of vacuum assisted closure system was started immediately. Serial quantitative wound cultures were positive (MRSA) and intravenous antibiotic therapy (vancomycin, 500 mg X 3) was also started. Vacuum system was changed every 2 to 3 days and used in total for 34 days. Vacuum system was removed when regional and systemic signs of infection resolved and quantitative cultures were negative. Finally, the patient underwent regional muscle flap closure (pectoralis flap) and a complete healing was achieved.

Conclusion: Vacuum system offers an effective and safe means of managing patients with postoperative mediastinitis acting as a bridge for reconstructive plastic surgery.

PO-100 NTpro-BNP LEVEL OF THE HEART DONOR AND GRAFT FUNCTION IN EARLY POSTOPERATIVE PERIOD
Erik Petrikovits, Helena Bedanova, Josef Necas, Pavel Studenik, Nikolaos Efstathiou, Ioannis Fessatidis. Cardiothoracic Surgery, General University Hospital/IKEM, Prague, Czech Republic.

Background: Graft failure in early postoperative period is serious complication after heart transplantation (HTx). Poor quality of graft is a frequent reason of graft failure. The most reliable marker of the donor heart function is echocardiography. This has some limitation and in case of boundary finding it does not give final information. Therefore, a new method for detection of graft dysfunction, is sought. The aim of our study was to assess if the level of NTpro-BNP corresponds with graft function in early postoperative period.

Patients and method: We analysed a group of 16 heart graft recipients (av. age 30y) and their donors (av. age 53y) undergoing Htx in our hospital between April 2003 and May 2004. Blood samples were drawn at the time of organ retrieval. In all patients eco-cardiography was used to document global ventricular function. We assessed early graft failure, higher catecholamines support, and rejection episodes first 30 days after Htx.

Results: We detected one early graft failure, seven patients required higher catecholamine support, five of them had higher level of NT-proBNP in time of organ harvest. On the contrary, out of seven patients without catecholamine support, five of them had higher level of NT-proBNP in time of organ harvest. In total for 34 days. We recommend NT-proBNP determination at the donor hospital. Further studies are indicated to determine its role in donor assessment and the response to treatment.

PO-101 REAL INCIDENCE OF “CHRONIC ALLOGRAFT REJECTION” AFTER ORTHOTOPIC HEART TRANSPLANTATION
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Introduction: Allograft vasculopathy (AV)-“chronic rejection” represents one of the most serious complications of late period after heart transplantation (HTx). Its incidence reaches 40-50% at one year after HTx. Despite huge progress in transplantontology its aetiology still remains to be fully answered. There is a huge discrepancy between experimentally and clinically established risk-etiologic factors of AV development. Donor related coronary artery disease (DRCAD), which does not “take place” in experimental studies of AV, might be a complicating factor for understanding AV development in clinical studies- in humans. The aim of this study was to establish the real incidence of chronic rejection (de novo developed coronary artery disease) after clinical HTx.

Study population and methods: Study group consists of 42 HTx recipients (33 male, 9 female, age 50.48±9.85 years) with both early and one year IVUS performed.

Results: Allograft coronary artery disease was detected by IVUS in 16 recipients (i.e. 38%) at one year after HTx. DRCAD was detected by early performed IVUS in 12 cases (i.e. 75%) out of these 16 HTx recipients. De novo developed allograft coronary artery disease was observed only in 4 cases (i.e. 9% of study group).

Conclusion: Our study demonstrates, that after HTx de novo developed allograft coronary artery disease is not common, the vast majority of allograft coronary artery pathology detected at one year after HTx derives from DRCAD.

PO-102 ABSTRACT WITHDRAWN

PO-103 HEPARIN INDUCED THROMBOCYTOPENIA (HIT) IN THORATEC ASSISTED PATIENTS: A WORD OF CAUTION
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Purpose: Anticoagulation with heparin in Thoratec assisted patients is recommended. Chronic exposure or re-exposure to heparin may initiate heparin antibody(Hp-Ab). To evaluate the incidence and management issues, we reviewed our experience.

Methods: Among 14pts supported with a Thoratec, 4pts tested positive for Hp-Ab by ELISA.

Results: The Thoratec was installed for post-cardiotoxicity failure in 3pts and myocardial infarct with shock in 1pt. HIT diagnosis was suspected by a platelet count <100000 in 3pts and a 50% decrease in platelet count in another pt. Anticoagulation was changed to an organ specific regimen in all patients. Sera-tonin released assay(SRA) confirmed the HIT diagnosis in 2pts. In 2pts the SRA test was not obtained owing to unavailability of the test in 1pt and the concomitant offer of a donor in another patient. This last patient underwent a successful transplantation under hirudin although significant intra-operative bleeding was encountered. Among the other 3pts, 2 died of multigorgan failure secondary to sepsis and one SRA+ pt, was successfully transplanted using hirudin once the ELISA Hp-Ab test was negative 3 weeks after the initial positive result. One pt sustained a thrombotic complication.

Conclusion: The incidence of Hp-Ab detected by ELISA in Thoratect pts is significant. To avoid false-positive ELISA tests, tests should be ordered in clinical settings compatible with HIT: platelet count <100000 or decrease >50% with at least 7-10days of heparin therapy or during heparin re-exposure. SRA confirmation should be obtained. In case of a SRA+ test, delaying transplantation until obtaining a negative ELISA Hp-Ab or undertaking transplantation under hirudin have to be considered.

PO-104 ABSTRACT WITHDRAWN

PO-105 ELECTIVE CONVERSION FROM CELLCAPT TO MYFORTIC UNDER CONTROL OF MYCOPHENOLIC ACID (MPA) CONCENTRATION IN STABLE HEART TRANSPLANT RECIPIENTS – PILOT PROSPECTIVE STUDY
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The aim: of the study was to evaluate a possibility to replace mycophenolate mofetil(CelleCept, Roche) with enteric-coated mycophenolate sodium (Myfortic, Novartis) in stable heart transplant recipients.

Material and Methods: An elective conversion of CellCept to Myfortic was performed in randomly selected 15 heart transplant recipients (13M/2F, 45.9±8.5y/o, 38±32mo. after transplantation). Recurrent acute cellular rejection was an indication to introduce CellCept in 13pts., however, at a time of conversion all subjects were without signs of significant rejection in the last endomyocardial biopsy. Conversion was performed according to CellCept dose, in 250mg/180mg of Myfortic ratio. Both CellCept and Myfortic dosage was leaded by MPA serum trough concentration (EMT), in order to achieve 1.2-2.0ug/ml.

Results: Follow-up was 5-7mo. Myfortic was converted back to CellCept at 1pt. due to intolerance. 1 acute rejection with hemodynamic compromise occurred, however Myfortic was continued. Average daily dose of CellCept at the time of conversion was 517±536mg, and MPA level 1.42±0.6ug/ml. Parallel dose of Myfortic after conversion was 1128±449, and MPA level after 1mo. of its use was 1.95±2.5ug/ml. Final MPA trough concentration increased to
2.82±2.2 Aug/ml (p=0.06, Mann-Whitney U test), achieved with a 1032±350mg daily dose of Myfolic. A final dose of Myfolic was increased in 5pts., decreased in 7pts., and unchanged in 3pts.

**Conclusion:** 250mg of CellCept/180mg of Myfolic conversion ratio seems to be proper for a majority of patients, however additional MPA measurement at 250mg of CellCept/180mg of Myfotic conversion ratio seems to be proper for a majority of patients, however additional MPA measurement

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**PO-108**

**THE RISK OF DEVELOPING NEW ONSET DIABETES MELLITUS AFTER HEART TRANSPLANTATION IS INCREASED UNDER TACROLIMUS THERAPY: AN ANALYSIS OF THE UNOS DATABASE**

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Diabetes mellitus emerging after transplantation (NODM) is a well documented complication of kidney and liver transplantation. Clinical trials and database analyses have linked this complication to immunosuppression, revealing a greater incidence with tacrolimus compared to Neoral® (CsA-ME). We examined this relationship in heart transplant recipients using the UNOS database. All patients receiving a first heart transplant in 2001 and 2002 who had at least six months of follow up, no evidence of diabetes pre-transplantation, and who were also receiving corticosteroids and mycophenolate mofetil at the time of initial hospital discharge were included in this analysis. The time period was selected in order to minimize possible effects of changing clinic practice while maximizing follow up duration and sample size. Statistical analyses included the computation of hazard rate ratios (HRR; tacrolimus vs. CsA-ME) for NODM and confidence intervals (CI) calculated using discrete-time multivariable hazard regressions. The incidence of NODM was 11.7% in the tacrolimus treated group (N=533) vs. 5.9% in the CsA-ME treated group (N=1,013). The HRR was 2.16 (95% CI 1.66 - 2.81, p<0.001), adjusting for recipient, donor and transplant-related characteristics. Graft survival also favored CsA-ME therapy (p<0.05, log rank test), with two-year survival of 93.3% vs. 90.3%. We conclude that the increased risk of NODM associated with tacrolimus reported in kidney and liver transplantation extends to the heart transplant population. This result, coupled with our finding of superior patient survival with CsA-ME in this population points to the importance of additional study.

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**PO-109**

**IMPROVING OUTCOMES OF HTx IN THE ERA OF DONOR SELECTION CRITERIA EXPANSION**

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Background: To fulfill increasing clinical needs, owing to organ shortage, selection criteria (SC) for donor in heart transplantation (HTx) have been widened. Use of marginal donors has been reported to increase early and late mortality. Aim: Aim of study was to assess whether donor SC expansion affected results following HTx.

**Method:** Between November 1985 and December 2004, 290pts underwent orthotopic HTx (294 HTx, 4 re-HTx censored) at our institution. On surgery date basis, 3 groups have been identified: Group 1 (G1) comprises pts transplanted in 1985-1991 (strict SC), Group 2 (G2) 1992-1998 (enlarged SC), Group 3 (G3) 1999-2004 (wider SC, plus different organ preservation and recipient immunosuppression).

Characteristics of G1 (58 donors), G2 (96) and G3 (136) were, respectively: Age 28±11yrs (14-54), 34±13 (15-60), 37±14 (15-65); Male/Female ratio 6.1, 2.5, 2.0; Trauma/Vascular death ratio 2.1, 1.6, 1.1; Prolonged Ipotension/Cardiac Arrest 7%, 7%, 10%; Ischemia Time 179±61min (92-237), 191±53 (82-307), 196±65 (62-385).

Cardioplegic solution was Bretschneider in G1 and G2, St Thomas in G3. On surgery date basis, 3 groups have been identified: Group 1 (G1) comprises pts transplanted in 1985-1991 (strict SC), Group 2 (G2) 1992-1998 (enlarged SC), Group 3 (G3) 1999-2004 (wider SC, plus different organ preservation and recipient immunosuppression).

Characteristics of G1 (58 donors), G2 (96) and G3 (136) were, respectively:

- **Conclusion:**
  - Early mortality (-30days) was 8.6%, 14.7% and 8.0%, respectively (p<0.05 G1 vs. G3).
  - Actuarial survival at 1, 5, 10 and 15 yrs was 82±2, 73±3, 59±4, 45±6, respectively.
  - Other clinical characteristics similar among Groups.

**Results:**

- Overall actuarial survival at 1, 5, 10 and 15 yrs was 82±2, 73±3, 59±4, 45±6, respectively.
- Early mortality (-30days) was 8.6%, 14.7% and 8.0%, respectively (p<0.05 G1 vs. G3).
- Actuarial survival at 1, 3 and 5 yrs was 88±4, 79±5, 72±6 in G1, 75±4, 70±4, 67±5 in G2, and 85±3, 83±4, 83±4 in G3 (p<0.05 G3 vs. G1-G2).

**Conclusions:** Despite more unfavourable donor variables, results of HTx in G3 are satisfactory, possibly due to better organ procurement and most tailored recipient immunosuppression. Data encourage using of marginal donors in selected cases.
PO-110
SOMATIC AND CARDIAC STATUS OF SURVIVORS MORE THAN 10 YEARS AFTER HEART TRANSPLANTATION IN THE CYCLOSPORINE ERA
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Heart transplantation (HTX) has a dramatic impact on both life expectancy and quality of life (QoL) in patients (pts) with terminal heart failure.

Methods: 461 HTX were performed between 1988-2004. 10 years survivors and their medical records (eg. cardiac catheter studies, echocardiography, ergospirometry) were examined to determine their somatic and cardiac status. Psychologic, social, and occupational status and QoL data were assessed by self-rating questionnaires.

Results: 43.4% survived 10 years and more. 63.2% of 1 year survivors were followed up 10 years or more (av. 11.44 years). We found generally excellent functional status, but a high incidence of hypertension, renal dysfunction, and graft CAD as well as malignancy.

Conclusions: The pts 10 years after HTX are mostly in good physical status [fig.1]. QoL is comparable to the general population, and only a few of them have significantly limited in their life style.

PO-111
INCIDENCE OF MACE AND ECONOMIC BURDEN IN DE NOVO HEART TRANSPLANT PATIENTS: A 4 YEAR COMPARISON OF EVEROLIMUS AND AZATHIOPRINE
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In trial RADB253, 1-year change in intravascular ultrasound (IVUS) showed that everolimus was associated with a significantly lower incidence of cardiovascular allograft vasculopathy (CAV) than azathioprine. The current study assessed whether the improved IVUS results at 1 year with everolimus are predictive of reduced risk of major adverse cardiovascular events (MACE).

Methods: The 4-year incidence of MACE was recorded in patients for whom IVUS measurements at baseline and 1 year were available. Since CAV manifests ~3 months post-transplant, only MACE after month 3 were included. US Healthcare Cost and Utilization Project (HCUP) 2002 data were used to estimate mean cost per hospitalization event for defined MACE events: acute myocardial infarction $36,666; percutaneous cardiac intervention $34,075; coronary artery bypass grafting $70,618; cerebrovascular accident $24,057; peripheral vascular disease $29,707; congestive heart failure $20,600; and implantable cardiac defibrillator $52,004.

Results: At 4 years post-transplant, there were more MACE events in azathioprine than everolimus patients. Two MACE patients died; both were in the azathioprine group and had developed CAV. MACE occurred in 9 azathioprine patients (14 events); 5 everolimus 1.5mg patients (5 events) and 5 everolimus 3mg patients (6 events). Applying the HCUP average costs per hospitalization, total treatment cost for MACE within 4-year follow-up was $376,753 for the azathioprine group, $116,064 for everolimus 1.5mg and $162,250 for everolimus 3mg.

Conclusion: Patients on everolimus experience fewer MACE by 4 years post-transplant than those on azathioprine, translating to reduced hospitalization and ultimately economic savings to healthcare payers.

PO-112
ONLY A FEW HEARTS FOR TO MANY PATIENTS: THE ROLE OF RETRANSPANTATION
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Objective: Last data have reported a one year survival of 76% after heart transplantation in our country. Patients with a previous heart transplantation may need another heart because of a new heart dysfunction. Therefore, a proper selection of patients should be done in order to make a well use of donors. Data outcomes after heart retransplantation are not well known in our country and there is a conflict about the convenience of using a new heart in these patients. We report the outcomes and survival of patients receiving a heart retransplantation.

Methods: All patients receiving a heart retransplantation in our hospital between 1992 and 2004 were selected (n=25). Baseline clinical characteristic, hospital outcomes and five years survival using a Kaplan-Meier curve, were analysed.

Results: Mean age was 55.4 ± 6.9 years with a male/female ratio of 5/1. Reasons for center in the heart transplantation waiting list were: 1) Primary graft dysfunction (n=11), 2) Graft vascular disease (n=14). A total of 12 patients had national priority for heart transplantation. Mortality after surgery was infectious (n=12) and neurological (n=5). One year survival was 67% and a better survival was seen in patients with primary graft dysfunction than in those patients with graft vascular disease can be seen (p=0.16).

Conclusions: Nowadays in our country, patients receiving a heart transplantation have one year survival close to those patient receiving their first heart transplantation (67% vs. 76%). Survival seems to be better in those patients with primary graft dysfunction than in those patients with graft vascular disease.

PO-113
FOURTEEN YEARS SURVIVAL AFTER A CARDIAC TRANSPLANTATION IN A DEVELOPMENT COUNTRY: THE COSTA RICA EXPERIENCE
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Purpose: We present the case of a patient who had a cardiac transplant 14 years ago for severe isquemic heart disease in functional class IV who has stayed in a class I since then.

Methods/Materials: This is a 38 years female patient with hyperlipidemia and smoking complained with severe CAD, multiple myocardial infarctions, refractory angor and severe LV dysfunction. In July, 1990 an orthotopic cardiac transplant was performed with an isquemic graft period of 120 minutes. She required peritoneal dialysis during 10 days being discharged at 21 postoperative days.

Results: The first endomyocardiacal biopsies revealed a light rejection grade 1 a, becoming negative after six months. A second rejection grade 2 was treated with prednisone and Azathioprine scheme, drugs that she has tolerated very well. The follow up angiograms have been normal. Lately, she has had an appendectomy, salpingectomy and hysterectomy. She is currently asymptomatic, living in a rural community, married and fully integrated to the society.

Conclusion: This case represents a landmark in the Social Security system of Costa Rica, improving the quality and life expectancy of a patient previously confined to the ICU with the high expenses that this condition represents. She is part of a group of patients admitted in a heart transplant program that started in 1990 in our country with one year survival of 80%.

PO-114
IS BNP A RELIABLE PREDICTOR FOR ACUTE REJECTION IN HEART TRANSPLANT RECIPIENTS?
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BNP levels are elevated in heart insufficiency and are a predictor for cardiac mortality. Recent findings suggest that elevated BNP plasma levels could form a basis for a non-invasive test for acute cardiac allograft rejection. Aim of this study was to evaluate the correlation between BNP-levels and acute rejection after heart transplantation. From 2001 to 2005 a total of 506 BNP measurements were taken immediately before routine endomyocardiacal biopsies. We analysed these measurements regarding the correlation between acute rejection and BNP as well as its sensitivity and specificity. Further covariables were patient age, fractional shortening (FS), left ventricular end diastolic diameter (LVEDD) and serum creatinine. Mean BNP in heart transplant recipients was 121.9±172.3 pg/ml. There was a significance in the correlation between BNP levels and the biopsy grade (ISHLT classification) (p=0.02), but the sensitivity and specificity was considerably low. The highest correlation was found between BNP and creatinine levels (p<0.001) and recipient age (p=0.001). There was no correlation between BNP and FS or LVEDD.

Circulating BNP is elevated in heart transplant recipients and increases with renal insufficiency. As a marker for acute rejection BNP is not reliable because the levels depend on many influencing factors. In addition great individual differences occur. This study is limited due to a low number of rejection episodes. BNP might be a marker for wall stress and volume overload, but not...
PO-115 ANTI-HLA ANTIBODY REPERTOIRE AFTER IVIG INFUSION IN HYPERIMMUNISED PATIENTS WAITING FOR KIDNEY TRANSPLANTATION

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IVIg reduces crossmatch positivity and increases transplantation in highly sensitized patients (HS). We quantified anti-HLA class I and II IgG antibodies (Ab) by CDC and we analyzed by Luminex the modulation of the specific Ab repertoire before and after three IVIg infusions (1g/kg/month) in 5 HS patients awaiting kidney transplantation. We focused our analysis on the anti-HLA Ab directly against HLA antigen expressed by previous transplants.

Results: Of the 5 patients who received IVIg, 1 showed a significant decrease in PR, from 40% to 17%. Analysis of the anti-HLA class I and II showed fluctuations of Ab repertoire during the IVIg treatment. The fluctuations were transient for 3 patients and but persist several months in two others. No change could be demonstrated in the anti-HLA repertoire of the patient with a strong and prolonged reduction of the PR. Similar analysis in 3 HS who don’t receive IVIg also demonstrated fluctuation of the repertoire.

Conclusion: IVIg treatment at 1g/kg is safe and induced significant reduction of the PR in one of the five patients. IVIg did not modify the long term anti-HLA repertoire in these patients. Our results suggest that at this dosage, the mode of action of IVIg to reduce anti-HLA Ab is not due to an anti-idiotypic effect.

PO-116 HLA CLASS I SENSITIZATION BY A KIDNEY GRAFT IS MAINLY DUE TO THE RECOGNITION OF A SINGLE MISMATCHED PUBLIC EPITOPE

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The conventional HLA donor/recipient compatibility takes into consideration the 6 polymorphic epitopes of the specific HLA-A,B, DR antigens. On the contrary, the humoral immune response against a kidney graft determines the production of antibodies reacting with multiple HLA specificity. The aim of this study was to define the epitope specificity of the HLA class I antibodies detected in the sera from 55 patients who had lost a kidney graft using the sensitive and allele specific FlowPRA Class I Single Antigen beads. We also investigated number, type and immunogenicity of potential donor “sensitizing epitopes” by analysis of HLA class I allele sequences of donors, recipient and antibody-reactivity. Eighty patterns of antibody-reactivity were identified; 76 (92.5%) of these were due to the recognition of a mismatched “public epitope.” Moreover the recognition of a single or few near mismatched donor residues caused the whole antibody-reactivity-pattern in the 98.2% (54/55) of the patients. As for the kind of “sensitizing epitopes”, 48 different residues (27 of HLA-A, 17 of HLA-B and 4 of HLA- A & B molecules) were identified. The more immunogenic epitopes were B2-83LR (75%), 80N (75%), 161D (60%), 625S (25%), 127K (37.5%). These data indicate that patients alloimmunized by a kidney graft produce HLA class I antibodies specific for donor “public epitopes.” The recognition of a “single” mismatched donor-residue determines the formation of a spread antibody-pattern. So, amino-acid based matching could enhance organ allocation criteria.

PO-117 THE FUNCTIONAL RELEVANCE OF HLA-DRB4 INCOMPATIBILITIES IN HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Selection of unrelated donors for hematopoietic stem cell transplantation (HSCT) is increasingly based on high resolution DNA typing for HLA-A/B/C/DRB1/DBR81 loci. Donor-recipient allele disparities correlate with higher risks of graft-versus-host disease, rejection, and mortality. Several studies have shown that a single disparity for A/B/C/DRB1 loci was associated with worse clinical outcome, as compared to matched donors. In most HLA-DR haptotypes a second DR antigen is encoded by one of the polymorphic DRB3, DRB4, or DRB5 loci. In this study we have investigated the functional relevance of the DRB4 locus encoding the DRB3 antigen.

HLA-DRB4 allelic polymorphism was analysed by PCR-SSP in a total of 125 DR4- or DR7-positive patient/donor combinations that were also typed for A/B/C/DRB1/DBR3/DRB5/DQB1 loci in the setting of related donor searches. Although some haptotypes were highly conserved, diverse DRB1- DRB4 associations were found for most DR4 and DR7 haptotypes. When analysing S9 patient/donor combinations (41 patients/55 donors) that were either fully matched or had a single class I incompatibility, a DRB4 mismatching rate of 10% was detected. All DRB4 incompatibilities, i.e. 0.01 versus 0.03 (n=5) or 0.01 versus 0.01 (n=1), did result in a negative in vitro bidirectional mixed lymphocyte reaction under conditions where a single DRB3 or DRB1 disparity was positive. The unresponsiveness of DRB4 disparities might be linked to a low expression of the DRB3 antigen and/or to the fact that DRB4*0101 and 0103 alleles differ at residue 135 only, a position that is not expected to affect T-cell allorecognition. We therefore conclude that HLA-DRB4 could be considered as a permissive locus for unrelated HSCT and that DRB4 typing could be omitted from the selection algorithm.

PO-118 INCOMPATIBILITY BETWEEN KIRZDL1 AND ITS HLA-C LIGANDS IS ASSOCIATED WITH ACUTE REJECTION IN KIDNEY TRANSPLANTATION

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Aim: Killer-cell-immunoglobulin-like receptors (KIRs) are expressed by natural killer (NK) cells and T cell subsets. Lately, it has been shown that KIR/HLA incompatibility exerts beneficial effects in bone marrow transplantation. Despite the knowledge about recipient NK-cell cytotoxicity against the graft in renal transplantation, as illustrated by the release of perforin or granzymes, little is known about the functional role of KIR-Ligand incompatibility in this transplant setting.

Methods: We designed a PCR-SSP for genotyping of 16 KIR genes amplifying gene products ranging from 107-455bp. Genotyping for HLA was performed routinely prior to Tx. In our study 63/142 patients suffered from one or more biopsy proven acute rejection (aRx) episodes after kidney transplantation.

Results: Data were analyzed for the entirety of activating and inhibitory KIR genes and their known HLA ligands for aRx patients compared to the control group. In summary, patients with an uncomplicated course displayed a higher number of KIR/HLA matches compared to the aRx group. This observation was made for inhibitory and activating KIR receptors. Furthermore the analysis revealed that aRx rejecting patients demonstrated a significantly higher number of mismatches between the inhibitory receptor KIRZDL1 and its corresponding HLA-C2 group 2 alleles (p=0.002).

Conclusion: Although our patient number is low, these are the first data illustrating the influence of KIR/HLA incompatibility in renal transplantation suggesting that allografts expressing KIR ligands or KIR molecules can be potential targets for NK-cell killing influencing graft outcome. Further studies are necessary to elucidate the functional role of polymorphic KIR receptors in kidney transplantation.

PO-119 EVALUATION OF ANTI-HLA CLASS I AND ANTI-HLA CLASS II ANTIBODIES IN SERUM OF PATIENTS AWAITING A RENAL ALLOGRAFT

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The presence of anti-human leucocyte antigens antibodies (HLA) in serum of renal allograft recipients can be a cause of hyperacute graft rejection. The detection of those antibodies in patients serum in crossmatch performed before transplantation is a basis of patients disqualification for transplantation.

The aim of the study was the identification of preformed antibodies (PRA) in sera of highly sensitized patients. Among 1 175 patients present on the kidney transplantation waiting list in Poland were chosen 32 with PRA level higher than 25% (25%-100%) and 8 patients with PRA value ranged 13-24%. Three patients with PRA=0% were chosen as controls. The class specificity of antibodies was evaluated with a solid phase Enzyme Linked ImmunoSorbent Assay using tests AbScreen HLA class I and AbScreen class II, Biostec.

In the group of highly immunized patients 3 (9%) had no IgG anti-HLA antibodie-
16 patients (50%) had only anti-HLA class I antibodies and 17 patients (53%) had antibodies against both HLA classes. One patient had only anti-HLA class II antibodies. In the group of low sensitized patients 3 of them (37%) had anti-HLA class I antibodies and 5 patients (63%) had both class I and class II antibodies. The control group had no anti-HLA antibodies. The confirmation of absence of IgG antibodies in highly sensitized patients permits the performing of kidney transplantation. The precise profiling of antibodies in low sensitized patients can protect them from acute graft dysfunction.

**Immunobiology / Basic Science**

**PO-120**

**FREQUENT AND LATE DONOR DIRECTED ANTIBODY FORMATION AFTER EARLY KIDNEY-TRANSPLANTATION**

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We retrospectively analyzed DDA formation in patients transplanted between 1992 and 2004 (n=600) who underwent transplantectomy (n=109). Patients with pretransplant HLA antibodies (ab) were excluded (n=28) as well as patients with retransplants (n=7) or combined kidney-pancreas transplantation (n=5). From the remaining 68 first transplant patients, we studied the patients with test within one month (n=34). Sera were collected and screened for class I and II antibody specificities by CDC and by ELISA. All patients except one were treated with CNI-based immunosuppression. Additional immunosuppressives were prednisolon, MMF and sirolimus. In 6/34 recipients an immunological event was proven to cause graft failure, i.e. rejection treatment or positive histology in the graft. Two out of 6 rejections were negative for HLA ab, the other 4 produced ab to class I+II (n=3) or class II only (n=1). In the total group, 19/33 patients became positive for DDA class I and/or II (56%). All ab were formed after transplantectomy, except in one patient who became positive with cl II ab 4 days before failure. Class I ab were produced in 17 (50%), 4A 7B 6A+B and class II in 14 (41%, 10DR, 1DQ, 2DR+DQ) recipients. Median day (+ range) of appearance of ab production was 122 days for class I and 132 days for class II.

HLA antibodies against donor antigens were produced in >50% of the transplantrecipients, even when the graft had been in situ for a short period only. Prolonged screening after transplantectomy is considered necessary in view of possible retransplantation.

**PO-121**

**CORRELATION OF MYCOPHENOLIC ACID PHARMACOKINETIC PARAMETERS WITH SIDE EFFECTS IN CHINESE KIDNEY TRANSPLANT PATIENTS TREATED WITH MYCOPHENOLATE MOFETIL**

Yiping Lu, Bo Li, Maozhi Liang, Youping Li, Li Wang, Feng Nan, Qin Yu, Keshi Tang. Transplantation Institute, West China Hospital, Sichuan University, Chengdu, Sichuan, China.

**Objective:** To investigate the relationship between the clinical events and the pharmacokinetics of mycophenolic acid (MPA) in adult renal transplant patients.

**Methods:** 22 adult kidney transplant recipients were included. All patients received a triple therapy of CsA, MMF and steroids. MPA-AUC0-12 was obtained. Further-

**Results:** Single-dose and multi-dose MPA-AUC0-12 were obtained. Furthermore, 151 MPA-C0 values were obtained from 22 patients. The 151 units were divided into three sub-groups: Group A, including102 units (67.5%) had un-eventolette outcomes, Group B including 43 units (28.4%) presented with MPA-related side effects, and Group C included 6 units (3.9%) experienced acute rejection. MPA-C0 in groups A, B and C was 0.88660.1063, 1.51140.2748mg/L and 0.53050.2863mg/L, respectively (P<0.001 between group A and B and P<0.0001 between group A and C). The 3 groups were also divided into initial phase (1 month, 78 units) and stable phase (>1 month, 73 units), the relation-

**Conclusion:** Our results suggest that there is a relationship between MPA pharmacokinetics and the clinical events. The MPA- C0 might be an appropriate pharmacokinetic monitoring parameter for kidney transplantation.

**PO-122**

**CONVERSION FROM CYCLOSPORINE TO MYCOPHENOLATE MOFETIL IMPROVES EXPRESSION OF A20 IN THE RET-KIDNEY ALLOGRAFTS UNDERGOING CHRONIC REJECTION**

Donghai Teng, Yiping Lu, Yupeng Xin, Rui Gao, Guihua Cao, Xiang Li, Li Wang, Jiqiang. Transplantation Institute, West China Hospital, Sichuan University, Chengdu, Sichuan, China.

**Aims:** We investigated whether conversion from cyclosporine to mycopheno-

**Methods:** The recipients were divided into three oral treatment groups: (1) vehicle group (CsA 10mg/kg.dX10d followed by vehicle), (2) CsA group (CsA 10mg/kg.dX10d followed by CsA 6mg/kg.d), (3) MMF group (converted from CsA 10mg/kg.dX10d to MMF 6mg/kg.d on day 1). The expression of four cy-lopoptotic genes, A20, heme oxygenase (HO)-1, Bcl-2 and Bcl-XL in these grafted kidneys were analyzed, by quantitative RT-PCR and immunohisto-

**Results:** The expression of A20 in grafted kidneys is significantly higher in MMF group than that in CsA group and in vehicle group (P<0.01). There is no significant difference between CsA and vehicle groups. In the total group, 19/33 patients became positive for A20 expression of HO-1, Bcl-2 and Bcl-XL. A20 is expressed in vascular structures, cellular infiltrates and at very low levels in glomerular structures. Expression of HO-1 mainly localizes in cellular infiltrates but is also detected in tubular structures. Expression of Bcl-2 and Bcl-XL are mainly in tubular structures.

**Conclusions:** We demonstrate for the first time that MMF can improve the ex-

**PO-123**

**COMPARISON OF RAMAPYCN VS, FK506 ON EXPRESSION OF CYTOPROTECTIVE GENES IN THE RAT-KIDNEY ALLOGRAFTS UNDERGOING CHRONIC REJECTION**

Yiping Lu, Donghai Teng, Rui Gao, Yupeng Xin, Guihua Cao, Xiang Li, Li Wang, Jia Wang. Transplantation Institute, West China Hospital, Sichuan University, Chengdu, Sichuan, China.

**Aims:** We investigate whether there is difference between rapamycin and FK506 in the ability of affecting expression of cytoprotective genes in the rat kidney allografts undergoing chronic rejection.

**Methods:** The recipients were divided into 3 oral treatment groups: 1. ve-

**Results:** Four cytoprotective genes are all detected in the rat-kidney allografts undergoing chronic rejection. The expression of A20 in grafted kidneys is significantly higher in rapamycin group than that in FK506 group and in vehicle group. No significant difference between rapamycin group and FK506 group was observed in the expression of HO-1, Bcl-2 and Bcl-XL. A20 is expressed in vascular structures, cellular infiltrates and at very low levels in glomerular structures. Expression of HO-1 is mainly localized in cellular infiltrates, but it is also detected in tubular structures. Expression of Bcl-2 and Bcl-XL are mainly in tubular structures.

**Conclusions:** We demonstrate for the first time that different immunosuppres-

**PO-124**

**THE EXPLORATIVE STUDY OF THE MECHANISM AND DRUG INTERVENTION OF CHRONIC ALLOGRAFT NEPHROPATHY INDUCED BY ISCHEMIA/REPERFUSION**

Yiping Lu, Yupeng Xin, Rui Gao, Xuhui Zhang, Jia Wang, Youping Li. Transplantation Institute, West China Hospital, Sichuan University, Chengdu, Sichuan, China.

**This study focuses on the mechanisms of IRI for CAN and the protective effects of the YM, an injecting solution from Traditional Chinese medicine.**

**Methods:** The rats were divided into four groups: Group A was only re-

**Results:** The rats were divided into four groups: Group A was only re-

**Conclusion:** The YM might be an appropriate pharmacokinetic monitoring parameter for kidney transplantation.
ROLE OF DIFFERENT IMMUNOSUPPRESSANTS IN VSMC

**PO-125**

**ROLE OF DIFFERENT IMMUNOSUPPRESSANTS IN VSMC BY AFFECTING THE TGF-b AND Smads SIGNAL PATHWAY**

Rui Gao, Yiping Lu, Yupeng Xin, Xihui Zhang, Jia Wang, Transplantation Institute, West China Hospital, Sichuan University, Chengdu, Sichuan, China.

**Objective:** The discovery of Smads proteins has revealed the intracellular signal transduction of TGF-β. We investigated the effect of different immunosuppressants on TGF-β1/Smad signal pathway in VSMC in order to clarify the role of immunosuppressants in CAN.

**Methods:** Vascular smooth muscle cell (VSMC) from rat aorta were incubated with different immunosuppressants (CsA 3mg/ml, FK506 1mg/ml, MMF 0.3mg/ml, Rapa 10mg/ml, CsA 1mg/ml+ MMF 0.3mg/ml), respectively for 6 or 12 hours, as control without anything. The immunohistochemistry and real-time fluorescence quantitative polymerase chain reaction, were used to comprehend the expression of TGF-β1 and Smad2, 3 and up-regulate expression of Smad7, whereas MMF and Rapa could down-regulate the expression of TGF-β1 and Smad2 and inhibit expression of Smad7, whereas MMF and Rapa could down-regulate the expression of TGF-β1 and Smad2 and inhibit expression of Smad7.

**Results:** Comparing with control groups, CsA and FK506 increased expression of TGF-β1 and Smad2 and inhibited expression of Smad7, whereas MMF and Rapa could down-regulate the expression of TGF-β1 and Smad2 and up-regulate expression of Smad7. We demonstrated that increased TGF-β1 was associated with overexpression of Smad2 and down-regulated Smad7 in VSMC. There was no significant difference between CsA group and FK506 group, as well as MMF group and Rapa group. We also showed that CsA and FK506 affected TGF-β1, Smad2 and Smad7 in VSMC in a time-dependent manner.

**Conclusion:** Our datas indicated that Smads proteins were expressed in VSMC and that they mediated TGF-β signaling in those cells. Different immunosuppressants can affect TGF-β1/Smad signal pathway in VSMC, CsA and FK506 can up-regulate the expression of Smad2 and down-regulate Smad7 expression in VSMC, and cause the overexpression of TGF-β1. This will contribute to atherosclerosis. However, MMF and Rapa have a protective role in VSMC compared with CsA and FK506.

**Conclusion:** Smads proteins were expressed in VSMC and that they mediated TGF-β signaling in those cells. Different immunosuppressants can affect TGF-β1/Smad signal pathway in VSMC, CsA and FK506 can up-regulate the expression of Smad2 and down-regulate Smad7 expression in VSMC, and cause the overexpression of TGF-β1. This will contribute to atherosclerosis. However, MMF and Rapa have a protective role in VSMC compared with CsA and FK506.

**PO-126**

**EXPRESSION OF FRACTALKINE, CX3CR1 AND VASCULAR ENDOTHELIAL GROWTH FACTOR IN HUMAN CHRONIC REJECTION GRAFT REJECTION**

Guihu Cao, Yiping Lu, Rui Gao, Yupeng Xin, Donghai Teng, Jia Wang, Youping Li, Transplantation Institute, West China Hospital, Sichuan University, Chengdu, Sichuan, China.

**Aim:** Fractalkine, as a unique chemokine, can induce both adhesion and migration of leucocytes. Fractalkine receptor (CX3CR1) mostly expressed in CD16+CD56+CD14, undergoes efficient binding to fractalkine-expressing cells and transendothelial migration in response to fractalkine. Fractalkine/CX3CR1 system may contribute to the pathogenesis of vascular and tissue chronic renal allograft rejection, VEGF is an endothelium protein produced largely by epithelial cells, myocytes, and macrophages, increased expression in inflammation and vasculopathy. This study is to comprehend the location of fractalkine/CX3CR1 and VEGF, first to investigate the relationship between fractalkine/CX3CR1 and VEGF in human chronic renal allograft rejection.

**Methods:** Renal biopsy tissue from 10 patients with chronic rejection was examined for fractalkine/CX3CR1 and VEGF protein by immunohistochemistry, and compared to patients with hyper acute rejection (N=10), acute rejection (N=10), and normal kidneys (N=10).

**Results:** Immunohistochemistry revealed that fractalkine/CX3CR1 is mostly expressed in tubulointerstitium, occasional in glomeruli, tubular epithelial and vascular endothelial cells in the chronic rejection group, VEGF is up-regulated mainly in the interstitial and perivascular components. There was increased expression of fractalkine/CX3CR1 and VEGF protein in the interstitial (P<0.05). VEGF co-localized with the expression of fractalkine/CX3CR1.

**Conclusion:** Fractalkine/CX3CR1 system and the relationship between fractalkine/CX3CR1 and VEGF in chronic rejection may play an important role in the development of interstitial fibrosis via mononuclear cell-induced cytokine production and myofibroblast stimulation. Further studies are necessary to identify the role of fractalkine/CX3CR1 and VEGF in the pathogenesis of chronic rejection.

**PO-127**

**COMPARISON OF CsA VS MMF ON EXPRESSION OF FRACTALKINE AND CX3CR1 IN CAN**

Guihu Cao, Yiping Lu, Rui Gao, Yupeng Xin, Donghai Teng, Jia Wang, Youping Li, Transplantation Institute, West China Hospital, Sichuan University, Chengdu, Sichuan, China.

**Aim:** This study is to investigate whether there is difference between CsA and MMF on affecting expression of Fractalkine/CX3CR1 in CAN.

**Methods:** The SDWistar rat accelerated kidney sclerosis model was performed following the procedure of Kamada with our modification. Before the transplantation, the kidney was preserved one hour in 0.4°C heparin sodium chloride solution for reinforcement of the injury of cold ischemia. The recipients were divided into three oral treatment groups (each group n=8): Group A, control group (CsA 10mg/kgd10 followed by vehicle), Group B, CsA 6 mg/kgd, Group C, MMF20 mg/kgd. Pathological changes according to Barff Standards were observed at the 4th, 8th and 12th weeks post-transplantation. The immunohistochemistry and real-time fluorescence quantitative PCR, were used to comprehend localization and expression of Fractalkine/CX3CR1 in the graft.

**Results:** The expression of Fractalkine/CX3CR1 in grafted kidneys is significantly lower in mycophenolate mofetil group than that in CsA and in control groups (P<0.05). There is no significant difference between CsA group and control group. Immunohistochemistry revealed that fractalkine/CX3CR1 is mostly expressed in tubulointerstitium, occasional in glomeruli, tubular epithelial and vascular endothelial cells.

**Conclusion:** Fractalkine/CX3CR1 may play an important role in the development of interstitial fibrosis in CAN. Different immunosuppressants have different effect on the expression of the Fractalkine/CX3CR1. Further studies are necessary to identify the role of fractalkine/CX3CR1 in the pathogenesis of CAN and the mechanisms of different immunosuppressants influence the expression of the Fractalkine/CX3CR1.

**PO-128**

**THE EFFECTS OF DIFFERENT IMMUNOSUPPRESSANTS ON CAN BY AFFECTING THE TGF-b AND Smads SIGNAL PATHWAY**

Rui Gao, Yiping Lu, Yupeng Xin, Xihui Zhang, Jia Wang, Youping Li, Transplantation Institute, West China Hospital, Sichuan University, Chengdu, Sichuan, China.

**Objective:** To investigate the effect of different immunosuppressants on CAN by affecting TGF-β and Smads Signal Pathway.

**Methods:** Vascular smooth muscle cell (VSMC) from rat aorta were incubated with different immunosuppressants (CsA 3mg/ml, FK506 1mg/ml, MMF 0.3mg/ml, Rapa 10mg/ml, CsA 1mg/ml+ MMF 0.3mg/ml), respectively for 6 or 12 hours. The rats were divided into 8 groups (each group n=8): Group A, psudo-OP; Group B, isotransplantation; Group C, CsA 6 mg/kgd; Group D, FK506 0.15 mg/kgd; Group E, MMF20 mg/kgd; Group F, Rapa 0.8 mg/kgd; Group G, CsA 3 mg/kgd; Group H, MMF 20 mg/kgd. The immunohistochemistry and real-time fluorescence quantitative polymerase chain reaction, (FO-PCR) were used to comprehend localization and expression of TGF-1 and Smad2, 3, 7 in VSMC and in the transplant kidney.

**Results:** MMF and Rapa could down-regulate the gene expression and protein production of TGF-β1, Smad2, 3 and up-regulate expression of Smad7. There is no significant difference between CsA group and FK506 group, as well as MMF group and Rapa group. The result in the group treated by CsA +MMF was similar to MMF and Rapa group.

**Conclusion:** Our study suggests that different immunosuppressants can affect TGF-1 and Smads Signal Pathway in a Rat VSMC and kidney graft differently. CsA and FK506 can cause CAN, owning to up-regulate the expression of Smad2 and smad3, and down-regulate smad7 expression. MMF and Rapa can prevent the progression of CAN because of down-regulating expression of smad2 and smad3, and increase smad7 production.
2002 to June 2004 were eligible for entry. After an overnight fast, patients participated in a single 1g dose of MMF PK study before renal transplantation. Then the patients received kidney transplantation and taken 1g MMF twice a day. On the 12th day post-operation, at 0.5, 1, 1.5, 2, 2.5, 4, 6, 8, 10, 12h after MMF administration, 4ml blood was drawn and concentration of MMF and MPAG was simultaneously measured by RP-HPLC using gradient elution.

**Results:** (1) The PK of MPA,MPAG showed that the MPA plasma concentration-time profiles were fitted as a two compartment open model and the MPAG plasma concentration-time profiles were fitted as a single compartment open model with a linear kinetic absorption.

(2) The parent drug MMF was undetectable in plasma during oral administration, confirming the rapid conversion of MMF to MPA. In mean MPA concentration-time curve after single and multiple dose, a secondary peak occurred for MPAG during 610 h, attributed to entero-hepatic recirculation.

(3) There was significant variation of MPA plasma concentration-time data among subjects, in either single dose study or multiple dose study. It is noticed that the therapeutic plan (1g oral MMF, twice a day), which is adopted popularly in clinical therapy, doesn't emphasize on the individual variation among patients. It is suggested that TDM should be applied in dosage optimization.

**PO-130 CYCLIC AMP PROTECTS STEM CELL (CD34+) APOPTOSIS**

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We have previously demonstrated that a CAMP-elevating agent such as prostacyclin (PGI2) inhibits nitric oxide (NO)-induced megakaryocyte apoptosis through a CAMP-dependent pathway. We have now investigated CAMP effect on stem cell (CD34+) survival. CD34+ cells were isolated from human cord blood by positive magnetic immunoselection (95% of purity). Apoptosis was triggered by two different stimuli: serum deprivation (SD) or exposing cells to the NO donor, PAPA/NO (100 µM). Cell death was evaluated 24 h later by detection of apoptosis/necrosis using fluorescence microscopy and identification of hypodiploid cells by flow cytometry. Results showed that PGI2 (3-30 µM) failed to protect CD34+ cell death (C: 4 ± 1%, SD: 26 ± 3%, PGI2+SD: 27 ± 1%, p<0.05 vs SD, &p<0.001). Nevertheless proliferation was reduced in RT on MMF (353.7 ± 217.7 vs. 395.3 ± 243.9, p = 0.454). Corticosteroids did not influence the concentration and proliferation of EPCs.

**PO-131 THE DONOR RISK FACTOR BRAIN DEATH EFFECTS SIGNIFICANTLY WITH TOLERANCE INDUCING PROTOCOLS**

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We have previously demonstrated that a CAMP-elevating agent such as prostacyclin (PGI2) inhibits nitric oxide (NO)-induced megakaryocyte apoptosis through a CAMP-dependent pathway. We have now investigated CAMP effect on stem cell (CD34+) survival. CD34+ cells were isolated from human cord blood by positive magnetic immunoselection (95% of purity). Apoptosis was triggered by two different stimuli: serum deprivation (SD) or exposing cells to the NO donor, PAPA/NO (100 µM). Cell death was evaluated 24 h later by detection of apoptosis/necrosis using fluorescence microscopy and identification of hypodiploid cells by flow cytometry. Results showed that PGI2 (3-30 µM) failed to protect CD34+ cell death (C: 4 ± 1%, SD: 26 ± 3%, PGI2+SD: 27 ± 1%, p<0.05 vs SD, &p<0.001). Nevertheless proliferation was reduced in RT on MMF (353.7 ± 217.7 vs. 395.3 ± 243.9, p = 0.454). Corticosteroids did not influence the concentration and proliferation of EPCs.

Impaired renal function may be a potent inhibitor factor of the cardiovascular repair mechanisms in RT patients by reduction of EPCs concentration, proliferation, differentiation and adhesion. Immunosuppressive therapy may have an additional deleterious effect in inhibiting EPCs proliferation.

Our data demonstrate that the risk factor donor BD influences tolerance induction. These results stress the importance of donor treatment as a potential approach to diminish organ injury before transplantation.
Cyclosporin A does not interfere with steroid-induced apoptosis of allointegen-activated T lymphocytes

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Background: Cyclosporin A (CsA) has been reported to have diverse biological effects besides the inhibition of interleukin-2 (IL-2) production in T cells. This study investigated the influence of CsA on methylprednisolone (MP)-induced apoptosis of allointegen-activated T cells.

Materials and Methods: The allointegen-activated T cells were obtained from the mixed lymphocytes culture (MLC) following 7 days of the culture. The MLC cells were incubated further for 24 hours in the presence or the absence of MP. The DNA fragmentation of the cells was assessed using diphthamide assay. Caspase activity and mitochondrial membrane potential were also evaluated with fluorogenic substrates and JC-1 staining, respectively.

Results: The DNA fragmentation of the 7-day MLC cells without any induc- tion was 24.4%. MP (5 μM) augmented DNA fragmentation up to 32.1%. The addition of CsA at the concentration of 100 nM, optimal in inhibiting the pro- liferation, at the beginning of the MLC inhibited apoptosis both with and with- out MP. The simultaneous administration of reconstituent IL-2 (10 IU/ml) with CsA restored significantly DNA fragmentation. Pretreatment with CsA did not cause any effect on DNA fragmentation, while IL-2 inhibited apoptosis of the MLC cells. CsA affected neither the enzyme activity of caspase-3, 8, or 9, nor JC-1 staining of the cells.

Conclusion: CsA suppressed the sensitivity to apoptosis when added at the beginning of the MLC, but did not interfere with the apoptosis induced by MP once T cells were activated with allointegens.

PO-135 TOLERANCE INDUCTION THROUGH SIMULTANEOUS DOUBLE BONE MARROW TRANSPLANTATION WITH TWO-SIGNAL BLOCKADE

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Purpose: There are difficulties in clinical application of tolerogenic strategy due to the shortage of bone marrow cells (BMCs) and organs from the same donors. We determined whether two different kinds of BMCs from allogeneic donors would be simultaneously engrafted and lead to induction of double chimerism-based tolerance to fully MHC-mismatched skin allograft in the recipi- ents treated with Busulfan conditioning and the two signal blockade.

Materials: BMCs from BLA/c (H-2d) and CBA mice (H-2k) were transplanted simultane- ously to recipient C57BL/6 mice (H-2d). Establishment and characteristics of double chimerism were determined and induction of donor-specific tolerance was evaluated by transplant of skin from two donors and third-party DBA mice (H-2k). In addition, proliferating activities were assessed in MLR assay.

Results: Both haplotypes (H-2d and H-2k) of BMCs could be engrafted and lead to double chimerism in the recipients treated with two-signal blockade. Higher (P < 0.05) levels of H-2d type of lymphoid and myeloid lineage cells existed in the primary and secondary immune organs compared with those of H-2k type cells. Double chimeric recipients showed induction of donor-specific tolerance to skin allograft (MST > 100 days) and lower allogeneic responses of splenocytes than non-chimeria.

Conclusions: Transplantation of two different kinds of BMCs with two-signal blockade was effective in induction of double chimerism-based tolerance to skin allograft. Therefore, the effectiveness of this tolerogenic protocol might suggest the potential to help solving problems in donor shortage and to de- velop a robust strategy for tolerance induction in allogeneic transplantation.

PO-136 TWO-SIGNAL BLOCKADE WITH ANTI-CD45RB AND ANTI-CD154 MONOCLONAL ANTIBODIES IS ACCOMPANIED BY CD4-DEPENDENT MECHANISM IN ALLOGENEIC SKIN TRANSPLANTATION

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Introduction: Allograft survival is prolonged by targeting T cell activation sig- nals 1 and 2 with combination of anti-CD45RB and anti-CD154 monoclonal an- tibodies. We performed studies on the effects of two-signal blockade on CD4 or CD8 T cells in a murine skin allograft model. Materials: C57BL/6 recipients of BALB/c skin allograft were treated with anti-CD45RB and anti-CD154 alone and their combinations. For depletion of CD4 or CD8 T cells, the recipients received CD4-depleting or CD8-depleting mAb. Proportion of splenocyte-derived naïve/effector and IFN-γ-secreting CD4 or CD8 T cells and phenotyped regu- latory T cells (Treg) were assessed.

Results: Anti-CD45RB, anti-CD154 plus CD4-depleting mAb-treated group showed acute rejection of skin allograft in contrast to CD8-depleting group treated with two-signal blockade. In the group treated with the two-signal blockade, the proportions of CD4+ T cells, especially CD4+CD25+ and CD4+CD45RBhigh Treg, were increased while those of CD62Llow and IFN-γ-secreting effector CD8+ T cells were decreased when compared with non- treated group. The expression of CD8+ CTLA-4 was up-regulated by the two- signal blockade. In contrast, CD4-depleting group treated with the two-signal blockade showed increased proportions of CD62Lhigh and IFN-γ-secreting ef- fector CD8+ T cells and decrease in expression of CD8+ CTLA-4.

Conclusion: The enhancement of allograft survival resulted in increased pro- portions of Treg and decreased proportions of effector CD8+ T cells. The two- signal blockade is accompanied by CD4-dependent mechanisms in allogeneic skin transplantation.

PO-137 COMBINATION OF MRP 8/14 COMPLEX AND PCT FOR RELIABLE MARKER OF DIFFERENTIAL DIAGNOSIS BETWEEN REJECTION AND INFECTION IN TRANSPLANTATION

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Purpose: Procalcitonin (PCT) is a highly specific analysis that shows signifi- cant diagnostic validities when non-viral infections are compared with rejection episodes. Myeloid-related protein (MRP) 8 and MRP 14 may be considered as an early and highly specific marker for acute allograft rejection. We investi- gated the usefulness of MRP8/14 complex and PCT for discrimination between rejection and systemic bacterial infection in transplant patients.

Materials: Specimens obtained from transplant patients for 7 days were grouped according to biopsy-proven rejection (n = 14), bacterial (n = 8), or viral (n = 15), infection, or surgical complications (n = 8). As a control, specimens was also obtained from healthy subjects (n = 35). Results: The serum levels of MRP and PCT were below the cutoff in healthy subjects. A significant increase in serum levels occurred in response to bacterial infection (16.4 ± 10.37ng/ml of MRP8/14; 2.4 ± 2.98 ng/ml of PCT). The serum levels of PCT remained low in the presence of kidney allograft rejection whereas MRP 8/14 levels were in- creased (p < 0.01). In the patients with viral infection and surgical complication, the basal serum MRP 8/14 and PCT levels were not changed.

Conclusion: It is concluded that combination of MRP 8/14 complex and PCT is a sensitive and specific method to diagnose between rejection (increased MRP 8/14 with normal PCT), systemic bacterial infection (increase in both parameters) and viral infection (Normal MRP 8/14 with normal PCT).

PO-138 TOLERANCE INDUCTION THROUGH MEGA DOSE BONE MARROW TRANSPLANTATION WITH TWO-SIGNAL BLOCKADE

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Purpose: The toxicity of the required host conditioning may make current clinical protocols for allogeneic bone marrow transplantation (BMT) unsuitable for ap- plication in organ transplant recipients. We explored tolerogenic effectiveness of mega dose BMT with anti-CD45RB and anti-CD154 mAb (two-signal block- ade) in murine recipients without conditioning. Methods/Materials: Recipient B6 mice of skin allograft received Busulfan conditioning and an optimal dose (2 × 107 cells) of BMT. For a mega dose of BMT model, the conditioning was not performed; instead, mega dose (2 × 107 cells) of bone marrow was trans- planted to the recipients. The recipients were then treated with anti-CD45RB mAb and anti-CD154 mAb alone or their combination. We analyzed the de- gree and distribution of donor-derived cells and peripheral deletion of donor- reactive T cells. Induction of chimerism-based tolerance to skin allograft was further determined.

Results: High levels of mixed and multilineage chimerism-based tolerance was induced in the recipients (91%) treated with the optimal dose BMT, show- ing peripheral deletion of alloreactive T cells in a stable long-term chimerism. Such chimerism that was detected in all lineage and distributed in all lymphoid organ could induce donor-specific tolerance to skin allograft.

Conclusion: The mega dose BMT with two-signal blockade could effectively establish multilineage and mixed chimerism and induce donor-specific toler-
POTENTIAL REGULATORY CELL ACTIVITY OF RAT ANERGIC LYMPHOCYTES GENERATED BY BLOCKING CD28 AND ICOS PATHWAYS IN VITRO

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Background: Regulatory lymphocytes may play a pivotal role in inducing and maintaining transplantation tolerance. We investigated the mechanism of anergic lymphocytes with regulatory cell potential generated in vitro by ICOS and CD28 co-stimulatory blockades as a source of cellular therapy for treating allograft rejection.

Materials and Methods: Anergic lymphocytes were generated by a mixed lymphocyte reaction (MLR) consisting of DA splenocytes as the stimulator and Lewis spleenocytes as the responder in the presence of anti-ICOS mAb and CD28 mAb. Immunoregulatory effects of these lymphocytes were evaluated by secondary MLR and using various other stimulations. DA heart was transplanted into 75 Gy-irradiated rat without intravenous administration of these cells or Lewis spleen lymphocytes.

Results: We observed that these lymphocytes were not anergic to alloantigens and polyclonal stimulations but also exhibited regulative activity to inhibit the allo-reactive T-cell response. Our adoptive transfer studies revealed that irradiated recipients that received both regulatory lymphocytes and naive Lewis lymphocytes had significantly prolonged DA cardiac graft survival compared with a group that received Lewis lymphocytes alone. Furthermore, some of the recipients accepted the graft indefinitely after receiving anergic lymphocytes alone.

Conclusions: These results demonstrated that regulatory lymphocytes can be generated through blocking co-stimulatory signals, CD28 and ICOS, simultaneously in vitro, and may advance a new immunomodulatory strategy for preventing allo-rejection in organ transplantation.

IMMUNE TOLERANCE INDUCED BY SEB FOR TREATING HIGH-RISK KERATOPLASTY REJECTION

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Immune rejection is the main reason leading to allograft failure after corneal transplantation, especially under high-risk status. SEB, the bacteria-derived superantigen, which is able to induce T cells deletion and anergy, was confirmed to prolong rat corneal grafts survival in our prior experiments. The SEB could also reduce CD4+ and CD8+ lymphocytes infiltration in the corneal grafts and the lymphatic organs. The lymphocyte proliferation ability was also inhibited. The ELISA results showed the concentration of IL-10 rising but IL-2 reducing in the rat serum of groups SEB treated. Recently, we had found that the DTH (delayed-type hypersensitivity) reactivity of rats could be inhibited by SEB from 84.6±10−3 mm to 12.5±10−3 mm at the tenth day after keratoplasty. The immunoregulatory cytokines produced by regulatory T cells in corneal grafts and aequous humor had been changed from balance between T helper 1 (Th1) and Th2 cells to express Th2 cytokines, such as IL-4, IL-5, IL-10, but IFN-γ and TNF-α express declined. So we concluded that peripheral tolerance induced by SEB is associated with immunoregulatory cytokine and can be used for treating rat high-risk corneal transplantation rejection.

ROLE OF FK778 ALONE OR IN COMBINATION WITH TACROLIMUS OR mTOR-INHIBITORS AS IMMUNOMODULATOR ON IMMUNO FUNCTIONS: IN VITRO EVALUATION OF T-CELL PROLIFERATION AND THE EXPRESSION OF LYMPHOCYTE-SURFACE ANTIGENS

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Purpose/Methods: The aims of this study are: to evaluate the in vitro capacity of FK778, alone or in combination with others immunosuppressive drugs (Tacrolimus: TRL, Sirolimus: SRL, Everolimus: EVL), to inhibit the proliferation of T-lymphocytes and the expression of lymphocyte surface antigens; and to compare the immunosuppressive potential of FK778 combined with TRL+SRL or EVL in comparison with the same combinations based in Mycophenolic acid (MPA) as antimetabolite. The lymphocyte proliferation assay was assessed by多少钱 (H)Thymidine incorporation, in whole blood cultures. The effect of FK778 over the alloresponse was evaluated by mixed lymphocyte culture and the expression of lymphocyte antigens by flow cytometry.

Results: FK778, TRL+SRL and EVL showed a high in vitro capacity to inhibit the lymphocyte proliferation. When FK778 was combined with TRL+SRL, or EVL an additive effect was observed, especially in the FK778+TRL+EV combination. The similar capacity to inhibit the proliferation was observed, when FK778 was combined with TRL, SRL or EVL, respect the same combinations but using FK778 alone.
MYOCARDIAL CCL-19 EXPRESSION AFFECTS CD8 T-CELL RECIRCULATION DURING ACUTE HUMAN CARDIAC ALLOGRAFT REJECTION

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Inflammatory and lymphoid chemokines (CXs) and their receptors (CRks) contribute differentially to T-cell homing after heart transplantation (post-HTx). We investigated circulating T-cell subset CK expression and intragraft CKR and CK mRNA levels in relation to acute rejection (AR). Twenty cardiac allograft recipients under triple maintenance immunosuppression were studied prospectively in a 9-month follow-up post-HTx. At the time of routine myocardial biopsies, CCR5 and CCR7 expression on peripheral blood CD4+ and CD8+ T-cells was measured by flow-cytometry. Intra- and inter-study differences in the %CCR5+ cells or %CCR7+ cells were found: %CCR5+ cells were higher during AR+ compared to AR- (p<0.05 and p<0.01) and in AR+ compared to AR- (p<0.01). In AR+ a 2- and 3.5-fold increase in CCR5+ cells or CCR7+ cells was found compared to time-points before AR+ (p<0.05 and p<0.01, respectively). Mean myocardial CCL5 and CCL19, but not CCL21 mRNA levels, increased significantly (2- and 3-fold) compared to time-points before AR+. Mean myocardial CCL5 and CCL19, but not CCL21 mRNA levels, increased significantly (2- and 3-fold) during AR+ (p<0.05 and p<0.01) compared to AR-. During AR+, intragraft CCR5 and CCR7 mRNA levels increased 2- and 3.5-fold compared to time-points before AR+. Rejection patients had higher myocardial CCR5 (p<0.01) and CCR19 (p<0.05) mRNA levels before AR+. Increased myocardial CCL19 expression represents a novel aspect of acute allograft rejection. Increased myocardium chemokine production may affect CD8 T-cell recirculation post-HTx, under the influence of homeostatic receptor CCR7.

PO-144

INDUCTION OF IMMUNOLOGICAL TOLERANCE AND GEROPROTECTIVE EFFECTS BY ALLOTRANSPLANTATION OF EMBRYONIC PLURIPOTENT PROGENITOR CELLS (EPPC) IN RATS AND MICE

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Introduction: It has been studied the probability of survival; reproductive function and reaction for skin and spleen allotransplantation after EPPC administration in mega doses into old males of rat and mice to examine the basic positions of the theory of organism stem spaces depletion, as a basis for mammalian organism aging.

Methods: In the process of aging in the experiment dynamic is determined. Reproductive function of old males was studied in biological experiment. There have been studied histological changes in testes, prostate gland and seminal vesicles with determination of testosterone level in blood. Results of skin and spleen allotransplantation were estimated by the grafts engraftment.

Results: EPPC administration in mega doses facilitates allograft engraftment that accompanies with external effect of animal rejuvenation, extension of span life, increase in sexual activity and enlargement of spermatogones amount in testes of old males.

Conclusion: Allograft transplantation of EPPC in mega doses induces the central immunological tolerance and extends stem spaces of organism that increases the life span of old rats and restores their reproductive function.

PO-145

IMMUNOSUPPRESSIVE DRUGS INHIBIT THE DEVELOPMENT OF CD4+CD25+CTLA4+ CELLS IN MLR

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In the last decade it has become clear that regulatory T(Reg) cells play a pivotal role in immune regulation through their control of T cell responses. Attention has focused in particular on a certain subset of CD4+ T cells that can be identified by their receptors constitutive expression of CD25 and CTLA-4. The balance between CD4+CD25+CTLA4+ cells and inflammatory cells will determine whether an immune response occurs. Upon transplantation strong inflammatory signals are induced in the recipient, which need to be controlled through the administration of immunosuppressive drugs. The global effect of immunosuppressive drugs on the immune system predisposes a patient to the development of infection and cancer and may have a deleterious long-term effect on graft function.

The aim of this study was to evaluate the influence of immunosuppressive drugs cyclosporin A, rapamycin on the generation of CD4+CD25+CTLA4+ regulatory T(Reg) cells in vitro (MLR). MNC were isolated from peripheral blood of healthy donors and activated in MLR in the presence of both cyclosporin A and rapamycin or single drug. After six days the cells were labeled with monoclonal antibodies. Immunosuppressive drugs prevents graft rejection, but also blocks induction of transplantation tolerance. We observed that immunosuppressive drugs cyclosporin A or rapamycin have decreased the percentage of CD4+CD25+CTLA4+ cells in vitro. The addition of both drugs enhanced the inhibition effect on CD4+CD25+CTLA4+ generation. The important was also the time when drugs was added to the cultures. The investigation and characterization of new features of regulatory T cells throw light on the mechanism of tolerance induction.

PO-147

A STUDY ON CYTOKINES AND LYMPHOCYTE POPULATIONS IN PERIPHERAL BLOOD IN LIVER TRANSPLANT PATIENTS DURING WITHDRAWAL OF IMMUNOSUPPRESSION

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Objectives: To analyze prospectively lymphocyte cell and cytokine profiles in the peripheral blood of patients undergoing withdrawal of immunosuppression (IS).

Patients and Methods: 8 Liver Transplantation patients with more than 2 years survival who were treated with cyclosporine (Cy) and underwent controlled withdrawal of IS were studied. Levels of IL-2, IL-10 and lymphocyte populations studied in peripheral blood are not predictive of patient response to withdrawal of IS. IL-2 levels and lymphocyte populations (CD3, CD4, CD4+CD28+ and CD8+CD28+) in peripheral blood were analyzed at baseline and monthly thereafter.

Results: Complete withdrawal of IS was possible in 3 patients (follow-up period of 36±0.8 months). In the 5 patients in whom withdrawal of IS could not be completed, 3 had portal infiltration and 2 had acute rejection. In patients who tolerated withdrawal of IS, IL-2 levels decreased during the period of withdrawal of IS (99.2 versus 59 pg/ml), whereas in patients who did not tolerate withdrawal of IS, IL-2 levels increased (33 versus 114 pg/ml). IL-10 levels increased in a higher proportion in tolerant patients (32 versus 65 pg/ml) than in non tolerant patients (32 versus 39 pg/ml). No significant changes were observed in the lymphocyte cell populations.

Conclusion: Withdrawal of IS is possible in some LT patients without the occurrence of rejection. IL-2 levels decrease and IL-10 levels increase during the period of tolerance after withdrawal of immunosuppression in LT patients. The lymphocyte populations studied in peripheral blood are not predictive of patient response to withdrawal of immunosuppression.

PO-148

ACUTE REJECTION DERIVED CA2+ INFLUX IN T CELL OF SKIN TRANSPLANTATION RAT

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Background: T cell activation and the Ca2+ concentration in the T cell are responsible for acute rejection in organ transplantation. Although it was reported that the elevation of Ca2+ concentration was attributable to a Ca2+ release from endoplasmic reticulum caused by T cell activation, a lot of researchers recently showed that the Ca2+ release-activated Ca2+ channel activation was caused by the elevation of a cytosolic free Ca2+ concentration.

Method: Skin transplantation rats were prepared in homoplastic group (Lewis-Lewis; LL group) and heteroplastic group (BN-Lewis; BL group). After transplantation, the rejection response was observed by histopathological examination. We collected T cell from spleens of transplantation rats at 2 and 5 days after transplantation. Ca2+ influxes in collected T cells were measured using radioactive 45Ca with and without BN rat antigen presented Lewis rat macrophages.

Results: From the histopathological results, we observed that the acute rejection was found 5 days after transplantation in BL group. On the other hand, Ca2+ influx was increased 2 days after transplantation in LL group. The rats in LL group were histopathologically and Ca-physiologically unchanged.
Summary: The elevation of Ca2+ influx in the T cell appeared at an early stage from histopathological observations in rat acute rejection model. This suggested that Ca2+ influx in T cell could be the early detection index of an acute rejection.

PO-149 ADMINISTRATION OF FTY720 INHIBITS TUMOR GROWTH IN VIVO AND DEMONSTRATES A STRONG ANTI-ANGIOGENIC EFFECT IN VITRO

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Aims: Tumor recurrence or de novo tumor development is one of the major fears of long term immunosuppression after organ transplantation. FTY720 is a unique immunosuppressant that induces apoptosis in activated lymphocytes, reduces numbers of lymphocytes in peripheral blood, and prevents infiltration of lymphocytes into allografts. Recently, FTY was shown to prevent tumor growth and metastasis. In this study we examined the efficacy of FTY720 in inhibiting tumor growth and angiogenesis.

Methods: To evaluate the effect of FTY720 on tumor growth 10th Lewis Lung Carcinoma (LLC1) cells were injected subcutaneously in the back of syngenic C57BL/6 mice. After establishment of a palpable tumor animals were treated with 1) saline, 2) FTY720 (1 mg/kg/d), 3) FTY720 (5 mg/kg/d) or 4) FTY720 (10 mg/kg/d). The anti-angiogenic properties of FTY720 were tested in a human umbilical vein endothelial cell (HUVEC) spheroid model.

Results: FTY720 significantly inhibited subcutaneous tumor growth in a dose-dependent fashion. On day 35 control animals showed a tumor volume of 1113±165 mm3, compared to FTY720 1 mg/kg/d 856±130 mm3, FTY720 5 mg/kg/d 688±151 mm3 and FTY720 10 mg/kg/d 520±143 mm3. Interestingly, FTY720 showed a strong in vitro antiangiogenic effect. The vascular sprouting of VEGF-stimulated HUVEC spheroids was significantly inhibited at concentrations as low as 1 nM and was completely inhibited at 10 nM.

Conclusions: FTY720 revealed strong anti-angiogenic activities in vitro and a substantial anti-tumor effect in vivo. Following organ transplantation a combination of FTY720 with an mTOR-inhibitor may proof to be useful to prevent tumor development or progression in high-risk patients.

PO-150 PERFUSION WITH MITOMYCIN C (MMC) CONTAINING SOLUTION PROLONGS HEART ALLOGRAFT SURVIVAL IN RATS

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Purpose: MMC is an agent which inhibits protein synthesis. We study the effect of rat heart allograft perfusion with MMC-containing solution on transplant survival and its mechanism of action.

Methods: (a) Hearts were perfused with Ringer solution without (control) or with MMC and transplanted into LEW rats. Recipients were injected intraperitoneally 1 week before with 106 BN dendritic cells (DCs). (b) Rat endothelial cells (ECs) or DCs were incubated in medium with MMC, washed, kept in culture for 24 hrs and analyzed by FACS. (c) MMC-treated DCs were incubated with allogeneic T cells and proliferation was measured.

Results: Heart perfusion with MMC-solution significantly prolonged graft survival (14±5.8 vs. 6.3±0.4 days = control). Two types of cells play a crucial role in graft rejection: DCs, the most immunogenic cell subpopulation among "passenger leucocytes", and ECs, the primary target of rejection. To clarify the mechanism by which MMC prolongs graft survival, we analyzed its action on DCs and ECs. FACS analyses showed that MMC treatment leads to downregulation of CD80, CD86 and ICAM-1 on DCs, whereas other molecules were unaffected. In contrast ECs, which weakly express these molecules, showed only reduced CD80 expression. The T-cell stimulatory capacity "in vitro" of allogeneic MMC-DCs was dramatically reduced; the same effect was obtained when DCs were preincubated with antibodies to CD80, CD86 and ICAM-1. Injection of donor MMC-DCs into the recipient prolonged graft survival (30±2 days vs 6±1 days after naive DCs injection).

Conclusion: Heart perfusion with MMC solution prolonged the graft survival. We speculate that this effect is mediated by downregulation of immunostimulatory molecules on immunogenic donor cells.

PO-151 ASSESSMENT OF VARIATION IN EPSTEIN BARR VIRUS SPECIFIC CYTOTOXIC T CELLS FOLLOWING TRANSPLANTATION USING MHC CLASS I-PEPTIDE COMPLEXES

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Cytotoxic T cells play an important role in viral immunity. This study was performed to evaluate the use of dextramer complexes to assess changes in the number of CD8+ T cells specific for Epstein Barr virus (EBV-CTL) following renal transplantation.

Methods: Twenty transplant and ten controls were studied on days 0, 7, 14 and 90. A range of APC-labelled class I-dextramer -peptide complexes was used to detect CD8+ T-cells specific for EBV-derived peptides. Whole blood-lyse-no wash staining method with 4-colour flow cytometry was used. A real time PCR was performed on DNA from whole blood to quantify EBV load.

Results: Within 7 days of transplantation there was a significant increase in absolute number and proportion of EBV-specific CD8+ T cells in patients who received EBV+ grafts compared with EBV- grafts.

Conclusion: Immediately post transplant there is a consistent rise in the EBV-specific CD8+ cells. A rise in EBV load post-transplant implies that the increase in EBV-specific CD8+ cells is in response to specific stimuli with intact immune surveillance. Inadequate immune response might predispose patients to development of PTLD.

PO-152 DEVELOPMENT OF A NOVEL METHOD OF EXPANDING FOXP3+CD25+CD4+ REGULATORY T CELLS ISOLATED FROM A LIVING DONOR LIVER TRANSPLANTATION RECIPIENT

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Although the existence of a "CD45RA+CD25+CD4" regulatory T cells (Treg) population has been reported, we recently confirmed that "CD45RA+CD25+CD4" but not "CD45RA-CD25-CD4" fraction acquires and retains regulatory activity after ex vivo expansion with allo-antigen stimulation. In this communication, we describe a novel modality of expanding Tregs ex vivo of living-donor liver transplantation (LDLT) recipients in a donor antigen-specific manner.

Methods: Recipient abdominal blood was collected by reservoir during removal of the native liver and "CD45RA+CD25+CD4" cells were purified by cell sorter,as a distinct population from "CD45RA-CD25-CD4" cells. Effluvients flushed out from hepatic graft were recovered to obtain donor antigens presenting cells (APCs). Cells from a 51y old female recipient with primary biliary cirrhosis were stimulated by irradiated donor APCs every 7 to 10 days in the presence of IL-2.

Results: 2600ml abdominal blood was obtained. 2.4±106 mononuclear cells were collected and 1.6±106 "CD45RA+CD25+CD4" cells were purified. Real time PCR revealed high expression of Foxp3 in this fraction. Co-culture of this fraction with donor APCs increased the cell number by approximately 100 folds for 50 days,MLR suppression assay showed that ex vivo expanded cells retained high regulatory activity to the donor antigen but not to 3rd party.

Conclusion: 1)Abundantly purified "CD45RA+CD25+CD4" cells from LDLT recipient successfully expanded ex vivo and retained regulatory property in a donor antigen specific manner.2)This novel modality may endorse feasibility of post-LDLT tolerance induction through adoptive transfer of effective Tregs.

PO-153 HUMAN SPLENIC DENDRITIC CELLS REACT DIFFERENTLY TO BACTERIAL AND ALLOGENIC ANTIGENS

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Toll-like receptors (TLR) on DC are involved in innate response to bacterial infections. It
has been suggested that TLR could respond to microbial and to endogenous substances. Such recognition would be critical for activation of responses to viruses, tumors and to transplants. AIM. To determine of ability bacterial and allogeneic antigens to stimulate DCs.

Methods: DCs were isolated by enzymatic digestion, separation on dense BSA and incubation in culture. The E.coli cells, LPS and bacterial DNA were incubated with DC for 24h. Mixed lymphocytes reaction was performed with DC and allogeneic lymphocytes. Immunohistochemical identification of DC was performed with HLA-DR, CD68, CD83, CD22, CD14 and CD123 mAbs. Expression of receptors was determined by Western-blot with TLR2, TLR3, TLR4, TLR9, CD83, CD123, Hsp60 and Hsp90 mAbs.

Results: In human, CD minimal expression of TLR2, TLR3 and CD123 was found. After incubation with bacteria increase of CD83, TLR3, TLR4 and TLR9 was observed. Treatment with LPS increased expression of TLR3, TLR4, Hsp60 and Hsp90. Stimulation by bacterial DNA resulted in Hsp60 and TLR9 expression. The percentage of HLA-DR+, CD83+ and CD123+ cells increased and the number of CD68+, CD22+ and CD14+ cells decreased in every case. After all stimulation expression of Hsp60 and Hsp90 increased.

Conclusions: The response of human splenic DC to bacterial and allogeneic antigens varies. It is suggested that the complementary effects of bacterial and allogeneic stimulation may increase the intensity of graft rejection.

ENDOTHELIN DIFFERENTLY REGULATES INTERLEUKIN-1 BETA AND INTERLEUKIN-1 RECEPTOR ANTAGONIST EXPRESSION IN NON-CARDIAC ORGANS OF THE HOST DURING CHRONIC CARDIAC ALLOGRAFT REJECTION

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Evidence suggests that systemic immune mechanisms are activated in transplanted organs. Little is known about immune activation in host organs. Endothelin-1 is a vasoconstrictor and growth-inducing peptide, is increased during chronic rejection. In the present study we investigated effects of chronic rejection on protein expression measured by ELISA. Protein levels of interleukin-1 (IL-1) beta and its inhibitor, interleukin-1 receptor antagonist (IL-1ra) in host plasma, liver, and lung during chronic rejection after heterotopic heart transplantation in the absence of immunosuppression using the Fisher/Lewis rat model were assessed. A subgroup of animals was treated with the endothelin receptor antagonist. Cardiac allograft rejection was associated with severe graft arteriolosclerosis and myocardial fibrosis. Circulating levels of IL-1beta and IL-1ra increased significantly. During rejection expression of IL-1beta increased in host liver, while no activation was found in the lung. In non-rejecting control animals, hepatic and pulmonary IL-1ra protein levels were more than 10-fold higher than IL-1beta levels. During rejection, levels of both cytokines increased in lung and liver. Endothelin receptor blockade markedly reduced circulating IL-1ra levels (p<0.05) whereas tissue levels were not significantly affected. Treatment had no effect on the severity of transplant vasculopathy. These data provide first evidence that during chronic rejection in the absence of immunosuppression very distinct proinflammatory activation occurs in the hepato-pulmonary system of the heart. The data further extend that endogenous circulating endothelin-1 receptor system is involved in the activation of cytokines. These findings may be important for the understanding and possibly treatment of tissue injury associated with rejection.

DNA MICROARRAY-BASED GENE EXPRESSION PROFILES OF CMV AND HHV-6 INFECTION IN LIVER TRANSPLANTS

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Purpose: An association between cytomegalovirus (CMV) and allorejection has been suggested. Human herpesvirus-6 (HHV-6), a close relative of CMV, has been described in liver transplantation. The CMV and HHV-6 associated gene expression of inflammatory factors were studied in liver transplants by DNA microarray.

Methods: Expression of inflammatory genes was studied at mRNA level in liver biopsies from patients undergoing CMV (3 patients) or HHV-6 infection (3 patients) and compared with acute rejection (5 patients). The RNAs were isolated and CNA microarray analyses were performed on the human immunochip (4600 sequences). RNA extracted from normal liver was used as control material.

Results: Among upregulated genes in CMV infection were various chemokines, TNF, TGF-β receptor, TNF-R, MHC class II, ICAM-1, IL-2, IL-2Ra, IL-4R, caspases and granzymes A-B. In allorejection most upregulated genes were chemokines, TNF, MHC class II, IFN-γ, caspases, granzymes A-B, IL-2Rβγ, and VCAT-1. Upregulated genes in HHV6 infection were IFN-R, TNF, chemokines, IL-4, IFN-γ, MHC class II, ICAM-2, IL-1, IL-10 and TGF-β. Upregulated genes common for CMV and HHV6 were chemokines, TNF, MCH class II and ICAM-3, Common for CMV and allorejection were glycoprotein A-B, TNF, caspases, MHC class II, IL-2Rβγ, Common HHV-6 and allorejection upregulated genes were TNF, MHC class II, chemokines. In CMV infection but not in HHV6 infection upregulated were ICAM-1 and glycoprotein A-B genes.

Conclusions: Microarray analysis defined different immunological entities of CMV, HHV-6 and allorejection. The differences and similarities of the gene expression profiles may help to understand the intra-graft immunological events.

HUMAN "CD45RA+"CD25"CD4+ T CELLS ACQUIRE TOLEROGenic CHARACTER FOLLOWING CULTURE IN THE PRESENCE OF ALLOANTIGEN

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For cp"CD25"CD4- regulatory T cells (Treg) expanded ex vivo is expected to be useful as cellular therapeutic tool in clinical transplantation. Neverthe- less, no reproducible and successful method exists to retain regulatory activity after ex vivo expansion in human. Treg, in addition to anergic/regulatory property, is characterized by memory phenotypes (CD45RO+,CD28-), while "CD45RA+CD25"CD4+ T cells have been thought to be a distinct entity from Treg.

Methods: "CD45RA"CD25"CD4+ and "CD45RA+CD25"CD4+ (conventional Treg) cells were purified by cell sorter from peripheral blood mononuclear cells (PBMC), respectively. Two different fractions were separately expanded using allogeneic PBMC as a source of an antigen presenting cells (APCs) added every 7 days for 1 month in the presence of IL-2.

Results: "CD45RA+CD25"CD4+ fraction exhibited anergic/suppressive properties while "CD45RA+CD25"CD4+ fraction showed proliferative but not suppressive property in response to allo-antigen. Surprisingly, however, "CD45RA+CD25"CD4+ fraction expressed higher Foxp3 than "CD45RA+CD25"CD4+ fraction. Both fractions expanded ex vivo in the number by 100 folds over 1 month. At the termination of culture, "CD45RA+CD25"CD4+ fraction derived cell line lost regulatory property. In contrast, "CD45RA+CD25"CD4+ fraction derived cell line acquired potent cytokine-specific regulatory property after expansion.

Conclusions: "CD45RA+CD25"CD4+ fraction, albeit having been regarded as a distinct entity from Tregs, expressed high Foxp3 level when purified and acquired potent regulatory property after ex vivo expansion. This may bring about a novel ex vivo Treg expansion strategy with efficiently retained regula- tory property.

INTRAOPERATIVE INTERLEUKIN LEVELS IN LIVER TRANSPLANT RECIPIENTS

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Purpose: To evaluate the levels of several interleukins (IL-2, IL-4, IL-6, IL-10, TNF-α, and IFN-γ) in plasma samples obtained before surgical intervention (T0) and during intra-operative liver transplantation: I-1 (after induction of anesthesia), I-2 (15 min of anhepatic phase), I-3 (5 min before reperfusion), I-4 (10 min after reperfusion), I-5 (20 min after reperfusion), I-6 (60 min after reperfusion), and I-7 (1h after reperfusion) using a FACScan flow cytometer by the CBA technique (Becton Dickinson) which combines an ELISA technique with flow cytometry. Quantitation of each interleukin studied was made using CBA Software provided by Becton-Dickinson.

Results: The study was approved by the local Clinical Research (Ethics) Committee. Written informed consent was obtained from patients' relatives. Fifteen patients (10 men, 5 women) aged 23-61 years, recipients of a liver transplantation were studied. IL-6 and IL-10 reached their maximum levels at I-6. Specifi- cally, each IL-6 enhancement was contributed to by TNF-α and IFN-γ uses. Likewise, IL-2 and IL-4 reached their maximum values at I-6, whereas TNF-α reached its maximum level at I-5 and IFN-γ at I-4.

Conclusion: The enhancement of cytokine production after reperfusion might act triggering the response of other cytokines such as IL-2, IL-4 and IL-6 (inflam- matory) or IL-10 (anti-inflammatory) which reached their maximum values 60 min after reperfusion.
INTRAVENTOUS IMMUNOGLOBULINS TARGET THE ADAPTIVE AND INNATE ARMES OF THE IMMUNE SYSTEM

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The adaptive and innate immune responses, which include T-cells and dendritic cells (DC) respectively, are crucial in acute rejection. To explore the suitability of intravenous immunoglobulins (IVg) as prophylaxis of rejection after organ transplantation, we investigated the effects of IVg versus calcineurin inhibitors (CNI) on these two cell types. T-cells and DC were isolated from blood of healthy individuals by immunomagnetic selection. T-cells were stimulated with phytohemagglutin (PHA) or allogeneic antigen-presenting cells and DC were stimulated with TNFα/L1b, either in absence or presence of IVg or CNI. The influence of tested agents on T-cell and dendritic cell stimulatory capacity was assessed by CFSE-labeling and thus in diminished allo-immune responses.

NKT CELL-DEPENDENT IgM RESPONSE TO THE HUMAN BLOOD GROUP A TRISACCHARIDE: EXPLORING THE ROLE OF Vv14 NKT CELLS IN ABO INCOMPATIBLE TRANSPLANTATION

Wendy Zhou, Hideki Ohdan, Yuka Tanaka, Asahara Toshimasa. Department of Surgery, Graduate School of Hiroshima University, Hiroshima, Japan.

Anti-human blood group Abs are a major barrier in organ transplantation across ABO blood group. This IgM response is believed to require no major histocompatibility complex class II (MHC-II)-restricted recognition by conventional T-cells and thus in diminished allo-immune responses. In conclusion, Vv14 NKT-B cell responses suggest lack of innate response to MHC products. Migrating human DC enriched population both reacted to and stimulated alloimmune responses. Conclusions: There was no increase of TLRs expression on DC after allostimulation what suggests lack of innate response to MHC products. Migrating splenic DC enriched population both reacted to and stimulated alloimmune responses.

PREVENTION OF CARDIAC ALLOGRAFT REJECTION BY 4-AMINO-TETRAHADROBIPERIN: MECHANISTIC INSIGHTS INTO THE IMMUNOSUPPRESSIVE FUNCTION USING cDNA MICROARRAY ANALYSIS

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DNA FROM ORGANO ALLOGRAFTS IN Recipient Tissues

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DNA from organ allografts in recipient tissues 7 days after allogeneic transplantation without immunosuppression and 30 days in recipients treated with Cyclosporin A (CsA) and FK506. Materials: Male BN (RTI14) rats served as donors and female LEW (RTI1A) as recipients. Skin flaps (SK), liver and limb (containing bone marrow) (HM), bone marrow cells (BMC) were transplanted. Results: Median graft survival of untreated hearts was 7.2±0.6days. Graft survival increased with the dose of ABH4 to 12.6±1.1days at 200mg/kg and 50mg/kg ABH4 (survived every Bisurvival 14.9±2.1days) produced results comparable to CsA-treatment (15.0±1.9days). Among 22626 genes surveyed, expression of 58 was reduced by more than 3-fold(containing genes involved in immune response and B-cell activation) in ABH4 treated grafts and expression of 85 genes was increased by more than 2-fold. CD11c-like antigen-presenting cells and DC were stimulated with TNFα/IL1b, either in absence or presence of IVIg or CNI. The influence of tested agents on T-cell and dendritic cell stimulatory capacity was compared to the effect of CNI. Moreover, IVIg-treated DC were not affected by CNI. IVIg functionally inhibited H-thymidine incorporation into proliferating T-cells by 31.15% after PHA stimulation (n=7; p<0.01) and by 71.15% after allogeneic stimulation (n=7; p<0.01). CFSE-labeling revealed less precursor T-cells responding to PHA in the presence of IVIg (8.4±6.7% vs 56.9±7.2%) in control; (p<0.01). IVIg or CNI added after stimulation still hampered clonal expansion. IVIg suppressed the numbers of IFNγ-producing T-cells upon PHA-stimulation (68±24 vs 21±15.5; n=3; p<0.05). The inhibitory effect of IVIg on T-cells was comparable to the effect of CNI. Moreover, IVIg-treated DC were suppressed in their capacity to stimulate allogeneic T-cells by 73±12% (n=6; p<0.01), whereas CD11c-like function was not affected by CNI. IVIg functionally inhibited immune cells of the adaptive and innate arms, i.e. T-cells and DC, while CNI only suppressed T-cells. Considering its favourable safety profile and strong immunosuppressive effect, IVIg may be a potential candidate to replace CNI for prevention of rejection.

DNA FROM ORGANO ALLOGRAFTS IN Recipient Tissues

Waldemar L. Olzewska1, Marek Durlik1,2, Bozenka Interwez1, Aleksandra Domicki1,1, Department of Surgical Research and Transplantology, Medical Research Center, Polish Academy of Sciences, Warsaw, Poland. 2Central Clinical Hospital, Ministry of Internal Affairs, Warsaw, Poland.

DNA from organ allografts in recipient tissues 7 days after allogeneic transplantation without immunosuppression and 30 days in recipients treated with Cyclosporin A (CsA) and FK506. Materials: Male BN (RTI14) rats served as donors and female LEW (RTI1A) as recipients. Skin flaps (SK), liver and limb (containing bone marrow) (HM), bone marrow cells (BMC) were transplanted. Seven days later bone marrow (BM), skin (SK), lymph node (LN), spleen (SPL), liver (L), and heart (H) were harvested. Mice-SRY-gene was identified by PCR in tissues and population harvest. Male-SRY-gene was identified by PCR in tissues and population harvest.
**Dissipation of Donor DNA in Graft Recipients**

**Increased Chronic Cyclosporin Nephrotoxicity**

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The destruction of the rejecting graft involves its cellular elements. They are disseminated in the recipient and in most part taken up by macrophages and dendritic cells (DC). Allogeneic transplantation is followed by cellular microchimerism and "seeding" of donor DNA from the rejecting graft cells. To prevent rejection immunosuppressants are routinely used. Irrespective of that DNA from the graft cellular debris and passenger cells is distributed throughout the recipient organs.

**Aim:** To localize DNA in recipient spleen dendritic cells (DC) and days after syngeneic heart transplantation without immunosuppression and 30 days after syngeneic and allogeneic transplantation in recipients treated with Cyclosporin A (CsA) and FK506. The phenotypic characterization of spleen dendritic cell enriched population.

**Methods:** In rat experiment, BN or LEW male hearts were transplanted to LEW females and the male-SRY-gene fragment was identified in enriched population of splenic dendritic cells. The phenotypic characterisation of recipient splenic cells was performed with OX27, OX6, ED1, W3/13 and OX62 antibodies.

**Results:** After 7 and 30 days donor DNA was not detected in DC after syngeneic transplantation. Whereas after administration of immunosuppressants the donor DNA was detected in DC enriched fraction in syngeneic and allogeneic combinations reaching even slightly higher values after FK506 treatment in syngeneic transplantation. The percentage of positive cells in recipient spleen dendritic cells after heart transplantation was 95% of OX6, 92% of ED1, 35% of W3/13 and 5% of OX62.

**Conclusions:** CsA and FK506 increase the optical density value of donor DNA in splenic DC both after syngeneic and allogeneic grafting. This may be caused by the cytotoxic effects of drugs in addition to rejection of allogeneic grafts.

**PO-164** INHIBITION OF SEMICARBAZIDE-SENSITIVE AMINE OXIDASE DECREASES LYMPHOCYTE INFILTRATION IN THE EARLY PHASES OF RAT LIVER ALLOGRAFT REJECTION

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Vascular adhesion protein-1 (VAP-1) has been shown to mediate lymphocyte adhesion to endothelia at sites of inflammation in vitro and in vivo. We have previously shown that blockade of VAP-1 by monoclonal antibody inhibits T-cell infiltration in rat liver allograft rejection. VAP-1 is also an enzyme with semicarbazide-sensitive amine oxidase (SSAO) activity. In this study we investigated whether inhibition of SSAO could influence the inflammatory infiltration in acute rat liver allograft rejection.

**Methods:** BN recipients of DA liver allografts were treated with 50mg/kg/d semicarbazide, an inhibitor of SSAO, or similar volume of saline. 10 rats/group were followed for graft survival, and 10 rats/group were sacrificed on day 7 post transplantation for histology and T-lymphocyte isolation. The area percentage of portal inflammatory infiltrates in the grafts were assessed from digital photomicrographs. The amounts of CD4+, CD8+ and IL-2 receptor-positive lymphocytes were studied with flow cytometry.

**Results:** At day 7, the proportional area of the portal fields and perivenous inflammatory infiltrates was significantly lower in the semicarbazide group (4.4±2.4% of total slide area) when compared to control (9.0±3.0%), indicating a lower amount of inflammatory cells in the grafts. CD4+, CD8- and IL-2 receptor-positive and -negative cells were equally affected. However, there was no significant effect on animal survival.

**Conclusions:** Blockade of the enzymatic activity of VAP-1 has an effect on lymphocyte adhesion in vivo. SSAO inhibition could be used as a component of immunosuppressive treatment.

**PO-165** BACTERIOPHAGES INHIBIT INTERLEUKIN-2 PRODUCTION BY HUMAN T LYMPHOCYTES

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Our most recent findings indicate that bacteriophages can exert immunosuppressive effects and therefore help control local inflammatory and autoimmune reactions (Cell Mol Life Sci 2005,62,511). In the present report we substantiate these claims by demonstrating that phages can inhibit interleukin-2 (IL-2) production by human T cells.

Mononuclear cells were cultured for 3 days in the presence of PHA and the culture supernatants were harvested and assayed for IL-2 using a standard ELISA system. Purified coliphages (T4, endotoxin concentration < 50 EU/ml) were added in a proportion of 1,000-10,000 phage particles/cell.

**Objective:** To investigate whether inhibition of SSAO could influence the inflammatory infiltration in rat liver allograft rejection. VAP-1 is also an ectoenzyme with semicarbazide-sensitive amine oxidase activity. In this study we investigated whether inhibition of SSAO could influence the inflammatory infiltration in acute rat liver allograft rejection.

**Methods:** BN recipients of DA liver allografts were treated with 50mg/kg/d semicarbazide, an inhibitor of SSAO, or similar volume of saline. 10 rats/group were sacrificed on day 7 post transplantation for histology and T-lymphocyte isolation. The area percentage of portal inflammatory infiltrates in the grafts were assessed from digital photomicrographs. The amounts of CD4+, CD8+ and IL-2 receptor-positive lymphocytes were studied with flow cytometry.

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**Conclusions:** Blockade of the enzymatic activity of VAP-1 has an effect on lymphocyte adhesion in vivo. SSAO inhibition could be used as a component of immunosuppressive treatment.
Materials and Methods: Male FVB mice (WT) and PGp knockout -mdr1a/b knock-out FVB mice (KO) received low-salt diet and daily subcutaneous injection of CsA (75 mg/kg), SRL (0.4 mg/kg) or vehicle (olive oil) for 6 weeks. After this period Creatinine, BUN, blood and tissue drug levels, and tubulointerstitial fibrosis (TIF) were measured semi-quantitatively. For statistical analysis groups were compared using non-parametric test
Results: There were no significant differences between drug levels of KO and WT groups: CSA 358.1 ± 1025 vs 2952.8 ± 845 ng/ml (p=ns); SRL 76.7 ± 72.4 vs 100.5 ± 66.0 ng/ml (p=ns) respectively. KO mice treated with CSA didn’t show different creatinine (0.46 ± 0.06 vs 0.46 ± 0.05 mg/dL, p=ns) or BUN (90.0 ± 39.5 vs 51.0 ± 10.8 mg/dL, P=0.08) compared with WT mice treated with CsA. However, KO-CsA group showed increased TIF score (7.5 ± 3.5%) compared with WT-CsA group (7.5 ± 3.5%) (p=0.003). There were no significant differences between renal function or TIF of KO and WT mice treated with SRL or vehicle, and between tissue drug levels of KO and WT mice.
Conclusion: PGp knock-out mice showed increased CsA nephrotoxicity. These new data prove the relation between PGp expression and CsA nephrotoxicity.

PO-168 INFLUENCE OF HEMATOPOIETIC MICROCHIMERSIM ON SOLID ORGAN TRANSPLANTATION
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Donor hematopoietic cell microchimerism after solid organ transplantation has been widely discussed. Residual immunity of the transplanted recipient could activate either a chain reaction of alloimmune rejection or tolerate these non-HLA identical cells, in which case there would be a better acceptance for the implanted organ.
Objective: To analyze the existence of microchimerism in peripheral blood after a solid organ transplant. A secondary objective was to determine the incidence of HLA discrepancies between donor and recipient and correlate it to the impact of microchimerism. Also, to determine which population of leukocytes may be affected by microchimerism.

Patients and methods: One hundred and fifty-six patients have been included in this study. Thirty-two patients were heart transplanted and 124 were kidney transplanted. DNA from peripheral blood cells was available from the donors, pre-transplant recipients and also 1, 6, 12 and 18 months post-transplant recipients. Microchimerism study was carried out by PCR-VNTR, PCR-STR, PCR-SSP, Q-SSP-PCR. RSCA was performed for the HLA typing and matching.
Results: We have seen that 42.6% of the recipients have demonstrated microchimerism, and 16% had rejection episodes while 81% did not. Furthermore, in the absence of microchimerism, 34% showed rejection episodes while 66% did not. HLA-A,-B,-DR mismatching from both donor and recipient showed several similar mismatches.
Conclusions: Hematopoietic microchimerism is fairly common in solid organ grafted recipients. Microchimerism detection pathways will be discussed. It also seems suitable to have peripheral blood circulating donor cells to show graft rejection.

PO-169 IDENTIFICATION BY PROTEOMIC TOOL OF ANTINUCLEAR ANTIBODIES (ANA) TARGETS IN AUTOIMMUNE HEPATITIS TYPE 1 (AIH-1) IN DE NOVO AIH AND CHRONIC LIVER ALLOGRAFT REJECTION
Stéphanie Huguet, Valérie Labas, Jean-Charles Duclos Vallee, Joëlle Vinh, Didier Samuel, Catherine Jhanetan, Eric Ballot. Hepatology-Clinical Center, Paul Brousse Hospital, Villejuif, France.
ANA are diagnostic markers of AIH-1. They have been shown in de novo AIH after liver transplantation, chronic liver allograft rejection (CR).

AIMS/Methods: We propose to identify ANA targets by using the proteomic tool. ANA-positive sera from 46 AIH-1, 5 de novo AIH, 14 CR and sera from 29 negative controls were analyzed. Immunoblots were performed using nuclear fraction proteins resolved either by SDS-PAGE, or by combination of isoelectrofocusing and SDS-PAGE (2D). Interest spots were identified by mass spectrometry type matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF). Identifications were confirmed by western blot and chromatography electrospray tandem mass spectrometry (LC-ESI-MS/MS).

RESULTS: Four main bands located at 30, 34, 36 and 38 kDa were statistically more frequently stained by sera from AIH than by sera from controls. These bands were stained unspecifically by de novo AIH and by CR compared to AIH-1. However, the 30 and the 38 kDa proteins were less frequently recognized by CR than by AIH (respectively 36% vs 65% and 7% vs 50%). Identification of surface holomRNA A2 for the 34kDa band, a mix of hnRNP B1 and A3 for the 36 and 38 kDa bands.

PO-170 MODIFICATION OF ALLOGENIC SPLENCYTES WITH IRRADIATION PRIOR TO PORTAL INJECTION REDUCES RECIPIENT ANTIGEN PRESENTING ACTIVITY TO ALLOGENIC T CELLS
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We have previously reported that portal injection (PI) of irradiated allogeneic splenocytes from class II-deficient (C2D) B6 mice into Balb/c mice led to an indefinite acceptance of subsequently transplanted donor-type heart allografts. In order to address the role of irradiation of splenocytes in tolerization by PI, we evaluated the capacity of splenoid antigen presenting cells (APCs) from Balb/c recipients of PI of either untreated or irradiated B6 C2D splenocytes to stimulate Balb/c T cells with indirect allospecificity. By PKH-26-labeling of B6 C2D splenocytes prior to PI into Balb/c mice, the injected B6 C2D splenocytes and Balb/c phagocytes that had taken up the injected splenocytes could be identified. The population density of injected splenocytes and phagocytes that captured the injected splenocytes in the spleen was significantly higher in consequence to PI of untreated splenocytes than that in consequence to PI of irradiated splenocytes in the observation period. On immunohistological examination, remarkable number of PKH-26-labeled untreated splenocytes were found to have penetrated the marginal zone and reached the T cell area whereas very few PKH-26-labeled irradiated splenocytes did so. The splenic APCs from the Balb/c mice treated with PI of untreated B6 C2D splenocytes efficiently induced proliferation of naïve Balb/c T cells, whereas the APCs from the Balb/c mice treated with PI of irradiated B6 C2D splenocytes did not so. These findings imply that the splenic APCs that have a capacity to present allogeneic antigens to T cells with indirect allospecificity exist in consequence to PI of untreated splenocytes, but not in consequence to PI of irradiated splenocytes.

PO-171 NUCLEO-CYTOPLASMIC TRANSLATION OF BACH1 REGURATES THE EXPRESSION OF HEME OXYGENASE-1, AN ANTI-OXIDANT DEFENSE ENZYME
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The heme oxygenase-1 (HO-1) system is among the most critical of cytoprotective mechanisms activated during cellular stress. HO-1 overexpression exerts beneficial effects in a number of transplantation models. While the expression of HO-1 is repressed by Bach1/small Hsfd of heme synthesis. Overexpression of MafK together with Bach1 resulted in significant nuclear accumulation of Bach1. Inhibition of heme synthesis enhanced the nuclear accumulation of Bach1 whereas cells having been treated with 10-7 M MafK together with Bach1 resulted in nuclear exclusion of Bach1. While the cadmium-inducible nuclear export signal of Bach1 was dispensable for the heme response, a region containing two of the heme-binding motifs were found to be critical for the heme-induced nuclear exclusion.

PO-172 REDUCTION OF PECAM-1 AT GRAFT ENDOTHELIIUM AFTER CARDIAC TRANSPLANTATION IS ACCOMPANIED BY THE REDUCTION OF LEUKOCYTE INFLTRATION INTO THE PERIVASCULAR SPACE OF ARTERIES. A COMPARATIVE STUDY WITH CA. PKG66 AND MMF
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Platelet endothelial cell adhesion molecule (PECAM-1), is expressed at the endothelium of vessels and is involved in T-cell activation and transendothelial migration of leukocytes into the perivascular space (pvs) or into the myocardium. We evaluated the effects of CAs, FK506 and MMF on PECAM-1 expression in an ex-perimental transplant model.
Methods: After cardiac transplants (Lewis to Fisher rats) animals were divided into four groups: CSA 3mg/kg/d (n=74), MMF 40mg/kg/d (n=96), FK506 0.3mg/kg/d (n=96) and Control (no therapy (n=74). 3-4 animals of each group were sacrificed in intervals of 1-4 days up to day 60. Using immunohistochemistry we investigated the quote of positive stained ves-sets, the intensity of staining and the geometric distribution of positive staining for PECAM-1 and analysed CD4, CD8, CD11a and CD18 positive leucocytes in the pvs of intra- and epicardial arteries.

Results: In controls we found an intensive and nearly circularment PECAM-1 staining. All used drugs reduced the intensity of staining, the quote of stained vessels as well as the geometry of staining. Comparing CsA and FK506, we did not find significant differences. In MMF treated animals the intensity and the geometry of staining were significantly reduced compared to both calcineurin inhibitors. When leucocyte infiltration into the perivascular space of arteries and into the myocardium was analysed (CD4/CD6 and CD11a/CD18) we found a significant correlation between the intensity of PECAM-1 staining and leucocyte infiltration. MMF therapy reduced PECAM-1 staining in graft endothelium as well as the amount of leucocytes in the perivascular space at intra- and epicardial arteries.

Conclusion: We conclude that the blockade of VLA-4 costimulatory receptors may contribute to development of pregnancy-induced tolerance. To further study its mechanisms could offer significant clues for mechanisms of transplant tolerance.

PO-175 ACTIVATION OF INNATE IMMUNITY – ROLE OF THE THROMBIN PARADOX

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Objectives: In own studies, reported elsewhere (Haemostaseologie, 2004), the thrombin paradox could be proven experimentally. Binding of thrombin to various endothelial receptors (thrombomodulin, thrombin receptor, heparan sulfate) hereby not only enhances endothelial antithrombogenic activity; recent studies demonstrated the binding of endothelial heparan sulfates to dendritic cell-derived Toll-like receptors (TLR). The aim of this study was to demonstrate the presence of the TLR-activating inducible heat shock proteins (HSP70) in the process of igniting the innate immune system (IIS)

Methods: As a model of activation of the IIS, in human recipients of renal allografts, during transplantation, before and after reperfusion, at least 2 biopsies were performed (0-biopsy and 1 h after reperfusion). By means of EPR-spectroscopy, we analysed renal venous blood after reperfusion for reactive oxygen species as marker for the ischemia reperfusion injury. We investigated formaldehyde-fixed specimen histopathologically by binding assays with HSP72.

Results: In all biopsies, qualitative proof of inducible HSP70, measured by HSP72, could be positively obtained, whereas control biopsies from normal renal tissue revealed negative results. Concentration of inducible HSP70 was highest, however, in 1-h-biopsies, at the time, when ROS formation was highest. Inducible HSP70 act as initiators of TLR4 on dendritic cells by “chaperoning” (by ROS) oxidized proteins thus triggering the alloimmune response.

Conclusions: The proof that inducible HSP70 are found to correlate with ROS concentrations in reperfused kidney transplants, hints towards the ability of endothelial (heparan-...) bound thrombin to inhibit the innate immune system. Hence, factor Xa-specific anticoagulants, leaving a sufficient amount of thrombin for binding to endothelial heparan sulfate intact, may interfere with the innate immune system.

PO-176 OUTCOME AFTER HUMAN LIVER TRANSPLANTATION IS NOT INFLUENCED BY DONOR HEME OXYGENASE-1 GENE POLYMORPHISM

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Background: The heme oxygenase-1 (HO-1)/carbon monoxide pathway has been proposed as a protective system with anti-inflammatory and anti-oxidant effects. The inducibility of HO-1 mRNA expression is modulated by a (GT) n-polymorphism. The aim of this study was to determine whether HO-1 genotype affects outcome after liver transplantation.

Methods: We investigated 186 renal transplant recipients and 100 liver transplant recipients. For each individual, we determined HO-1 promoter length polymorphism and genotypic outcome. Outcome was defined as death or return to dialysis. As this was an observational study, no statistical power calculations were performed.

Results: In univariate analysis, there were no significant differences for genotype distributions between livers with cold ischemia time 15h, or a subgroup with acute rejection was also not different. In contrast to kidney transplantation, the HO-1 promoter length polymorphism does not affect graft survival or incidence of acute rejection after liver transplantation. Organ specific differences in the protective properties of HO-1 could be an explanation for this discrepancy.
IS SIROLIMUS A TOLERANCE PROMOTING DRUG?

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**Purpose:** Induction of transplant tolerance is a desired long-term outcome for renal transplant patients. This ongoing study is aimed at identifying whether in contrast to calcineurin inhibitors, sirolimus promotes immune tolerance in man. Prospective donor-specific response frequencies are compared in de novo renal allograft recipients on two different treatment arms of an open-label, randomised study.

**METHODS/MATERIALS:** Immunosuppressive regimes compared are daclizumab induction followed by either 1) sirolimus or 2) tacrolimus, adjunctive with MMF and steroids. Donor antigen-specific responses from recipient PBMCs are studied pre- and 1-12 months post-transplantation. Quantitative assessments of recipient IFNy responses to donor and 3rd-party antigens are made by ELSpot analysis. Direct responses are detected by stimulating T cells with donor APCs and indirect responses by stimulating PBMCs with donor cell membrane-derived proteins. Depletion of CD4+CD25+ cells from responder populations uncovers Treg function.

**Results:** Interim data analysis shows pre-transplant direct frequencies against donor and 3rd-party are similar. Significant donor-specific hyporesponsiveness is not detected 1 and 6 months post-transplantation although anti-donor responder frequencies diminish over time. In contrast, donor-specific indirect frequencies increase with time post-transplantation. No significant differences are found between each treatment arm as yet. Interestingly, CD4+CD25+ cells are reduced in peripheral blood 1 month post-transplant in both groups, probably due to daclizumab therapy.

**Conclusions:** Donor-specific assays developed for this study provide an insight into the development of recipient responses following transplantation and will help to elucidate the governing role of Tregs. We expect that with more patients studied by the trial end-point, a clinically important answer should be obtained.

PO-177  DENDRITIC CELLS IN PATIENTS UNDERGOING RENAL TRANSPLANTATION UNDERGO CHARACTERISTIC CHANGES IN RESPONSE TO STANDARD IMMUNOSUPPRESSIVE THERAPY

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**Purpose:** Dendritic cells (DC) appear to play a key role in the induction of immunotolerance against allograft transplants. The effect of standard immunosuppression on lymphocytes is described, little is known about DC fate. To assess the impact of immunosuppression, DC subsets were monitored using CD62L, CD80, CD83 and CD86 cell surface markers in renal transplant recipients undergoing standard immunosuppressive therapies.

**Materials:** Blood samples were taken from 25 patients receiving renal transplants under standard immunosuppressive therapies with prednisolone, mycophenolate mofetil and tacrolimus in renal transplantation.

**Results:** Patients on MMF and steroids. Donor antigen-specific responses from recipient PBMCs were made by ELISpot analysis. Direct responses are detected by stimulating T cells with donor APCs and indirect responses by stimulating PBMCs with donor cell membrane-derived proteins. Depletion of CD4+CD25+ cells from responder populations uncovers Treg function.

**Conclusions:** Donor-specific assays developed for this study provide an insight into the development of recipient responses following transplantation and will help to elucidate the governing role of Tregs. We expect that with more patients studied by the trial end-point, a clinically important answer should be obtained.

PO-178  EFFICIENT EXPANSION OF REGULATORY T CELLS AND Prolongations of Cardiac Allograft Survival by CD28 SUPERAGONIST TREATMENT

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**Background:** It is well known that CD4+CD25+ regulatory T-cells play a critical role in the suppression of autoimmunity, inflammation and allograft rejection. We investigated the efficient expansion of regulatory T-cell and the prolongation of cardiac allograft survival by CD28 superagonist treatment.

**Materials and Methods:** After stimulation of Lewis T-cell with CD28 superagonist, cell population was analyzed with flow cytometry. Three days after injection of CD28 superagonist, populations of lymphocytes from Lewis rat were examined. Cytokine and FoxP3 mRNA expression of these lymphocytes were analyzed by RT-PCR. Regulatory activity of these lymphocytes was examined in the mixed lymphocytes reaction (MLR). Furthermore, CD28 superagonist was intravenously administered into the recipient of cardiac transplant recipients.

**Results:** CD28 superagonist exerted remarkable proliferation of CD4+CD25+ lymphocyte population in vitro and in vivo study. In MLR, lymphocytes from the rat treated with CD28 superagonist showed anergy and regulatory activity. These cells showed mRNA expression of IL-2, IL-4, IL-10, TGF-β and FoxP3. CD28 superagonist treatment significantly prolonged the cardiac allograft survival compared with no treatment.

**Conclusions:** CD28 superagonist may expand the regulatory T-cell population in vitro and in vivo without loss of function and represent a major advance towards the therapeutic use of these cells in the treatment of allograft rejection.

Immunosuppression / Acute Chronic Rejection

PO-178.5  FIVE-YEAR RESULTS OF A STEROID WITHDRAWAL PROTOCOL WITH MYCOPHENOLEATE MOFETIL AND TACROLIMUS IN RENAL TRANSPANTATION

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**Object:** To describe the long-term evolution (60 months in 37 patients and 56 months in another 4) of a steroids withdrawal protocol with mycophenolate mofetil and tacrolimus in renal transplantation.

**Methods:** Follow-up of 42 kidney transplant patients treated in the immediate post-transplantation period with mycophenolate mofetil (1 g/2 h), tacrolimus (0.10 mg/kg/12 h) and a steroid withdrawal protocol: 250 mg i.v. in the pretransplant phase, 125 mg i.v. on day 1, 20 mg after day 2, and with a progressive dose reduction to withdrawal after 3 months.

**Results:** Steroids were withdrawn in all patients after 3 months, and 2 patients presenting post-transplant diabetes converted after 2 years from tacrolimus to cyclosporine A. Acute rejection was recorded in 7% of the patients (one requiring OKT3 therapy), and chronic rejection in 7% (1 patient started hemodialysis after 6 months). Patient and graft survival is 100% and 97.6%, respectively, with a mean serum creatinine concentration and creatinine clearance of 1.98±0.97 and 76.75±3.57, respectively. The incidence of hyperlipidemia, arterial hypertension and hyperglycemia was 36, 66 and 12%, respectively. Eight patients presented hyperparathyroidism, while 4 developed infections: respiratory unknown origin in 1 case, varicella-zoster in 2, and CMV in another. One patient presented Bowenoid in situ carcinoma.

**Conclusions:** The association of mycophenolate mofetil and tacrolimus allows early steroid withdrawal, with good long-term results.

PO-180  MONITORING MYCOPHENOLIC ACID: WHAT TO MEASURE AND HOW OFTEN?

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Exposure to mycophenolic acid (MPA) is highly variable between patients on standard dose therapy. In addition, exposure increases over time and is predictive for the development of acute rejection. Consequently, therapeutic drug monitoring (TDM) of MPA may optimize exposure, although a large within-patient-variability could be a limitation. This study aims to analyze the extent of
within-patient-variability of MPA exposure for area-under-the-curve (AUC) and trough concentrations (C₉₀). For day 3, 7, 11, and 21, and months 1, 2, 3, 4 and 5 after transplantation, AUC and C₀ values from 45 renal transplant recipients were divided into quartiles. When AUC or C₀ changed 1, 2 or 3 quartiles within a patient from one occasion to the next, a score of respectively 1, 2 or 3 points was assigned. For all 8 between-occasion-intervals, this results in a maximum score for within-patient-variability of 24.

For C₀, the mean overall score (± stdev) was 6.3 of maximal 24 ± 2.9. For AUC measurements this score was 4.1 ± 3.0. The higher score for C₀ was explained by a higher mean score on day 7 (0.91 (of maximal 3) vs 0.58 for AUC) and day 1 1.95 vs 0.49.

The within-patient-variability for MPA exposure is low in kidney transplant recipients during the first 5 months after transplantation. In the first weeks after transplantation within-patient-variability is larger for C₀ than for AUC. Based on this observation the following TDM scheme may prove to be useful: one measurement of exposure, preferably by AUC, in the first week after transplantation to determine the optimal MPA dose and a second measurement after 2 months to compensate for the increase in exposure over time.

**PO-181 ESTIMATION OF MYCOPHENOLIC ACID AREAS UNDER THE CURVE IN SIROLUSUM CO-TREATED PATIENTS USING A LIMITED SAMPLING STRATEGY**

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Pharmacokinetic analyses of MPA (C₀, C₄₀min, C₆₀min, C₉₀min, C₁₅₅min, C₂₅min, C₃₅min, C₄₅min, C₅₅min, C₆₅min, C₇₅min, C₉₅min, C₀) were performed at week 2 and at months 1, 2 and 3 post-transplant. MPA and C₀ were given simultaneously and plasma MPA was analysed using an EMIT assay. Reference AUCs over 12h were calculated analysed using an EMIT assay. Reference AUCs over 12h were calculated. The multivariate analysis included 1074 patients and assessed a strong, independent negative impact on graft survival for donor recipient age > 60, DGF, and CMV infections, while a MPA dose maintained at 2 g and a Neoral dose >3mg/kg/die at M12 were strongly associated with better GFR (p < 0.001 for all). Also stratifying patients according Neoral dose (cut of 3 mg/die) didn’t influence the beneficial effect of maintaining stable the MPA dose.

Maintaining the MPA dose at 2 g results in a better renal function at 12 months.

**PO-182 RITUXIMAB – RESCUE OF A KIDNEY GRAFT WITH C4d POSITIVE REJECTION IN A PATIENT WITH A HISTORIC CROSS-MATCH POSITIVITY**

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Acute humoral rejection (AHRe) carries a poor prognosis and necessitates a more intensive rescue regimen. Rituximab, monoclonal antibody targeting B-cells promotes in these situations. We report a case of a 34-years old woman with panel reactive antibodies 41%/3%, who obtained a cadaveric kidney graft with 1 A and 1 B HLA miss-matches. Immunosuppression protocols associating sirolimus (Srl) with MPA have been proposed. The aim of the present study was to develop a limited sampling strategy (LSS) to estimate MPA area under the curve (AUC) in patients co-treated with Srl.

Twenty-one renal recipients treated with Srl, MPA and steroids were included. Pharmacokinetic analyses of MPA (C₀, C₄₀min, C₆₀min, C₉₀min, C₁₅₅min, C₂₅min, C₃₅min, C₄₅min, C₅₅min, C₆₅min, C₇₅min, C₉₅min) were performed at week 2 and at weeks 1, 2 and 3 post-transplant. Srl and MPA were given simultaneously and plasma MPA was analysed using an EMIT assay. To determine AUCs over 12h were calculated using a linear trapezoidal method. We estimated MPA AUC through multilinear regression with a limited number of samples (N ≤ 4). The highest coefficient of determination between MPA AUC and a single concentration was observed with C₀ (r² = 0.85). Trough concentration (C₀) was well correlated with AUC (r²=0.71). The best coefficient of determination of MPA AUC using a short sampling period was the model using C₀, C₄₀min, and C₆₀min (r² = 0.92).

Trough levels are well correlated with MPA AUC and can be estimated through a LSS in Srl co-treated patients. The 3 sampling times of our model are close to those proposed for tacrolimus co-treated patients.
PO-188  
**GRAFT WEIGHT/STANDARD LIVER VOLUME RATIO IMPACTS ORALLY TAC DOSE AND LEVEL AFTER RIGHT SPLIT LIVER TRANSPLANTATION**  
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**Background:** The aim of this study was to evaluate clinical factors influencing orally TAC dose and level after right split liver transplantation.

**Patients and methods:** A total of 21 patients after right split liver transplantation (living related, LR, n=13; cadaveric split, CS, n=8) were included in this study. Tac based immunosuppression started at a dose of 25x mg/day (n=17) or 2x mg/day (n=4) perorally. Tac dose was adjusted according to initially aimed Tac serum trough of 12-17 mg/dl. ID described initial time duration until reaching target level. CD indicated continuous Tac dose necessary for reaching aimed Tac level. Both parameters were correlated with several clinical factors.

**Results:** There were significant differences (P<0.05) between CS- and LR-group regarding warm and cold ischemia time, blood loss, initial allograft function and GWS/LV. Mean ID was 2.1 days in the CS-, and 2.5 days in the LR-group. Mean CD was 4.6 mg in the CS-, and 5.3 mg in the LR-group, respectively. There was no significant clinical correlation with ID in either group. Conversely, CD was significantly correlated with initial allograft function in the CsA-group (r=0.72). In the LR-group, CD revealed a significant correlation with recipients' age (r=-0.75) and GWS/LV (r=0.63).

**Conclusion:** Orally maintenance Tac dose after right split liver transplantation is influenced by recipient's age, initial allograft function and, above all, GV, providing an early post-LT available parameter. Thus, adequate initial orally Tac dose adjustment and thereby reduced Tac-induced toxicity might be possible in right split-liver transplantation.

PO-189  
**IMPROVED KIDNEY FUNCTION 2 YEARS AFTER SWITCH FROM CNI IMMUNOSUPPRESSION TO SIROLUSM + PREDNISOLON**  
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CNI immunosuppression is considered to be associated with progressive decrease in kidney function due to CNI toxicity in the majority of NTX pts. We therefore studied effects of a switch from a CNI regimen (CNI+MPA+P) to SRL+P in 26 pts with moderately impaired kidney function (S-Crea 1.5 <1.0) due to either CNI toxicity or clinical evidence for CAD.

13 pts received regimen 1 consisting of SRL 12mg dosage on day 1 and from day 2 to 5 SRL 4mg + CSA half of maintenance dosage. From day 6 SRL 8mg, CSA was withdrawn. MPA or AZA were halved for 4 to 6 weeks. P was kept constant.

Target level for SRL was 12 to 20 µg/ml. 13 pts received regimen 2 consisting of SRL 12mg and CSA withdrawal on day 1 and from day 2 to 6 SRL 6mg was administrated for a target level of 7 to 10 µg/ml. MPA or AZA were halved for 4 to 6 weeks and P was kept constant.

With regimen 1 there were 6 dropouts due to adverse events whereas with regimen 2 only 2 dropouts occurred. 45% of the patients showed a decrease of S-Crea, 20% were unchanged and only 25% showed an increase. Overall there was a significant increase cholesterol and triglycerides, whereas other parameters were unchanged.

**Conclusion:** switch from CNI containing immunosuppression to a dual regimen of SRL+P results in an improved transplant function after 24 months in a substantial number of patients. A regimen with target levels of SRL from 10 to 20 and an overlap in immunosuppression shows a high rate of adverse events and is associated with a 3-fold dropout rate.
Treatment regimen was associated with acute Banff 97 sum score, which was 0.6 higher for CsA. Odds of acute score > 2 were higher for CsA (OR 2.48). Mean chronic Banff 97 sum score did not differ between groups but odds of chronic score > 2 were higher for CsA (OR 2.18). After adjustment for other variables the CADI score was 0.6 higher for CsA and odds of CADI > 4 were higher for CsA (OR 2.2). Of the individual histological components the interstitial inflammation and tubulitis scores were higher in the CsA group. There was also a trend towards more intestinal fibrosis and mesangial matrix increase in the CsA treated group.

Conclusion: We found that both acute and chronic histopathology scores were higher in renal transplant recipients receiving CsA than FK.

**PO-193 RAPID CONVERSION FROM CYCLOSPORINE TO SIROLIMUS IN RENAL TRANSPLANT RECIPIENTS: FIRST CLINICAL EXPERIENCE**

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Sirolimus (SRL) has demonstrated its potential to substitute for calcineurin inhibitors because it lacks significant nephrotoxicity and shows a short-term immunosuppressive capacity comparable with that of cyclosporine (CsA). However, recent evidence suggest that de novo use of SRL may have disadvantages in terms of wound-healing and recovery from a delayed graft function. To overcome these clinical problems, we designed a rapid conversion protocol starting with ATG (single shot) + CsA + mycophenolate mofetil (MMF) + steroids (ST), followed after 2-3 weeks by an immunosuppression with SRL (trough level: 6-10ng/ml + MMF (1.5g) + ST). A cohort of ten low-risk renal transplant recipients (PRA<30%) subjected to this protocol showed a patient and graft survival of 100% after 6 months of follow-up. Graft function was excellent with a calculated GFR (Cockcroft-Gault formula) of 82±14.1 ml/min. During 6 months, one (10%) steroid-sensitive, acute rejection (Banff 4a) occurred. In the observation period, one patient discontinued medication due to rash and two patients interrupted sirolimus because of scheduled reoperation. This first clinical experience demonstrates that our rapid conversion approach is feasible and safe and might successfully bypass the problems associated with the early use of sirolimus following renal transplantation.

**PO-194 TACROLIMUS-BASED VS. CYCLOSPORINE-BASED MONOTHERAPY IN LIVER TRANSPLANTATION. SHORT-TERM RESULTS FROM A PROSPECTIVE, RANDOMIZED TRIAL**

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Background: the tacrolimus (Tac)-based monotherapy regimen has been successfully administered in humans. As well, our group adopts either cyclosporine (A) or Tac in monotherapy since 2001. The two drugs, in the context of mult-drug regimens, have been compared in different studies, with contrasting results.

Aim: To compare Tac- vs. CsA-based monotherapy.

Patients and METHODS: Fifty-five patients were randomly assigned to receive either CsA (26) or Tac (19), since the first postoperative day. No induction therapy, nor intra-operative steroids were given. For CsA dosage, C2 was considered. Endpoints of the study were patient and graft survival; incidence of acute rejection (AR), infections, complications (IC) and de novo diabetes (NDDM); liver and kidney function, cholesterol and triglycerides.

Results: At 1 year, patient and graft survival were 78% (CsA) vs. 80% (Tac), and 80% vs. 80%, respectively (p=ns). Six cases of AR were recorded in the CsA group (3 mild, 1 moderate, 2 severe), whereas just 1 mild in the Tac (p=ns). When the other issues are considered, the two groups were comparable, except for the blood levels of alkaline phosphatase at month 12 (203±163 vs. 102±169, p=0.01).

Conclusions: Monotherapy is safe and effective, warranting results similar to the standard. Tac seems to better control the immune response of the host. Long-term results and larger population are needed.

**PO-195 THE DIFFERENT GENE EXPRESSION IN SEB INDUCED ANERGY IN TREATING HIGH-RISK CORNEAL TRANSPLANTATION IN RAT MODEL**

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Objective: To investigate the different genes involved in SEB (Staphylococcal enterotoxin B) induced anergy in treating high-risk corneal transplantation in rat model.

Methods: Fisher344 rats were used as donors and Lewis rats were used as recipients. Conical neovascularization was induced by suture. All the animals were divided randomly into two groups. The SEB-treated group was intraperitoneally injected with 0.2ml SEB of 25µg/kg before keratoplasty. The control group received saline buffer in the same way. 10d after surgery, the anergy

**PO-191 CYCLOSPORINE SPARING WITH THE USE OF MYCOPHENOLEATE MOFETIL, DACTILUMAB AND CORTICOSTEROIDS IN RENAL ALLOGRAFT RECIPIENTS – 18 MONTH RESULTS**

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356 of 356 patients consented at 18 month (mo) followup of a 12 mo open label, multicenter study assessing cyclosporine (CsA) withdrawal or reduction in de novo renal transplant recipients. Patients were randomized into 3 groups: (A) dactilumab (dac), mycophenolate mofetil (MMF), corticosteroids (CS), low dose CsA with weaning (mo 4/5 withdrawal (6); (B) dac, MMF, CS, low dose CsA; (C) MMF, CS, standard dose CsA. Creatinine clearances (CrCl) were measured in 228 patients.

At mo 18, mean CrCl's were slightly better in Groups A and B (69.1 and 69.9 ml/min, respectively) than in Group C (66.3 ml/min). The mean GFR for Group B at mo 18 (54.4 ml/min/1.73m²) was higher than that for Groups A (46.8 ml/min/1.73m²) and C (48.6 ml/min/1.73m²), possibly due to Group B having fewer rejections than A and less CsA than C. The incidence of first biopsy proven acute rejection in Group B (29.4%) was lower than in Group A (40.8%) and comparable to that of Group C (31.3%). Reported deaths (D) and graft losses (GL) were least in Group B (4 D, 6 GL), compared to Group A (8 D, 14 GL) and Group C (6, 9 GL).

Use of low dose CsA with MMF, CS, and dac induction is clinically safe and effective for renal transplant patients through 18 mo posttransplant.

**PO-192 RAPAMICIN ASSOCIATES WITH A STRONGER INHIBITION OF DONOR-RECIPIENT MIXED LYMPHOCYTE REACTINS AMONG KIDNEY TRANSPLANTS**

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RAPA is a new immunosuppressive drug currently used in kidney transplantation (KTX). Its mechanism of action is different from calcineurin inhibitors (CNI) and contrary to those don't seem to modulate the transcription of cytokines. MLR tests the indirect and direct antigen presentation and provides an indication of the strength of the alloimmune response. We tested the influences of RAPA on MLR as compared with CNI.

32 KTX were divided into 2 groups; Group I (n=17) was treated with RAPA/MMF/pred and Group II (n=25) with CsA/MMF/pred. No KTX received antibody induction and all were first cadaver KTX. MLR were done between 6 and 12 month post-KTX in donor-recipient (D/R) and third-party-recipient combinations (R/T) with donor spleen cells thawed for culture. Proliferation was evaluated at 96h.

No significant differences were observed in both groups when comparing demographic data and serum creatinine values. No patient suffered an acute rejection before MLR. The cpm were for D/R: Group I: 3404±7373 and Group II: 5017±6274 (P=0.017); for R/T Group I: 35998±41544 and Group II: 35417±27671 (P=0.582). Relative Response was for Group I: 5.7±14.8% and Group II: 11.4±14.8% (P=0.003).

Our results are the first evidence that RAPA treatment associates with a significant down-regulation of anti-donor response while third-party response was not affected. Whereas some doubts have been raised that CNI may abrogate significant down-regulation of anti-donor response while third-party response was not affected. Our results are the first evidence that RAPA treatment associates with a significant down-regulation of anti-donor response while third-party response was not affected. Whereas some doubts have been raised that CNI may abrogate significant down-regulation of ant-donor response while third-party response was not affected. Therefore, some doubts have been raised that CNI may abrogate significant down-regulation of anti-donor response while third-party response was not affected.
status of the recipients' lymphocytes were evaluated and different genes in the spleen lymphocytes between the two groups were identified with gene chips (Oligo rat gene library, Qiagen Company). The difference expression ratio less than 0.5 or more than 2.0 was deemed significant (Ratio=experiment/control).

Results: The SEB-treated group could prolong the survival time of the allo- grafts significantly. The proliferation ability of lymphocytes and the DTH (Delayed-Typer Hypersensitivity) degree was significantly weakened. Gene chips showed there were mainly 23 different genes between the two groups. The genes have an extensive distribution: some were involved in the nervous system, some related to tumor growth and some to enzymes coding.

Conclusions: SEB could induce anergy in treating high-risk corenal trans- plantation. The different genes regulated by SEB lied in many systems. The function of the genes should be further studied.

PO-196 IMPACT OF TACROLIMUS EXPOSURE ON SUBCLINICAL REJECTION 3 MONTHS AFTER RENAL TRANSPLANTATION
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Background: At present, there are no prospective studies relating steady- state tacrolimus dose-interval exposure to subclinical acute rejection (SAR).

Methods: A total of 32 Caucasian kidney allograft recipients, all treated with the combination of mycophenolate, mycophenolate motil and corticosteroids, under- went a percutaneous allograft protocol biopsy 3 months after transplanta- tion. Tacrolimus exposure (expressed as AUC0-12) was measured simultane- ously, using a validated abbreviated 4-hour sampling equation. The biopsies were scored by a blinded pathologist according to the Banff 1997 criteria.

Results: SAR was seen in 6/32 (18.75%) of patients. 60% of patients (3/5) with a tacrolimus AUC0-12 < 151 ng.h/mL (mean AUC0-12 134±16) had SAR on protocol biopsy 3 months after transplantation, while only 11.1% of patients (3/27) with a tacrolimus AUC0-12 > 151 ng.h/mL (mean AUC0-12 199±33) met the criteria for SAR (Fisher's exact test p=0.0342). Corresponding tacrolimus trough levels (mean C0 respectively 7.5±5.1 and 11.5±6.2 ng/mL; Wilcoxon p=0.0006) and tacrolimus Cmax (mean respectively 19.8±3.4 and 31.0±10.7; Wilcoxon p=0.0256) differed significantly between the respective AUC0-12 so- horts. Tacrolimus trough levels per se could however not differentiate between absence/presence of SAR. Except for the mean HLA mismatch (4.2±1.3 and 2.6±1.4; Wilcoxon p=0.0364), no other variables differed between groups (donor and recipient sex, donor and recipient age, PRA, cold ischemia time, operation time, delayed graft function, creatinine, proteinuria, immunosuppres- sant and corticosteroid dose).

Conclusion: This study suggests that steady-state tacrolimus exposure, mea- sured by abbreviated 4-hour concentration sampling, has an impact on the incidence of subclinical acute rejection at 3 months after transplantation.

PO-197 DISCONTINUATION OF CNI AND TAPERING OF MMF IMPAIRS THE CYTOTOXIC FUNCTION OF DONOR DIRECTED LYMPHOCYTES
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Patients with stable renal graft function were withdrawn from calcineurin in- hibitors (CNI) to receive 2x1 g/d MMF with 5-10 mg/d prednisone. Subse- quently, the MMF dose was tapered to 50%. MMF was not tapered in a control group. We questioned whether tapering of immunosuppression would af- fect T-cell reactivity. Before and after discontinuation of CNI and after tapering only 2/18 patients. Detectable num- ber of T-cell reactivity. Before and after discontinuation of CNI and after tapering only 2/18 patients. Detectable num- erate T-cell reactivity. Before and after discontinuation of CNI and after tapering only 2/18 patients. Detectable num-

Conclusions: SEB could induce anergy in treating high-risk corenal trans- plantation. The different genes regulated by SEB lied in many systems. The function of the genes should be further studied.

PO-198 CONVERSION FROM CYCLOSPORINE TO TACROLIMUS IN KIDNEY TRANSPLANT PATIENTS WITH HYPERLIPIDEMIA IS RELATED TO AN IMPROVEMENT IN CARDIOVASCULAR RISK PROFILE
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The aim of this prospective and multicenter study was to evaluate the effect of the conversion from cyclosporine (CsA) to tacrolimus (Tac) on cardiovascular risk factors in stable kidney transplant patients with hyperlipidemia. Twenty six patients were included being switched from CsA to Tac at 81±4.5 months after transplantation. Tac was started at 0.15 mg/kg/day. Patient outcome was evaluated up to 6 months after conversion.

Systolic blood pressure significantly diminished after conversion (143±13 baseline vs 136±6 mmHg at 6 months, p=0.028), as well as the need for antithy- pernseptive medication, with no changes in diastolic blood pressure. There was a significant reduction in total cholesterol (247±41 baseline vs 221±35 mg/dl at 6 months, p=0.003), LDL cholesterol (150±24 baseline vs 127±27 mg/dl at 6 months, p=0.001), total cholesterol/HDL-cholesterol ratio (4.5±1 baseline vs 3.9±1 at 6 months, p=0.02) and triglyceride levels (228±175 baseline vs 148±71 mg/dl at 6 months, p=0.026). No significant modifications in HDL- cholesterol, Apo A and Apo B levels, nor in the need for lipid-lowering med- ication were observed. Blood pressure and plasma lipids were significantly improved at 6 months in 11 patients, while no modifications were observed in the 15 remaining patients. In conclusion, elective conversion from CsA to Tac in stable kidney transplant patients with hyperlipidemia was related to a reduction in systolic blood pressure and total cholesterol levels, which determined an improvement in the Framingham risk score.

PO-199 THE IMMUNOREGULATORY CYTOKINES EFFECT ON FETUS AS AN ALLOGRAFT
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FETUS AS AN ALLOGRAFT

The mammalian fetus, will express paternally inherited antigens that are al- logeneic to the mother. Nevertheless fetuses are not normally reject by the mother. An understanding of how the fetus escapes the maternal immune sys- tem may be relevant for the prevention of rejection in transplantation. It has been suggested that the same immunosuppressive cytokines contribute to successful pregnancy and transplantation. Recent reports suggest a role for Transforming growth factor beta (TGF-β) in the generation of T-regulatory lym- phocytes. On the other hand interleukin-12 (IL-12) is the unique stimulator of differentiation of T helper lymphocytes (Th) to Th1 cells. This study was car- ried out in 70 pregnant women in the 21-36 weeks, gestation, and 32 healthy non-pregnant controls. The ELISA method was used for estimation of TGF- β1 and IL-12 in serum from all cases. The results showed that TGF-β1 is present in high concentration in all pregnant women compared with the non- pregnant controls. No significant differences in expression of IL-12 was found in pregnant women compared with the controls. The results suggest that: (1) the cytokine milieu of the placenta plays to play a critical role in the mater- nal acceptance of the fetus. (2) TGF-β1 may function as a regulatory factor in fetal alloagraft survival during pregnancy.

PO-200 ONE YEAR RESULTS OF TOLERIZING PROTOCOLS WITH CSA, MMF AND 4 DAYS OF PRENISONE: DOES THE TYPE OF ANTIBODY MAKE ANY DIFFERENCE?
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We studied the efficacy of Simulect (Sim), and Thymoglobulin (Thymo) on non sensitized primary cadaver renal transplant recipients subjected to tolerizing protocols using short course of steroids(Pr), CSA and MMF.

Methods: Single center retrospective study of 147 consecutive patients trans-
planted from May 2001 to December 2003. Group I (n=52) CSA + MMF + P. Group II (n=31) received additional Sim. Group III (n=30) received Sim + CSA + MMF + 4 days of P. Group IV (n=34) patients under 60 years without diabetes, heart and vascular disease received Thymo + CSA + MMF + 4 days of P. One year admissions and re-admissions were captured from ICD-9 codes, finance department records and house labs. Charges were expressed in 2004 dollars. Chi-square was used to analyze categorical data, ANOVA for continuous data and Kaplan-Meier for rejection and graft survival. Data is expressed as mean ± SD.

Results: The 4 groups are similar with regards to donor and recipient age, gender, race, cold ischemia time. Other findings are:

| Group | Admission | Re-Admission | DGF | Rejection | PS | GS | Charges |
|-------|-----------|--------------|-----|-----------|----|----|---------|
| I     | 6.9±3.9   | 7.8±3.8      | 40.4| 45.3      | 96.2| 94.2| 131,226 |
| II    | 7.7±3.3   | 3.1±3.1      | 35.8| 38.7      | 96.6| 93.3| 120,672 |
| III   | 8.2±3.6   | 6.4±3.2      | 40.0| 19.4      | 96.7| 97.6| 141,649 |
| IV    | 6.8±2.1   | 5.1±2.5      | 35.5| 36.5      | 97.1| 91.2| 130,511 |

No significant difference was seen between these groups.

Conclusions: The use of antibiotics has not improved the primary and re-admission LOS, rates of delayed graft function, rejection, patient and graft survival and charges at one year. Long term follow up is necessary to assess patient and graft survivals under these tolerizing protocols.

PO-201 THE EFFECT OF FK778 ON ACUTE RAT RENAL ALLOGRAFT REJECTION AND PDGF EXPRESSION

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Background: Acute rejection is the single most important risk factor for the subsequent development of chronic allograft nephropathy (CAN). Platelet derived growth factor (PDGF) is a major mitogen mediating mesenchymal cell proliferation in CAN. FK778, is a new promising immunosuppressive drug. Here we investigated the effect of FK778 on acute rejection and PDGF expression both alone and in combination with cyclosporin A (CsA) or tacrolimus (Tac).

Methods: Kidney transplants were performed from DA to WF rats and syngenic controls were performed between DA rats. Allografts were immunosuppressed either alone with FK778 (5, 10 or 20 mg/kg/d po) or with CsA (1.5 mg/kg/d sc) or Tac (1.5 mg/kg/d po). Grafts were harvested on day 3 for histology and immunohistochemistry (PDGF-A, -B, PDGFRα, -β).

Results: No acute rejection was seen in syngenic grafts. FK778 ameliorated inflammatory response in a dose dependent manner both alone and with Tac or CsA. Tac with FK778 10 mg/kg-dose decreased inflammatory response at the level of syngenic grafts whereas with CsA a 20 mg/kg-dose of FK778 was required for the same effect. FK778 together with calcineurin inhibitors showed synergy, which was stronger with Tac than with CsA. FK778 also decreased PDGF expression in a dose dependent manner and combination with CsA or Tac decreased expression more than FK778 monotherapy.

Conclusions: Our results demonstrate that FK778 is a potent immunosuppressive drug having synergistic effect with calcineurin inhibitors. This synergy seems to be stronger with Tac. Our data also shows that FK778 decreases PDGF expression suggesting FK778 to be a promising therapy for CAN.

PO-202 THERAPEUTIC APPROACHES TO ACUTE ONGOING REJECTION: LONG TERM RESULTS

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To determine clinical outcome in pts. with continuing cardiac acute rejection (CAOR) treated with two protocols, records of 110 patients (pts.) operated between 1994 and 1999 were reviewed. May 1994 to December 1999 110 pts. had OHT. Analysis revealed that 24 pts. (21%) had higher occurrence of acute rejection (5.4± 0.2eppt/pts. vs. the remaining 86 pts. (6.02 ± 0.06 eppt/ p.v. 0.003). Eleven pts., Group1, had CyaA, Methotrexate 5 mg/week and Prednisone), while 13 pts., Group2, FK506, MMF and Prednisone. No difference was found neither in sex, nor age nor indication for OHT distribution. Acute Rejection dropped in G1 from 5.3 ± 0.07 to 0.62 ± 0.03, while in G2 from 5.7± 0.02 to 7± 0.07 p<0.008. Overall 10yrs. survival was 83% and 83% in G1 vs. 84% in G2.p.v. n.s. Nobody died of AR. Two pts. (1 G1 and 2 G2) died 12 mos. after HTX due to B lymphoma and Curvularia infection. Chronic rejection was responsible of 1 G1 and 1 G2 pts. death, p.v. n.s. Two and seven infective episodes requiring hospitalization were recorded on G1 and G2.p.v.0.005. Annual angiographic revealed chronic rejection in 7/1 1G1pts. (63%) vs. 6/13 (46%) G2 pts., p.v. n.s. Renal failure was found in G2 (8/13, 69%) vs. G1(4/11, 36%) p.v. 0.004 while neoplasia G4 pts. 36% vs. G2 1/13, 8% G2 p.v. 0.004. CAOR is sensible to both therapies. MTX is linked to higher incidence of leucopoenia and neoplasia, while FK 506 and MMF intake lead to major infection occurrence. Chronic rejection is controlled in both protocols.

PO-203 MOFETIL MYCOPHENOLATE REDUCES THE FIBROSIS PROGRESSION RATE OF HCV RECURRENT IN LIVER GRAFTS

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Background: Mycophenolate (MMF) is known to have anti-fibrotic and antiviral effects. The Berlin group recently confirmed this finding in HCV+ liver transplant recipients.

Aim: To test this hypothesis in our HCV patients receiving MMF monotherapy.

Patients and Methods: Eighteen patients (MF 17/1, mean age 62.4 years, mean follow up from transplantation 6.3 months) were enrolled and followed prospectively, as part of a larger study in which MMF was introduced as rescue treatment from calcineurin-inhibitors (CNI, Cyclosporine A 15 cases, tacrolimus 3 cases) based-immunosuppression, having caused invalidating side effects. Primary endpoint of the study was the impact of MMF on graft histology. Fluctuation of cytolysis and cholestasis markers, as well as of HCV RNA was investigated.

Results: After a mean follow up of 24.8 (from enrolment) and 17.6 (from complete weaning off CNI) months, staging and grading improved (from 2.9 ± 1.2 at baseline to 2.3 ± 1 at last available biopsy, and from 4.2 ± 1.8 to 4.1 ± 1.5, respectively), despite statistical significance was not reached. Interestingly, the yearly fibrosis progression rate (FPR) was very low (0.07), similar to that registered in immunocompetent and tolerant patients (-0.3 and 0, respectively). Liver tests and HCV viremia did not significantly improve, except direct bilirubine (1.4 ± 0.8 vs. 0.8 ± 0.2, p = 0.03).

Conclusions: MMF positively impacts on HCV recurrence in liver grafts, via a marked reduction of FPR.

PO-204 IMPACT FACTORS ON RENAL FUNCTION AND GRAFT SURVIVAL IN CADAVERIC RENAL TRANSPLANT PATIENTS

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Purpose: Improvements in long-term cadaveric kidney graft survival have been described, though the reasons are unclear. Serum creatinine during the first year is a good predictor of long-term graft survival. This prospective study analyzed the variables impacting on renal function and graft survival in cadaveric renal transplant (CRT) patients during the first year.

Methods: A total of 2042 CRT patients were followed from January 2000 to December 2002 at 13 hospitals; 1449 treated with Tacrolimus (TaC) and 593 with Cyclosporin (CsA) with MMF+ F Multivariate analysis was performed using logistic regression and Cox model adjusted for variables known or suspected to impact on renal function and graft survival. Patient and graft survival for the study groups were computed by Kaplan-Meier estimates and test of equality survival curves were performed with the Log-Rank test.

Results: At one year post-transplant serum creatinine (1.48±0.54 vs. 1.70±0.64 mg/dL; p<0.0005; OR 0.66, 95% CI 0.51-0.85; p<0.0005), creatinine clearance-Cockcroft (58.5 vs. 47.9 ml/min.; p<0.0005), graft (92.2 vs. 88.8%; p=0.006) and patient (96.7 vs 95.7%; p<0.04) survival were significantly better in patients treated with TaC. Variables with a significant negative impact on graft survival were donor age, previous transplant, acute rejection, delayed graft function, renal function and proteinuria.

Conclusion: TaC has a significant impact on CRT results. CRT patients treated with TaC have a better renal function and graft survival than those receiving CsA.
PO-205 RENAL FUNCTION IN PATIENTS WITH CADAVERIC KIDNEY TRANSPLANTS TREATED WITH TACROLIMUS (TaC) OR CYCLOSPORIN (CsA). COMPARATIVE ANALYSIS
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Purpose: Comparison of TaC and CsA for renal transplant (RT) patients has led to great debate. Serum creatinine during the first year is the best predictor of long-term graft survival. We analyzed prospectively renal function in patients treated with TaC or CsA, with mycophenolate mofetil (MMF) and prednisone (P).

Methods: A total of 2042 cadaveric RT patients were followed from January 2000 to December 2002 at 113 hospitals, 1449 treated with TaC+MMF+P and 593 with CsA+MMF+P. Multivariate analysis was performed using logistic regression analysis adjusted for variables known to impact on renal function.

Results: At one year post-RT, patients treated with TaC had significantly lower serum creatinine levels than those treated with CsA. 1.48±0.54 vs 1.70±0.64 mg/dL (p<0.0005), with acute rejection (1.65±0.62 vs 2.02±0.83 mg/dL; p=0.0005) and recipients from donors older than 55 years (1.69±0.54 vs 1.85±0.68; mg/dL; p=0.002). Also, the percentage of patients with serum creatinine lower than 1.5 mg/dL was higher in those treated with TaC: total, 68.8 vs 39.2% (OR 0.52; 95%CI 0.43-0.65; p<0.0005) and recipients from donors older than 55 years, 61.7 vs 38.3% and 54.5 vs 45.5% (OR 1.34; 95%CI 1.12-1.60; p<0.001). Treatment with TaC was an independent risk factor for renal function (OR 0.66; 95%CI 0.51-0.85; p=0.001).

Conclusion: RT patients treated with TaC have a better renal function than those receiving CsA.

PO-206 INCIDENCE OF MALIGNANCIES IN HEART AND/OR LUNG TRANSPLANT RECIPIENTS – AN AUSTRALIAN EXPERIENCE
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Purpose: To determine the incidence and outcome of malignancies in heart and/or lung transplant recipients at The Alfred Hospital, and to compare this with the non-transplant general Victorian population.

Methods: Recipients of heart and/or lung transplants at The Alfred Hospital between February 1989 and January 2004 were cross-referenced with the Victorian Cancer Registry. The medical records of all patients with a cancer diagnosis before 1 January 2005 were reviewed to confirm the diagnosis and examine specific outcomes. Data on baseline demographics, including cancer type, stage, treatment received and survival were collected. The incidence of specific cancer types was then compared with the Victorian population based rates.

Results: 908 transplants (Tx) were conducted between February 1989 and 1January 2004: 425 heart Tx, 56 heart/lung Tx, 200 single lung Tx and 227 double lung Tx. The most common cancer diagnoses were non-melanoma skin cancer, lymphoproliferative disorders and non-small cell lung cancer. The complete data will be presented at the meeting.

Conclusion: Certain malignancies are more common following heart and/or lung transplantation, which in our cohort were non-melanoma skin cancers, lymphoproliferative disorders and non-small cell lung cancer. The outcome of heart and/or lung transplant recipients diagnosed with solid organ malignancies was very poor.

PO-207 SIROLIMUS (SRL) AND CYCLOSPORINE (CyA) COMBINATION: LOOKING BEYOND THE HIGH END
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RMR study showed benefits of high dose SRL (level 20-30ng/ml) however some patients cannot tolerate this dose. We evaluated our low risk patients who received low dose (L)SRL and low exposure (L)CyA. Low risk was defined by the absence of PRA, delay graft function or retransplantation. Subjects included denovo kidney recipients who received L-SRL, L-CyA, steroid (Gr1) and patients who were switched to L-SRL, L-CyA, steroid due to chronic rejection or HUS (Gr2). End points were acute rejection (AR) and change of serum creatinine. 26 patients were enrolled. 10 were Gr 1 and 16 were Gr 2. Median dose of SRL was 2.0 mg. For Gr 1 and 2, duration of SRL was 102 ± 74 and 38 ±18 weeks, SRL level (HPLC)was 7.2 ± 2.8 and 9.4 ± 2.9, CyA dose was 1.23 ± 0.29 and 1.10 ± 0.26 mg/kg/D. CyA level was 80 ± 37 and 68 ± 24. No patient developed AR. Final serum creatinine was 0.59 mg/dL for Gr 1, For Gr 2, mean serum creatinine before SRL was 2.22 ± 0.56 and improved to 1.84 ± 0.54 (p =0.04). MAP improved from 98 ± 6.8 to 91 ± 7.4 mm Hg. 24/26 patients required statin therapy (22/26 had HUS that required dialysis and change to MMF). Graft survival was 10/10. Other adverse events were proteinuria (n =2), squamous cell CA (n =1) and intestinal lung disease (n =1). We conclude that combination of L-SRL, L-CyA and steroid is effective and associated with good clinical outcomes.

PO-208 FK778: NEW CELLULAR AND MOLECULAR MECHANISMS OF ACTION
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FK778 is a malononitrilamide that inhibits T- and B-cell proliferation/function. Its most popular mechanism is the inhibition of the pivotal enzyme of pyrimidine biosynthesis. This report reveals new mechanisms of action on different cell types which are involved in acute and chronic allograft rejection. Brown-Norway rat-aortic-endothelial-cells (EC) were pre-treated with low or high-concentrations of FK778. Endothelial adhesion molecule expression (ICAM-1/CAM-1) was quantified by FACS-analysis/immunofluorescence and western blotting. Lewis rat-lymphocytes were incubated with FK778 and stimulated via TCR/CD28-signals. Uridine addition was used in all assays to reverse the pyrimidine-synthesis-blockade. Lymphocyte-EC-interaction was assessed by two different adhesion-assays. TNF-alpha-receptor-binding-assays were performed using radiolabelled TNF. SMC-proliferation and -migration were analysed in comparison to tacrolimus and sirolimus. TNF-alpha-stimulation and TCR/CD28-costimulation significantly increased EC-ICAM-1/CAM-exression and lymphocyte CD25-surface-expression, respectively. These effects were dose-dependently inhibited by FK778 and were not reversed by the addition of uridine. FK778 dose-dependently attenuated lymphocyte adhesion to EC in both adhesion assays. FK778 did not interfere with TNF-receptor-binding. The dose-dependent inhibition of SMC-proliferation by FK778 was abolished by uridine addition, whereas the inhibitory effect on SMC-migration was not affected by uridine supplementation. The latter effect was comparable to the sirolimus potency. FK778 directly reduces ICAM-1/CAM-1-up-regulation, inhibits lymphocyte activation, and attenuates lymphocyte-endothelium interaction, a critical early step in graft rejection. These effects can be separated from its blockade on pyrimidine synthesis and are not mediated via TNF-receptor blockade. The antiproliferative potency of FK778 on SMC may be an important mechanism to inhibit the fibroproliferative lesions of chronic organ rejection.

PO-209 THE INFLUENCE OF IMMUNOSUPPRESSIVE THERAPY ON THE DEVELOPMENT OF REGULATORY T (TR) AFTER RENAL TRANSPLANTATION
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Immunosuppressive drugs, which suppress the host immune system in a non-specific manner make a transplant recipient susceptible to infections and may also affect graft function. The ideal solution would be to make recipients tolerant towards donor antigens. Regulatory T cells (Tr) are essential for the induction and maintenance of transplantation tolerance. Various subpopulations of CD4+ cells, e.g. CD4+CD25+FoxP3, CD4+CD25+CTLA-4+ and CD4+CD25-CD122+ cells have been shown to have suppressive properties. In this study we have examined how immunosuppressive therapy influence the development of CD4+CD25+FoxP3, CD4+CD25+CTLA-4+ and CD4+CD25-CD122+ cells on patients after renal transplantation. The study was performed on renal allograft recipients with uneventful stable course. The patients have received immunosuppressive therapy: group I (Prednisone+Simulimus) and group II (Prednisone+CyA+Azathioprine). The central panel of the donors. We examined the surface expressions of CD4, CD25, CTLA-4, and CD122 in T cells from the peripheral blood of the renal allograft recipients. Flow cytometry was performed using FACS Calibur (Becton Dickinson). In our study we observed a significant decrease in percentage of CD4+CD25+ cells after re-

Immunosuppression / Acute Chronic Rejection
PO-210 DETERMINATION OF THE INOSINE 5’-MONOPHOSPHATE DEHYDROGENASE (IMPDH) ACTIVITY IN CD4(+) CELLS DURING MYCOPHENOLIC ACID TREATMENT FOLLOWING RENAL TRANSPLANTATION

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IMPDH catalyses the oxidation of inosine 5’-monophosphate (IMP) to xanthine 5’-monophosphate (XMP). This rate-limiting step in the biosynthesis of guanine/deoxyguanine nucleotides is an established target in immunosuppression following organ transplantation. Mycophenolic acid (MPA) is an IMPDH inhibitor that is widely used as co-immunosuppressant in rejection prophylaxis. Reduced production of guanine/deoxyguanine nucleotides retards the proliferation of activated lymphocytes. A method for the determination of IMPDH activity in CD4(+) cells was developed to assess MPA pharmacodynamics in renal allograft recipients. Paramagnetic polystyrene beads coated with anti-CD4 monoclonal antibody were utilised for the isolation of CD4(+) cells. The intracellular MPA concentration was restored by incubating the isolated cells in plasma separated from the original whole blood sample. Subsequently, plasma was removed and the maximal XMP formation rate was determined by a liquid chromatography-based method.

Adequate XMP production was achieved by incubating lyses of 200 000 - 400 000 cells in 120 minutes. Addition of IMP 1.79 mM and NAD 0.377 mM saturated the reaction kinetics. The XMP production versus incubation time showed linearity up to 240 minutes. Linear XMP formation rate was seen in the interval 0 - 8.70 pmol XMP/minute. Reproducible IMPDH inhibition profiles were observed during MPA exposure.

We have developed an assay for the determination of IMPDH activity in CD4(+) cells isolated from whole blood during MPA exposure and may improve the understanding of MPA pharmacodynamics in patient populations.

PO-211 KAPOSI’S SARCOMA IN TRANSPLANT AND IN HIV-INFECTED PERSONS: AN EPIDEMIOLOGICAL STUDY IN ITALY AND FRANCE

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Kaposi’s sarcoma (KS) in persons with HIV infection and in transplants.

Methods: 8074 HIV-positive persons and 2755 transplants (1844 kidney, 702 heart, 159 liver and 50 lung transplants) were followed up between 1970 and 2004. Standardized incidence ratios (SIR) with 95% confidence intervals (CI). Incidence rate ratios (IRR) were estimated by Poisson regression analysis.

Results: 356 KS cases were observed (317 in HIV-positive) and the overall incidence rate of KS was higher in HIV-positive (7.22/10^5 PYs) than in transplants (1.78/10^5 PYs). In comparison with the general population, KS was 451-fold more frequent in HIV-infected persons and 127-fold more frequent in transplants. In HIV-infected individuals, higher KS risks were observed in homosexual men (IRR=6.7, in France; IRR=6.7 in Italy), and increasing CD4+ cell counts were associated with reduced KS risks. Italian transplants born in the South had a 5-fold increased risk of KS. Moreover, KS occurred earlier in transplants (median=1.6 years) than in HIV-seroconverters (median=2.5 years).

Conclusions: Our findings suggest that type, duration and degree of immunosuppression are crucial risk factors for KS and that a high level of immunosuppression reached in a short time interval increased the chance of KS occurrence.
suppression (Group I = 25) were compared with earlier DKTs in recipients treated with CI-based therapy (Group II = 24). Patient and graft survival, surgical and medical complications, rejection episodes and renal function were retrospectively analysed.

Results: There were no deaths after a mean follow-up of 9.7±1.6 months (Group I) and 47.6±14.6 months (Group II). The graft was lost in one patient in Group I (due to bilateral renal vein thrombosis) and in 3 in Group II (1 PMN, 1 chronic rejection, 1 Kaposi’s sarcoma). The incidence of acute rejection was 20% in Group I and 17% in Group II. DGF was 16% and 54%, respectively. Renal function was better in Group I, with a mean S-Cr of 138±52 vs 210±141µmol/L at 1 month (p=0.04) and 120±31 vs 149±49µmol/L at 6 months (p=0.04).

Conclusions: A CI-free immunosuppressive regimen after DKT from elderly donors affords excellent results, with a lower DGF rate and better renal function.

LATE INTRODUCTION OF SIROLIMUS INDUCES ANEMIA OF INFLAMMATORY STATE IN RENAL TRANSPLANT RECIPIENTS

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Background: The responsibility of sirolimus (SRL) for post renal transplant anemia has never been proven, because SRL is usually combined with myelotoxic drugs, and because of the high incidence of anemia in the post-transplant period.

Methods: We retrospectively analysed anemia in 46 renal transplant recipients, who had been switched from calcineurin inhibitors to SRL for biopsy-proven chronic allograft nephropathy.

Results: The mean decrease in hemoglobin (Hb) after SRL introduction was 2.8 g/dl. The 26 patients, whose Hb fell by >= 2g/dl, displayed microcytic anaemia with low serum iron despite high ferritinemia, consistent with anemia of chronic inflammatory states. We subsequently focused our study on 8 patients without confounding factors of anemia. Anemia improved in all eight after SRL withdrawal. I6 and TNFα at the nadir of anemia were significantly higher than before SRL introduction and after its withdrawal. Decreasing in Hb correlated with rises in pro-inflammatory cytokine levels in a linear regression model. Unchanged serum IL10 levels measured at the nadir of anemia were discordant with the inflammatory state.

Conclusion: We conclude that, late introduction of SRL after renal transplantation, may induce anemia of chronic inflammatory states, possibly due to defective IL10-dependent inflammatory autoregulation.

THE EFFECT OF CYP3A4, CYP3A5 AND MDR-1 POLYMORPHISMS ON DOSE-ADJUSTED TACROLIMUS TROUGH LEVELS IN STABLE RENAL TRANSPLANT RECIPIENTS

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Tacrolimus is a widely used immunosuppressive drug with a narrow therapeutic index. Differences in P-glycoprotein, cytochrome P450 (CYP) 3A4 and CYP3A5 activity may alter its absorption and the rate of hepatic and intestinal metabolism. The objective of this study was to determine the role of CYP3A4, CYP3AS and MDR-1 polymorphisms on tacrolimus dose requirement and trough blood concentration. Stable renal transplant recipients receiving tacrolimus (n=92) were genotyped by PCR followed by restriction fragment length polymorphism analysis. Tacrolimus concentrations were measured by EMIT method. Dose-adjusted trough levels were determined at 1, 6 and 12 months after transplantation and correlated with the genotype. Of the 92 patients, the MDR-1 wild-type genotype (3435 CC) was observed in 28 patients, whereas 44 patients were heterozygous (3435 CT) and 20 patients were homozygous (3435 TT). The variant CYP3AS-1 allele was found in three of 92 patients. The number of the homozygotes patients for the CYP3AS*3 was 88, whereas 4 patients were heterozygotes (CYP3AS*3/*1). Tacrolimus trough levels were lower in patients with the variant CYP3AS-4 allele (p<0.05). Significantly lower tacrolimus dose-adjusted trough levels were found in patients carrying a CYP3AS*1 allele compared with patients with the CYP3AS*3/*3 genotype (p<0.05). Significant differences were also found for the tacrolimus doses in patients with different MDR-1 C1435T genotypes. Our findings suggest that genotyping for CYP3A4, CYP3AS and MDR-1 could contribute to a better individualization of immunosuppressive drug treatment.

PLASMAPHERESIS PLUS INTRAVENOUS HUMAN IMMUNOGLOBULIN AND RITUXIMAB IN TREATING ACUTE HUMORAL REJECTION – AN EFFECTIVE THERAPEUTIC APPROACH

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Previous sensitization to human leukocyte antigens (HLA) is a known risk factor for the development of acute humoral rejection. Furthermore, 30% of steroid-resistant acute rejections have been proven to be humoral related. The authors describe the clinical evolution and complications of three patients previously sensitized (previous kidney transplant) and the impact of the rescue therapy applied. All patients were diagnosed acute humoral rejection, presenting with graft dysfunction, anti-HLA specific antibodies and diffuse peritubular capillaries C4d deposition. The rescue treatment protocol included daily plasmapheresis (PMF) sessions with administration of intravenous human immunoglobulin (IVIG). Rituximab was administered as a single dose immediately after PMF. Immunoglobulin was later administered for two occasions. All patients maintained an immunosuppressive regimen that included mycophenolate mofetil plus tacrolimus and all received anti-lymphocyte induction therapy. After initiating treatment with PMF and IVIG, a rapid diuresis recovery was observed with a slower improvement of the graft function. Although this protocol achieved a rapid decrease in the anti-HLA antibodies, rituximab allowed those levels to remain low, allowing host accommodation and endothelial phenotype modification to occur. In all patients, the graft biopsies made after treatment showed no signs of humoral rejection. Although this therapy showed very good results, only one graft remains functional after 6 months transplantation with a serum creatinine level of 1.2mg/dl. The other two patients lost their graft due to causes related to hemodynamic and late surgical complications but not to acute humoral rejection. This therapeutic strategy showed to be highly effective in treating acute humoral rejection, allowing 100% graft survival, at least in the short-term.

AN EARLIER STEROID WITHDRAWAL USING LOW DOSE MYCOPHENOLATE MOFETIL DECREASE DELAYED/REFRACTORY ACUTE REJECTION IN ADULT LIVING DONOR LIVER TRANSPLANTATION

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Adult LDLT has an inevitable and unique complication named small for size syndrome (SFS). We investigated whether Mycophenylate mofetil (MMF) has beneficial effects as a less bone-marrow suppressive agent in Adult LDLT. [Method] Forty eight adult LDLT recipients who could be followed more than 1 year, were studied. The recipients divided into two groups by administration of 20mg/kg/day MMF. Group 1(n=23): CNI + Steroids + MMF; Group 2(n=25): CNI + Steroids. The incidence of delayed or refractory acute rejection was significantly lower in group1 (p<0.05). Twelve and 18 months steroid withdrawal rates in Group 2 was significantly higher than those in group 1 (65%, 85% vs 26.3%, 47.4%, p<0.05). In Group 1, AZ was discontinued in 5 cases by leukocyteperia derived from SFS whereas no recipient dropped out from MMF protocol. [Conclusion] Triple regimen including low dose MMF, safely administered to adult LDLT recipients, induces earlier withdrawal of steroids and decrease infection associated death of the adult LDLT recipients.

DO HLA ANTIBODIES INDUCE TRANSPLANT GLOMERULOPATHY?

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The influence of humoral rejection in the development of chronic allograft nephropathy is actually controversial; specially transplant glomerulopathy.
The aim of our study was to analyse the influence of post-transplant HLA antibodies on the development of transplant glomerulopathy (c0, c1, c2g and c3 Banff’97). We selected renal transplant functioning for at least 6 months (1975-2003), which had chronic glomerular changes in a clinically indicated biopsy showing chronic allograft nephropathy (case group). We studied the presence of anti-HLA antibodies (Ab) in the last serum with functioning graft, and divided them into 3 groups according to the severity of glomerular lesion. We also selected 52 cases without transplant glomerulopathy (control group). A total of 77 specimens had transplant glomerulopathy, 39 c0g, 29 c2g and 9 c3g. Results on pre and posttransplant HLA Ab are shown in the following table.

| PRA at TX (%) | Maximum PRA (%) | Posttransplant Ab | Type I Ab | Type II Ab | Type III-IV Ab |
|--------------|----------------|-------------------|-----------|-----------|---------------|
| c0g (52)     | 3.3 ± 12.4     | 7.7 ± 16.8        | 8 (15.3%) | 2 (25%)   | 4 (50%)       |
| c1g (39)     | 5.7 ± 13.9     | 16.5 ± 24.4       | 13 (33.3%)| 4 (12.5%) | 6 (15.3%)     |
| c2g (29)     | 11.1 ± 46.6    | 7.6 ± 10.6        | 7 (24.1%) | 1 (4.2%)  | 2 (6.9%)      |
| c3g (9)      | 10.1 ± 12.5    | 26.8 ± 27.6       | 6 (66.6%) | 3 (50%)   | 1 (16.7%)     |

According to our experience the presence of HLA Ab is a key factor in the development of transplant glomerulopathy and chronic allograft rejection.

### PO-220 CAN FLOW-CYTOMETRY IMPROVE THE ACUTE REJECTION DIAGNOSIS OF RENAL ALLOGRAFTS?

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**Introduction:** The mean half-life of renal allograft is reducing under acute rejection episodes. Renal biopsy is the golden standard in rejection diagnosis, but isn’t always possible. There are screening laboratory and ultrasonographic investigations for graft function but are also some flow-cytometric panels from peripheral blood and urine that can provide significant data for graft function.

**Objective:** To assess a flow-cytometric panel in combination with creatinine levels and Doppler parameters in attempt to evaluate graft function.

**Methods and Methods:** We prospectively investigated 20 consecutive renal allograft recipients with acute rejection suspicion between March 1 2003 and August 1 2003. They were living-donor recipients with triple immunosuppression therapy; similar cold/warm ischemia time, the same reperfusion solution, without DGF, and similar blood pressure and atherosclerotic lesions. The panel for flow-cytometric investigation included CD45-FITC, CD14-PE, IgG1-FITC, IgG2-PE, CD3-FITC, CD4-PE; CD8-PE, CD19-PE and CD16-56-PE.

After the laboratory analyses (serum creatinine level, calcineurin inhibitors level, and t-half-life) were completed, patients were further investigated with this panel.

**Results:** The better correlation (95%) with the graft function was for the triad of CD3+CD4+CD3-CD8+ outside of the normal range for graft age with the rise of serum creatinine level and rise of RI Doppler index. Important findings were the alteration of monitoring panel even before marked clinical events occurred and some particular modification in other pathological cases than acute rejection.

**Conclusion:** Further studies will be needed but such a panel provides a quick and noninvasive method to achieve valuable information for graft function.

**PO-223 OLDER RECIPIENTS OF RENAL ALLOGRAFTS DEMONSTRATE A STRONG IMMUNE RESPONSE IN THE EARLY PERIOD AFTER TRANSPLANTATION**

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Increasing demands for organ transplants in parallel to demographic changes are reflected by the utilization of organs from older donors and the enrollment into older recipients. Age-adapted immunosuppressive protocols are currently debated controversially.

63 renal allograft recipients were followed from 04/04-11/04. Patients ≥65 years (66/8±21) of the European-Senior-Program (ESP) receiving kidneys from donors ≥65 (69±3) were compared to recipients ≥65 (49±19±42) of kidneys from donors ≤65 (46±10±; ≤0.0001). Age-dependent immune response was analysed on day 0 (pretransplant) and day 7 (FACS, CBA, ELISPOT). Patient survival was 100% in both groups. Graft function was 100% for the younger vs. 78% in the elderly population (2 grafts with early acute rejections). Cold ischemia was significantly shorter in the ESP group (7.5±2.8 vs. 12.3±3.4 hours, p≤0.01). Immunosuppressive treatment was comparable in both groups. Recipients ≥65 demonstrated elevated numbers of memory T-cells after transplantation while amounts of naive T-cells were reduced (CD45RO+: 66.6±6% vs. 53.3±3% and CD45RA+: 22.4±14% vs. 35.3±3%; p≤0.05). Numbers of T-reg had decreased with increasing age (CD4+CD25+: 0.4±2.2% vs. 0.1±0.2% vs. ≤0.2% vs. ≤0.05). Serum levels of TNF-α, IL-10 were elevated in elderly recipients. Cytokine levels of TNF-α, IL-10 were elevated in elderly patients (TNF-α: 636±163 vs. 116±19 pg/ml, p≤0.01; IL-10: 73±22 vs. 46±6 pg/ml, p≤0.05). The increase in alloreactivity from day 0 to 7 was significantly more pronounced in older recipients.

Our data demonstrate an initially pronounced immune response in elderly recipients and support the concept of a potent immunosuppression in the early posttransplant period.
Lymphocyte's Phenotype Following (CTLA4-Ig) LEA Treatment, A Second Signal Blocker, in Patients Receiving Renal Allograft Transplantation

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Aims: Experiments in rodents but not in primates have shown that CTLA4-Ig may induce allograft tolerance. LEA have been used to prevent allograft rejection in human.

Methods: This study is to describe lymphocyte profile and the possible expansion of regulator T cells 6 months after transplantation. 28 patients enrolled in the LEA phase II study have been studied. They were receiving LEA, mycophenolate mofetil and steroids (LEA group) and 10 Neoral, mycophenalate mofetil and steroids (CTRL group) patients.

Results: The number of T lymphocytes and the percentage of CD3+ T cells were similar in both groups. However, the percentage of CD3+ CD4+ T cells was lower in LEA group than in Ctrl group (52.9% ± 9 vs 42.5% ± 13.7; p < 0.0005) and the percentage of CD3+ CD8+ cells higher (32.9% ± 6.7 vs 19.5% ± 8.2; p < 0.0002). The percentage of CD19+ cells were similar in both groups. CD8+ CTLA4+ cells were higher in the LEA group than in CTRL group (3.6% ± 1.7 vs 2.3% ± 0.8; p < 0.0002).

Conclusion: Our results indicates that LEA does not induce regulatory T cells in human. Further studies are needed to evaluate the role of both CTLA4-Ig and OKT3 in the development of regulatory T cells.

TACROLIMUS INDUCED NEUTROPENIA AFTER RENAL TRANSPLANTATION

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Neutropenia commonly occur after renal transplantation (RT) and is mainly related to viral infections or drugs. Conversely to the well-established haematological toxicity of the purines synthesis inhibitors (azathioprine or mycophenolate mofetil (MMF)), calcineurin inhibitors usually have an excellent haematological tolerance. Herein, we report two cases of neutropenia after renal transplantation which were definitively cured after tacrolimus (FK) withdrawal.

Observation 1: A 67 years old patient received a first cadaver renal transplantation which were definitively cured after tacrolimus (FK) withdrawal, and the absence of other cause of neutropenia suggest the responsibility of tacrolimus.

Observation 2: A 43 years old patient underwent a second cadaver renal transplantation under a sequential immunosuppressive regimen associating basiliximab, FK (0.2 mg/kg/d), MMF, and steroids. After 3 months he developed severe neutropenia (100/mm^3). The viral screening (CMV, EBV, HHV6) remained negative. Despite MMF withdrawal, neutropenia persisted requiring the recurrent use of granocytes-colony stimulating factor. Neutrophilic antibodies were negative. A bone marrow biopsy performed confirmed a central neutropenia and osteomyelitis. The patient was progressively switched from FK to sirolimus. After a complete FK withdrawal, the neutropenia definitively disappeared.

Conclusion: We report two cases of neutropenia after renal transplantation which were definitively cured after tacrolimus withdrawal due to its immunosuppressive role of pharmacologically applied tetrahydrobiopterin.

TETRAHYDROBIOPTERIN COMPOUNDS PROLONG ALLOGRAFT SURVIVAL INDEPENDENTLY OF THEIR EFFECT ON NITRIC OXIDE SYNTHASE ACTIVITY

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Purpose: The 4-amino analogue of tetrahydrobiopterin, a novel, selective inhibitor of inducible nitric oxide synthase, has been shown to prolong survival of murine cardiac allografts comparable to high-dose cyclosporin-A (CsA) treatment.

Methods: To further elucidate the underlying molecular immunosuppressive mechanism, we compared the effect of 4-amino tetrahydrobiopterin with that of the unsubstituted parent compound tetrahydrobiopterin and of N6-(iminoethyl)-L-lysine (L-NIL), a non-competitive inhibitor of inducible nitric oxide synthase using a murine cardiac transplant model. We observed allograft survival, intragraft gene expression by microarray analysis and real-time polymerase chain reaction, graft nitrotyrosine staining by immunofluorescence and plasma nitrite plus nitrate levels by high performance liquid chromatography.

Results: Graft survival was significantly prolonged by pterins and CsA, but not by L-NIL, although impaired plasma nitrite plus nitrate levels confirmed nitric oxide synthase inhibition in vivo. As compared to allogeneic untreated controls, intragraft peroxynitrite formation and hence nitrotyrosine staining was significantly lowered in all groups except in CsA-treated animals. Gene expression profiles obtained by microarray analysis identified several candidate genes like insulin-like growth factor-1 (IGF-1), CD163, proteasome (prosome, macropain) subunit, alpha type 6, or the inhibitory receptor NKR-P1D that might be responsible for the potent immunosuppressive features of tetrahydrobiopterin compounds.

Conclusions: These results demonstrate that the tetrahydrobiopterin structure rather than the nitric oxide inhibitor action is responsible for the immunosuppressive effect of 4-amino tetrahydrobiopterin and describe a novel, potent immunosuppressive role of pharmacologically applied tetrahydrobiopterin.

COMPARATIVE OF TWO IMMUNOSUPPRESSION REGIMENS BASED ON DACLIZUMAB IN NON-HEART BEATING DONOR KIDNEY RECIPIENTS

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Immunosuppressive regimens using reduced dosage of calcineurin inhibitors are desirable on renal transplant recipients from non-heart beating donor in order to minimize delay graft function (DGF). We have compared two immunosuppressive regimens based on low-dose tacrolimus, MMF and steroids plus daciuzumab 1 mg/kg (group 1D) or 2 mg/kg (group 2D) given as induction therapy. Weeky graft biopsies were performed during the period of delay graft function. Periperal blood CD4+, CD8+ and CD25+ T lymphocytes were accounted on day 7, months 1 and 6 post-transplantation. 104 renal transplants were analysed: 62 patients in group 1D and 42 in group 2D. Group 2D patients exhibited a deeper reduction on CD25+ TL on day 7 (2.34 ± 0.15 10^5/L vs 4.06 ± 7.13 10^5/L, p < 0.06). 1 month CD25+ TL were significantly higher on group 2D and CD4/CD8 ratio was persistently higher on group 2D. Biopsy proved acute rejection Banff grade IIb or more occurred in 12 patients on each group (21.8% group 1D, 34.3% group 2D, p=0.05), however DGF was similar in both groups. Graft function estimated by serum creatinine was significantly better on group 2D at 1 and 6 months post-transplantation: 1D: 3.0 ± 1.6, 1.9 ± 0.5, 1.8 ± 0.5 mg/dl vs 2D: 2.4 ± 0.5 mg/dl (p < 0.01).

We conclude that induction with daciuzumab 2 mg/kg results on significantly improved renal function compared with 1 mg/kg.
**PO-229 EVEROLIMUS WITH REDUCED-DOSE CYCLOSPORINE VS. MYCOPHENOLEATE MOTEFIL IN FULL DOSE CYCLOSPORINE: A EUROPEAN HEALTH ECONOMIC PERSPECTIVE IN DE NOVO RENAL TRANSPLANT RECIPIENTS**

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**Objective:** To compare the economic impact of everolimus 1.5mg with reduced-dose cyclosporine (CsA) vs. mycophenolate mofetil (MMF)g2 and with full-dose CsA in de novo renal transplant recipients.

**Methods:** In a previous trial (B201) using full-dose CsA, everolimus and MMFg2 showed similar economic outcomes. One-year direct medical costs (excluding everolimus, CsA and MMF) were mostly dependent on key clinical events: hemodialysis, length of stay (LOS) due to adverse events (AE) or infection (INF), biopsy proven acute rejection (BPAR) and days on cytomegalovirus (CMV) therapy. A subsequent trial of everolimus with reduced-dose CsA demonstrated similar efficacy (A2306). This later trial did not record resource utilization. We fitted a multivariate model on the B201 data to predict direct medical costs and applied the coefficients to the A2306 data.

**Results:** In France, incremental costs were €544 per hemodialysis session (p<0.001), €635 per day of AE hospitalization (p<0.001), €656 per day of INF hospitalization (p<0.001) and €7,881 per BPAR (p<0.001). After adjusting for recipient age, living donors, and CMV treatment between B201 and A2306, everolimus with reduced-dose CsA decreased 1-year costs (excluding CsA, MMF and everolimus) by €2,845 vs. MMF with full-dose CsA. Higher potential savings were found in Germany (€3,259) and Austria (€3,841), and lower savings in Belgium, Spain and Italy: €1,696, €1,524, and €1,461 respectively.

**Conclusion:** In this population, everolimus 1.5mg with reduced-dose CsA shows potential cost-savings as compared to a MMF-based regimen. Further prospective analyses are recommended to document the cost-saving of everolimus 1.5mg.

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**PO-230 INTERIM RESULTS OF A 12-MONTH STUDY WITH ENTERIC-COATED MYCOPHENOLEATE SODIUM (EC-MPS, MYFORTIC), BASILIKIMAB, AND NEORAL C-2 COMPARING DIFFERENT CORTICOSTEROID PROTOCOLS IN DE NOVO KIDNEY RECIPIENTS**

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The aim of this 12-month, 3-arm comparative study was to evaluate three different steroid protocols: none; short term or maintenance in conjunction with EC-MPS 720mg b.i.d., Neoral C2 cyclosporine monitored, and basiliximab in de novo kidney transplant recipients, as measured by calculated GFR. A 3-month interim analysis investigated the incidence of biopsy proven acute rejection (BPAR).

338 de novo primary kidney transplant recipients aged 18-75 were randomized to each of the groups (113, 117, 108). Interim analysis was performed after all patients completed 3 months' treatment or were lost to follow-up. BPAR rate was 6.5% in the standard arm, 24.1% in the steroid avoidance (P<0.001) and 19.0% in the steroid withdrawal arm (P=0.005, ITT population). ITT subpopulation (without DGF patients): 9.9% BPAR in the maintenance arm, 29.9% in the steroid free (P<0.006), and 15.6% in short term. Safety was comparable in the 3 arms. Lowest post-baseline creatinine values before and after occurrence of BPAR showed no worsening in 87.5% in the steroid free group, 50% in the short term steroid group and 25% in the standard steroid group. Interim 3-month results of this 12-month study showed that a regimen of EC-MPS with Neoral C2, basiliximab and steroids provided excellent BPAR rates. Data of the 12-month analysis are planned to be presented at the congress.
TOXIC TACROLIMUS BLOOD LEVELS WITH RIFAMPICIN ADMINISTRATION IN A RENAL TRANSPLANT RECIPIENT

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Induction of the hepatic cytochrome P450 3A4 system by rifampicin is difficult to be overcome in other drugs and require substantial increase in tacrolimus dose when given concurrently.

Case summary: A 24 years old lady had chronic renal failure due to membranous glomerulonephritis. She received kidney transplantation in 1988 complicated by chronic rejection, and a second renal transplant in 1993 which is functioning well. She was on prednisolone, azathioprin and tacrolimus. She has close relatives infected with tuberculosis. She was started on isoniazide prophylaxis in April 2002 and tacrolimus was maintained on therapeutic levels. She had chronic anemia, fever, night sweating, nausea, vomiting, chronic diarrhea, and loss of weight. Detailed investigations including multiple gatnsintestinal biopsies didn’t conclude definite diagnoses apart from mild gastritis. She was started on antituberculous treatment in November 2002(rifampicin, isoniazide, ethambutol, and pyrazinamide). She continued to have significant symptoms requiring multiple drugs to be controlled. She was getting omeprazole 20 mg twice daily, frequent doses of antacids(which decrease rifampicin absorption), metoclopramide(which inhibits tacrolimus metabolism), loperamide, acetaminophen and ondasetron hydrochloride. She had very high tacrolimus blood levels requiring successive dose reduction from 7mg/day up to 0.5mg every other day with rise of serum creatinine from 100 to 140µmol/l. Tacrolimus was changed to low dose sirolimus in April 2003 and renal function improved to its baseline.

Conclusion: Gastrointestinal disturbances and multiple drug administration may cause unexpectedly toxic tacrolimus levels even in presence of rifampicin. Combination of enzyme P450 inhibitors and low absorption of rifampicin may overcome its strong enzyme induction effect.

INTERACTION WITH TACROLIMUS: VORICONAZOLE DISTINGUISHES FROM ITROCONAZOLE

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Voriconazole, itroconazole and tacrolimus are drugs with extensive oxidative metabolism involving several cytochrome P450 isoenzymes. Both triazoles interact with tacrolimus, resulting in significantly elevated tacrolimus blood trough levels. We report a case of a 25-year-old tacrolimus-treated lung transplant, who was directly switched from itroconazole (100mg/day) to voriconazole (200mg/day). In this case itrocanazole was added 9 weeks before the switch and tacrolimus was reduced to 2mg/day at that time, leading to tacrolimus blood trough levels between 5.8-6.9ng/ml. Additional immunosuppression compromising mycophenolate mofetil (1g/day) and prednisolone (2.5mg/day). When itrocanazole was stopped, voriconazole was added the next day under the estimation that both drugs interact with tacrolimus the same. First day after the switch tacrolimus blood trough levels increased to 21ng/ml. The following 4 days tacrolimus blood trough levels decreased to 9-12ng/ml, but remained higher in comparison to the data before the switch. Tacrolimus dosage was not adapted during that time. The elevated tacrolimus blood trough levels after switch to voriconazole can be interpreted as an additive pharmacokinetic interaction of itroconazole and voriconazole with tacrolimus, because of the long elimination half-life time of itroconazole. In conclusion tacrolimus monitoring is required when voriconazole is added even when itroconazole therapy has finished and tacrolimus must be reduced after the switch.

C0 VS. C2 ADJUSTED CYCLOSPORINE IN DE NOVO KIDNEY TRANSPLANT PATIENTS; A PROSPECTIVE RANDOMISED SINGLE-CENTRE STUDY

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C2-based dosing of CyA has been promoted as improving the results of kidney transplantation (TX). No randomised, controlled studies in de novo patients have been published. Between June 2003 and August 2004, 160 consecutive cadaveric kidney TX patients allocated to CyA, MMF and steroids were randomised 1:1 to either C0 or C2 based dosing for the first 3 weeks after TX. Both C0 and C2 levels were measured, but the values of one method were blinded until 3 weeks. Initial CyA dose was 10mg/kg/day in both groups. Target C0 was 200-300 µg/L and C2 1500-2000 µg/L. From the 4th week on only C0 was used. Median follow up time was 337 days.

The clinical characteristics are in Table 1. CyA dose and C0- and C2-levels were nearly 50% higher in C2 group (p<0.00001). Delayed graft function (DGF) was similar but the length of oliguria in DGF was mean 2.7 days longer in C2 group than in C0 group. At 3 weeks the plasma creatinine tended to be higher in C2 group (N.S.). The overall rejection frequency was low, 8.3%, slightly higher in C2 group (10.5% vs. 7.5%). C2 based dosing of CyA led to much higher daily doses and higher blood levels than C0 based dosing. No advantages in TX results were achieved.
Effects of CYP3A5 and MDR1 Polymorphisms on Tacrolimus Pharmacokinetics After Renal Transplantation

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Background: Since 1994 Tacrolimus is used as an immunosuppressive drug after solid organ transplantation. Tacrolimus has a narrow therapeutic index but exhibits a broad inter-individual variability of pharmacokinetic characteristics, e.g. plasma half-life ranges from 4 to 50 hours. It is known to be a substrate of both, cytochrome P450 3A (CYP3A) as well as P-glycoprotein (P-gp), the product of the multidrug resistance (MDR1, ABCB1) gene. CYP3A5 is active in only 20% of the Caucasian population, thus explaining in part the variability of tacrolimus dose requirement, whereas the role of MDR1 polymorphisms is discussed.

Subjects and Methods: To investigate the significance of CYP3A5 and MDR1 polymorphisms to tacrolimus dose requirement in kidney transplant recipients and the clinical outcome we launched a prospective study enrolling 200 patients. Genotyping is carried out for CYP3A5*3A and MDR1 677G>T and 3435C>T using pyrosequencing technique. Tacrolimus trough plasma concentrations were determined by routine micro-particle immuno-assays.

Results: Preliminary results obtained from the first 36 patients, indicate that subjects having at least one active CYP3A5*1 allele, required significantly higher tacrolimus doses (mean 10.83 mg; P = 0.005). There was lack of evidence for an association of MDR1 polymorphisms and tacrolimus levels.

Conclusion: The data indicate the usefulness of the pharmacogenetic approach for individual dosage recommendation. The impact on the clinical outcome, however, needs to be further elucidated.

Comparative Study of Two Immunosuppression Protocols in Renal Transplantation: With and Without Calcineurin Inhibitors

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Purpose: To compare our results using two immunosuppression protocols: with and without calcineurin inhibitors.

Patients and Methods: In our department we started two different immunosuppression protocols in recipients of a renal allograft:

Protocol A - 62 patients started an immunosuppression protocol without calcineurin inhibitors consisting of basiliximab, sirolimus, mycophenolate mofetil and steroids.

Protocol B - 55 patients with a calcineurin inhibitor based immunosuppression: basiliximab, cyclosporine, mycophenolate mofetil and steroids.

We analyzed patient and graft survival, acute rejection episodes and renal function. There were no differences between the two groups in the characteristics of the recipients (such as age, sex distribution, weight) or the donor.

Results: See Table 1.

Results of the Protocols

| Protocol       | Immediate graft function | Acute rejection | Chronic Dysfunction | Graft Survival 1 year | Graft Survival 2 years | Graft Survival 4 years | Patient Survival 1 year | Patient Survival 2 years | Creatinine 1 month | Creatinine 1 year | Follow-up (years) |
|----------------|--------------------------|----------------|---------------------|-----------------------|-----------------------|-----------------------|-------------------------|-----------------------|------------------|----------------|------------------|
| Protocol A     | 77%                      | 37%            | 14%                 | 88.4%                 | 80.1%                 | 75.4%                 | 96.5%                   | 89.6%                 | 84.6%            | 1.5             | 1.3              | 1.8±0.9          |
| Protocol B     | 83%                      | 23%            | 20%                 | 88.6%                 | 84.6%                 | 84.6%                 | 94.1%                   | 94.1%                 | 89.9%            | 1.7             | 1.4              | 3.2±2.0          |
| P              | <0.05                    | NS             | NS                  | NS                    | NS                    | NS                    | NS                      | NS                    | NS               | NS              | <0.05            |

Conclusions: The two immunosuppression protocols have similar results in terms of immediate graft function, graft survival and renal function. Sirolimus based protocol has a higher frequency of acute rejection episodes but there is a lower chronic dysfunction. A longer follow-up is needed to see how it does influence the long-term graft function and survival.

Impact of Cytomegalovirus (CMV) Infection on Histopathology in Renal Allograft Protocol Biopsies

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Purpose: CMV seronegative recipients of renal allografts from CMV seropositive donors (seromismatched) have higher rate of acute rejection than other recipients. A relationship between CMV infection and chronic allograft nephropathy (CAN) has been demonstrated in animal studies although human studies using creatinine clearance as a surrogate for CAN found no association. Our objective was to determine if CMV seromismatching (D+R-) and/or CMV infection is associated with histological markers of CAN.

Methods: Retrospective single center study of all six-month transplant protocol biopsies from October 97 to March 04. Dependent variable was chronic allograft dysfunction index (CADI) score > 4. Exploratory variables were CMV seromatching, CMV infection and other donor and recipient variables potentially associated with the development of CAN. CMV infection was treated with IV gancyclovir. CMV seromismatched patients and CMV positive recipients receiving prophylaxis treatments also received prophylactic gancyclovir.

Results: 268 protocol biopsies were reviewed. 19% of biopsies were from recipients of CMV seromismatched kidneys. CMV infection prior to biopsy biopsy was diagnosed in 15.7% of recipients. CADI score > 4 was observed in 49.0% of CMV seromismatched recipients vs. 36.9% of others (p = 0.73). CADI score > 4 was observed in 35% of CMV infected patients vs. 35.7% of others (p = 1.0).

Conclusion: CMV seromismatch and CMV infection were not associated with a higher incidence of CAN on six-month protocol biopsy. Use of antiviral agents may explain in part the discrepancy between animal studies and human studies.

Tacrolimus and FK778 Prevent the Development of Obliterative Bronchiolitis Via Different Mechanisms

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Objective: In this experimental study we investigated the effectiveness of FK778 to prevent the development of obliterative bronchiolitis (OB) as a model of chronic rejection in comparison to tacrolimus.

Methods: Tracheae from Brown-Norway-donors were heterotopically transplanted in the greater omentum of Lewis-rats. Recipients were treated for 28 days with FK778 (5 or 20mg/kg), tacrolimus (1 or 4mg/kg) or combination regimens at varying doses (5±1mg/kg, 10±2mg/kg or 20±4mg/kg). Grafts were harvested and processed for histological and immunohistochemical evaluation (Trichrom Masson-Goldner/H.E., alpha-actin/PAS/C4D/CD6/CD5/ED1). Lymphocyte surface antigen expression was quantified and in vitro smooth-muscle-cell (SMC) proliferation assays were performed.

Results: In untreated recipients, huge amounts of infiltrating CD4+, CD8+ and ED1+ mononuclear cells were observed peritracheal with epithelial loss and complete luminal obliteration. Granulation tissue consisted of alpha-actin-positive cells and collagen-rich fibrosis. FK778 and tacrolimus as well as combination regimens of both agents dose-dependently inhibited peritracheal intiliration and luminal obliteration. Only tacrolimus treated recipients showed preserved luminal epithelial coverage with airway goblet cells, whereas in animals that received FK778 no epithelium was found. Both agents equally suppressed in vivo lymphocyte CD25-expression. PK778 but not tacrolimus showed potent antiproliferative effects on SMC in vitro.

Conclusions: Although both agents proved effective to prevent OB development, histology revealed major differences. The antiproliferative potency of PK778 on SMC may be an important mechanism of action. Combination regimens showed favourable drug interaction and allowed dose reduction of both agents to achieve maximal immunosuppressive efficacy.
Immunosuppression / Acute Chronic Rejection

**PO-242 OPERATIONAL TOLERANCE CORRELATES WITH THE INDUCTION OF REGULATORY T-CELLS: A 2-YEARS FOLLOW-UP OF THE WOFIE-PROTOCOL IN RENAL TRANSPLANT RECIPIENTS**

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**Background:** According to the WOFIE-concept we analyzed the effect of an 72 hours immunosuppressive window during the time of observation (10%) in the WOFIE vs. 40% in the control cohort, p<0.05). Whereas all but one of the WOFIE-patients could be stopped from steroids, 23.6% of the control had to be taken on steroids again. Serum creatinine levels were significantly lower in patients who received an immunosuppressive window. Six months posttransplantation WOFIE-patients revealed a lasting increase of CD4+CD25+ T-cells (15.4 % in the WOFIE vs. 5.7 ± 3.8% CD4+ T-cells in the control 2 years p. Tx, p<0.05) which strongly correlated with a significantly higher expression level of FOXP3-mRNA.

**Conclusions:** Initial interruption of immunosuppression (WOFIE) induced a significant increase of regulatory T-cells and allowed early and safe steroid withdrawal.

**PO-243 CALCINEURIN INHIBITOR (CNI) PHARMACODYNAMICS IN LIVER TRANSPLANTATION (LT)**

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Everolimus is a signal proliferation inhibitor studied for the prevention of transplant organ rejection.

**Material and methods:** Among 142 renal transplants performed between May 2000-January 2004, 20 were included in studies with Everolimus, Cyclosporin and Steroids (18-68 year-old patients, donors between 10 and 65, no previous transplants, negative HbsAg and HCV, no cardiovascular disease nor severe hyperlipidemia). An homogeneous control group of 31 patients in therapy with Cyclosporin, Mycophenolate Mofetil, Steroids and Basiliximab was selected.

**Results:** In the Everolimus group patients survival was 95% at 3 years, with 90% and 85% of actuarial graft survival at 1 and 3 years. In the control group patients survival was 86.5% at 3 years with graft survival rate of 87.1% (1 year) and 80.6% (3 years).

In the Everolimus group 10 patients (50%) presented BPAR 5 (25%) suffered from drug toxicity. In the control group 15 patients showed BPAR (48.3%), and 12 patients (38.7%) had drug toxicity.

Best creatinine mean level was 1.91 mg/dl in the Everolimus group vs. 1.81 mg/dl in the control. In the Everolimus group eight patient experienced severe hyperlipidemia vs no episodes in the control. No patient in the first group showed CMV, Herpes or other viral infections vs 9 patients in the control group. Eight patients of the Everolimus group suffered from de novo IFG or diabetes mellitus vs 5 in the control group.

**Conclusion:** Everolimus group showed better patients and graft survival rate, a reduced incidence of drug toxicity and the absence of viral infections, while a greater incidence of glvicidic and severe lipidic alterations were recorded.

**PO-244 THE EFFECT OF SEVELAMER ON TACROLIMUS TARGET LEVELS**

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We report on a 55 year old male patient who received his second kidney transplant because of recurrent IgA nephropathy in 1999. The graft function had been stable during the first years following the transplantation, with the immunosuppressive therapy consisting of tacrolimus, mycophenolate mofetil and low-dose steroid. Following cardiac surgery performed because of severe coronary artery disease and aortic stenosis, the patient was dependent on dialysis. In spite of a persistently low creatinin clearance the patient refused to return on a chronic hemodialysis program and was therefore kept on low doses of tacrolimus and steroid. Mycophenolate mofetil was discontinued. Sevelamer (Renagel®) was started because of a high calcium-phosphate product.

The oral medication was otherwise retained unchanged. Subsequently, a progressive decline in tacrolimus blood levels was observed. Target levels were measurable only temporarily in the context of further deteriorations of kidney function in spite of an increased tacrolimus dosage. Significant reductions in the peak level of tacrolimus (Cmax) and the area under the curve (AUC) after intake of one oral dose of 1.5mg tacrolimus were found when compared to tacrolimus kinetics in the same patient three days after discontinuation of sevelamer, with 0.9 vs 15.5 mg/ml and 4.02 vs 17.97 mg/ml.

AUC of hydroxychlorid is a non-adsorbable phosphate salt. It is known to reduce absorption of vitamin D, E, K and folic acid. Decreases in the peak concentration and AUC of mycophenolate mofetil were described. Data regarding the interaction with cyclosporine are controversial. This is the first time a decrease in tacrolimus blood levels with concomitant intake of sevelamer is reported.

**PO-245 EVEROLIMUS AND REDUCED DOSE CYCLOSPORIN VS STANDARD CYCLOSPORIN THERAPY IN RENAL TRANSPLANTATION**

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**Methods:** A Pharmacokinetic study: concentration-time curve (0-12 h) after the intake of one oral dose of 1.5mg tacrolimus were found when compared to tacrolimus kinetics in the same patient three days after discontinuation of sevelamer, with 0.9 vs 15.5 mg/ml and 4.02 vs 17.97 mg/ml. Whereas all but one of the WOFIE-patients could be stopped from steroids, 23.6% of the control had to be taken on steroids again. Serum creatinine levels were significantly lower in patients who received an immunosuppressive window. Six months posttransplantation WOFIE-patients revealed a lasting increase of CD4+CD25+ T-cells (15.4 % in the WOFIE vs. 5.7 ± 3.8% CD4+ cells in the control 2 years p. Tx, p<0.05) which strongly correlated with a significantly higher expression level of FOXP3-mRNA.

**Conclusions:** Initial interruption of immunosuppression (WOFIE) induced a significant increase of regulatory T-cells and allowed early and safe steroid withdrawal.

**PO-246 MYCOPHENOLATE MOFETIL (MMF) DOSE AND RENAL FUNCTION AFTER KIDNEY TRANSPLANTATION**

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MMF reduces acute rejection (AR) rate, but this could not fully explain its long-term results on graft survival. The relationship between the MMF dose and the long-term graft function has not been fully explored:We measured creatinine clearance(ml/min/1.73 m²) CrClL in patients receiving a cadaveric kidney graft between 1999-2003. Patients were divided in two groups according MMF doseday at Month 1: (M1) Group A (N=46) with 2 g Group B (N=36) with a lower dose (1.5 g in 24 patients and 1 g in 11). The same dosage was con-
INCIDENCE OF POST TRANSPLANT DIABETES MELLITUS WITH SIROLIUMS+CNI IMMUNOSUPPRESSION IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction: The new American Diabetes Association (ADA) criteria for diagnosing diabetes have allowed for the detection of previously unrecognized cases. This study evaluated the incidence of post transplant diabetes mellitus (PTDM) in kidney transplant recipients (KTx) immunosuppressed with sirolimus + calcineurin inhibitors (SRL+CNI), in comparison with cyclosporine (CsA).

Methods: One-hundred-eight consecutive KTx, performed at a single institution from 1997 to 2004 were evaluated. The incidence of PTDM was analysed in two groups according to immunosuppression: SRL+CNI (52 pts) and CsA (56 pts). Inclusion criteria: no pre-transplant treatment for diabetes, post-tx follow-up > 6 months, no conversion from initial immunosuppression. All pts received steroids during the first 6 months post-tx. Mean follow-up was 61.6 ± 23.2 months. PTDM and impaired fasting glucose (IFG) were defined according to the ADA criteria.

Results: Nineteen/108 pts (17.6%) were diabetic (8 IFG, 7.4%, 11 PTDM, 10.2%). PTDM treatment was started in 7/19 pts (6.5%), requiring insulin in 5 (4.6%), oral hypoglycemic drugs (OHD) in 2 (1.9%). PTDM incidence was higher in SRL+CNI (8/52 pts, 15.4%) compared to CsA (3/56 pts, 5.4%). IFG was similar in both groups (7.7% vs 7.1%, respectively). More patients required treatment in SRL+CNI compared to CsA (9.6% vs 3.6%, respectively); 4 pts (7.7%) became insulin-dependent in SRL+CNI, vs 1 pt (1.8%) in CsA. Use of OHD was similar in both groups (1.9% SRL+CNI vs 1.8% CsA).

Conclusions: The combination of SRL with CNI may increase the diabetogenic potential of CNIs. The high incidence of PTDM in the SRL+CNI combination may be explained as a sign of toxicity, due to the high CNI doses used in the early experiences with SRL+CNI.

IS THERE ANY RELATIONSHIP BETWEEN GLUCOCORTICOID RECEPTOR GENE POLYMORPHISMS AND GRAFT REJECTION IN PATIENTS AFTER KIDNEY TRANSPLANTATION?

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The aim of the study was to evaluate the frequency of polymorphic variants of GR gene (N363S and ER22/23EK, which determine various sensitivity to GC) and their relationship with transplanted kidney function and incidence of acute rejection. We have studied 100 KTx patients (68 treated with CsA, Aza/MMF and prednisone, 32 treated with Sirolimus, MMF and prednisone). Control group consisted of 104 healthy volunteers. GR variants were identified using the allelic discrimination assays.

Results: Six percent of KTx patients were heterozygous for N363S and 8% for ER22/23EK polymorphism. In the control group these values were 7% and 4% respectively. All the remaining KTx patients and controls were of wild type. In patients carrying N363S polymorphism 4 episodes of acute rejection occurred (66.7%) compared to 46% in wild types. The frequency of acute rejection was 37.5% in ER22/23EK carriers vs. 44.3% in the wild types. Serum creatinine level after first year was insignificantly higher in patients with N363S polymorphism in comparison to wild types (150 vs. 120 umol/L). There were no significant differences regarding age of recipients, donors, number of HLA A,B,DR mismatches between group of patients with gene polymorphisms and wild types.

Conclusions: Our data exhibits that N363S GR gene polymorphism is 3 fold less frequent in the renal transplant patients than in healthy population. The N363S and ER22/23EK polymorphisms in the GR gene do not seem to influence the incidence of acute rejection and kidney graft function.

FTY720 AND TACROLIMUS LONG-TERM ADMINISTRATION: EVALUATION OF RENAL AND BLOOD PARAMETERS

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Despite of the efficacy in prevailed acute graft rejection calcineurin inhibitors based immunosuppression causes renal toxicity. In opposite to CsA and FK506, FTY720 does not bind to calcineurin and does not prevent T cell proliferation/cytokine secretion. FTY720 may provide an opportunity for a reduction in calcineurin inhibitor dosage in transplant recipients with side effects, especially on renal toxicity. Therefore it was our aim to investigate whether FTY720 alone or in combination with FK506 could reduce renal toxicity and changes in leucocytes when administered for 21 days in mice. C57BL/6 mice were submitted to administration for 21 days of 1mg/kg/day of FTY720 and/or 2mg/kg/day of FK506. 24 hours urine, blood, and kidneys were collected for evaluation. Groups were analyzed by ANOVA. Table 1 shows that FTY720+FK506 combination had no effect at plasma creatinine and Na.

PO-250 FTY720 IMPAIRS ACUTE TUBULAR NECROSIS AND KIDNEY T CELL INFECTION AFTER ISCHEMIA-REPERFUSION (I/R) INJURY

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I/R injury is a common early feature in transplantation that can contribute for the kidney delayed function. Immunosuppressive drugs are harmful to renal function in addition to I/R. FTY720 is a new compound that has shown immunosuppressive properties without nephrotoxic effects. In order to investigate whether FTY720 could protect from I/R injury we submitted C57BL/6 mice to 30 minutes of bilateral renal vessels clamp. Mice were treated either with FTY720 (G1) or vehicle (G2) immediately before I/R. 24 hours urine, blood, and kidneys were harvested to evaluate renal function (creatinine Cr and sodium Na), and structure (percentage of acute tubular necrosis and T cell infiltration) at 3 and 7 days after I/R. Groups were analyzed by ANOVA test.

Infiltrating lymphocytes (x104) and area of acute tubular necrosis (%) in kidneys from C57BL/6 mice

Table 1. C57BL/6 mice evaluation after 21 days of FTY720/FK506 administration

| Groups | T cells (%) | Neutrophils (%) | Monocytes (%) |
|--------|-------------|----------------|--------------|
| Control | 70±4.0      | 13±2.0         | 3±0.5        |
| FTY720 | 32±4.0      | 50±5.0         | 15±3.0       |
| FK506  | 57±1.0      | 37±2.0**       | 6±1.0        |
| FTY720+FK506 | 68±4.0 | 68±1.4         | 13±7.0       |

p value <0.001 versus control; **P =0.015 versus control and FK506

However, there as a significant decrease at K plasma levels in this drug combination. Peripheral (blood) T cells presented a dramatic decrease in mice treated with FTY720+FK506, whereas neutrophils had a significant increase in the peripheral blood of the same group. No significant changes were observed in kidneys (histology) from all groups. Our data suggest that FTY720+FK506 combination is not nephrotoxic and probably acts preventing rejection by remotion of lymphocytes from peripheral blood.

FTY720 treated group presented an early recovery of renal function in comparison with vehicle treated group. Infiltrating T cells and acute tubular necrosis were improved in FTY720 treated group. Our results show that FTY720 could be protective against I/R injury.
**PO-251**

**EVALUATION OF RENAL FUNCTION AND STRUCTURE AFTER LONG-TERM ADMINISTRATION OF FTY720 AND/OR CYCLOSPORINE**

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Prevention of allograft rejection without the renal toxicity caused by calcineurin-inhibitors immunosuppression is the major goal to be achieved in transplantation. FTY720 is a synthetic drug that modulates immune responses in many animal models of transplantation, autoimmune disease, and ischemia-reperfusion injury. However, before its introduction in clinical transplantation there is still to be confirmed whether FTY720 has any nephrotoxic effect when administered continuously alone or in combination with CsA. In the present study FTY720 (1mg/kg) and/or CsA (10mg/kg) were administered for 21 days to C57BL/6 mice. 24 hours urine, blood and kidneys were harvested for creatinine (Cr)/sodium (Na)/potassium (K)/albumin (A) evaluation and histology.

**Table 1. Characteristics of C57BL/6 mice during 21 days of evaluation**

| Groups       | Urine (mL) | Cr (mg/dL) | Na (mEq/L) | K (mEq/L) | A (mg/dL) |
|--------------|------------|------------|------------|-----------|------------|
| Control      | 1.8±0.5    | 0.46±0.11  | 150±2.7    | 3.7±0.4   | 0.03±0.02  |
| Vehicle      | 1.1±0.3    | 0.38±0.03  | 149±3.0    | 3.4±0.3   | 0.04±0.008 |
| FTY720       | 0.9±0.2    | 0.38±0.06  | 149±2.0    | 3.9±0.7   | 0.03±0.009 |
| CsA          | 1.8±0.6    | 0.43±0.14  | 146±2.9    | 3.8±0.6   | 0.02±0.10  |
| FTY720+CsA   | 2.1±0.7    | 0.57±0.13  | 143±3.3    | 3.8±0.4   | 0.45±0.29  |

*p<0.05 versus control group

Our results suggest that FTY720 in association with CsA could cause changes at renal function and structure after long-term administration. The project was supported by a grant from FAPESP number 03/13009-4

**PO-252**

**FTY720+CsA PROLONG SKIN ALLOGRAFT SURVIVAL WITHOUT PREVENTING T CELL ACTIVATION**

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FTY720 modulates immune responses in animal models of transplantation through mechanisms related to lymphocyte migration to peripheral lymph nodes instead of inflammatory sites. However, the mechanisms associated with FTY720+CsA immunosuppression is still unknown. C57BL/6 were submitted to skin tail transplantation from BALB/c mice. C57BL/6 received FTY720 (1mg/kg) by gavage and/or CsA (10mg/kg) intravenously for 21 days. Five days after transplantation blood and draining lymph nodes were collected from C57BL/6 to evaluate immune response. Sneeze blood (SB) and flow cytometry (FC) of T cells (MHC II, CD54, Annexin V-apoptosis) were performed. Median survival time of skin grafts was 15 days in FTY720, 18 days in FTY720+CsA and 9 days (non-treated). T cells in SB presented a dramatic decrease in mice treated with FTY720 and FTY720+CsA. However, cells from lymph nodes showed no changes at activation/apoptosis markers except for increase at MHC II expression in recipients treated with the drug combination. At the rejection time, recipients treated with FTY720 presented a slight increase at blood T cells (33±14%). It was also seen an increase of MHC II (49.5±3%) and decrease of Annexin-V (10.8±7.6%).

Table 1. Percentage (%) of T cells in smear blood (SB) and activation/apoptosis markers in T lymphocytes from axillary lymph node

| Groups | T cells (SB) | MHC II | CD54 | Annexin-V |
|--------|-------------|--------|------|-----------|
| Control| 54±8.0      | 33.7±7.0| 93.6±0.30| 33.4±12 |
| Tx     | 31±12       | 35.6±6.8| 96.0±0.07| 31.2±14 |
| Tx FTY720| 31±12   | 37.0±1.6| 95.7±1.60| 32.3±4.5|
| Tx FTY720+CsA| 23±4.0 | 56.0±3.5| 97.6±0.80| 31.3±25|

Our data suggest that the mechanism of prolonged skin graft survival was T cell migration from peripheral blood but not inhibition of T cell activation even when CsA was associated. The project was supported by a grant from FAPESP 04/14726-4

**PO-253**

**SUDDEN HEARING LOSS ASSOCIATED WITH HIGH DOSES OF CALCINEURIN INHIBITORS AFTER LIVER TRANSPLANTATION**

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Purpose: To up to now, hearing impairment in patients after liver transplantation (OLT) has only been reported sporadically. However, a high rate of potential ototoxic side effects is known to be related to immunosuppression with calcineurin inhibitors, especially regarding cardiovascular and neurotoxic side effects.

Methods: We report a series of 5 patients after liver transplantation (3 female) who developed sudden hearing loss. At the same time, all patients presented high doses of calcineurin inhibitors.

Results: In 4/5 patients, sudden hearing loss was bilateral. Patients’ age was highly variable (18-59 years) when hearing loss occurred. Liver transplantation dated back 0-5 years. Underlying liver disease was heterogeneous as well as HCV, PSC, autoimmune hepatitis, malignant hemangiome- lhoma. Sudden hearing loss occurred under high doses of tacrolimus (n=3), mean serum levels at the time of hearing loss: 24 ng/ml and cyclosporine A (n=2, 343 ng/ml), respectively. Further immunosuppression consisted of prednisolone (n=4) and azathioprine (n=1). There were no other risk factors like administration of ototoxic drugs (e.g. aminoglycoside antibiotics). Serum lev- els of immunosuppressants rapidly normalised after the event. Nevertheless, in 4/5 patients hearing impairments (3/4 bilateral) became necessary during follow-up. Furthermore, two patients suffer from tinnitus since the hearing.

Conclusions: High doses of certain immunosuppressants after liver transplantation seem to be a risk factor for sudden hearing loss. In most cases, hearing loss was irreversible and resulted in need of a hearing aid. Neurotoxicity may be a probable mechanism. Further systematic evaluations are necessary to allow a better understanding of the problem.

**PO-254**

**THE INFLUENCE OF IMMUNOSUPPRESSIVE DRUGS ON THE GENERATION OF CD8+CD28- CELLS IN VITRO (MLC)**

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Patients with organ allograft require lifelong immunosuppression therapy to inhibit host’s immune response to alloantigens. Within the immune cells there are not only cytotoxic cells but also regulatory cells that play potentially an essential role for inducing and maintenance transplant tolerance. Human CD8+CD28- regulatory cells were previously shown to be involved in the control of immune response to transplanted allografts. The aim of this study was to evaluate the influence of selected immunosuppressive drugs - Cyclosporine A (CsA) and Rapamune (RAPA) on the generation of CD8+CD28- cells in vitro. Mononuclear cells were obtained from peripheral blood of healthy volunteers and were cultured in Mixed Lymphocyte Culture in the presence or without investigated drugs. Drugs were added to respective culture for every 24 hours. After six days lymphocyte subsets were evaluated using monoclonal antibodies and analysed by flow cytometry (FACSCalibur). We observed that RAPA added from 1 to 4 days of activation decreased the percentage of CD8+CD28- in vitro. CsA did not have significant influence on the level of CD8+CD28- cells. Mechanism of action immunosuppressive effects of RAPA results from inhibition of cell cycle progression. Influence of RAPA on generation CD8+CD28- probably depends on time of activation these cells and is the most in early phase of activation. CsA blocks signal 4 through TCR and inhibit cytokine trans- scription. Generation of CD8+CD28- cells might be partial or complete inde- pendent of cytokine withdrawal. RAPA might inhibit generation of CD6+CD28- regulatory cells while CsA might not interfere in this process.

**PO-255**

**PREVENTION OF EARLY ACUTE REJECTION WITH ANTI-INTERLEUKIN-2 RECEPTOR MONOCLONAL ANTIBODIES AND TRIPLE IMMUNOSUPPRESSION IN CADAVERIC RENAL ALLOGRAFT RECIPIENTS**

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In prospective randomised we assessed safety and efficacy of basilix- imab or daclizumab combined with triple immunosuppression in adult recipients of at least 1 HLA-mismatched cadaveric renal allografts. All studied patients received following immunosuppression: basiliximab or daclizumab in standard doses, cyclosporine, mycophenolate sodium and myco- phenolate mofetil in equal initial dosage. Dose of cyclosporine was adjusted to achieve target level.
Results of 3 months follow-up are presented in table [mean±SD (range)]. No statistically significant differences were found among study groups.

| Basiliximab (n=56) | Daclizumab (n=61) |
|-------------------|-------------------|
| Recipient age (y) | 48±10 (19-60)     | 48±10 (22-60)     |
| Recipient sex (%) |                  |                  |
| Male              | 37 (66.1)         | 39 (68.8)        |
| Female            | 20 (33.9)         | 22 (35.2)        |
| Donor age (y)     | 37±14 (8-60)      | 39±14 (9-58)     |
| Donor sex (%)     |                  |                  |
| Male              | 32 (57.1)         | 44 (72.1)        |
| Female            | 19 (32.9)         | 8 (12.9)         |
| ≥25°C conduction |                  |                  |
| Male              | 24 (42.9)         | 17 (27.9)        |
| Female            | 19 (33.9)         | 17 (27.9)        |
| Cold ischemia time (h) | 21.0±6.5 (7.0-35.0) | 19.0±6.5 (9.5-39.5) |
| 2nd renal allograft (n) | 4                  | 5                |
| Delayed graft function (%) | 17 (30.4%)        | 15 (24.6%)      |
| Acute rejection episodes (n) | 0                  | 3                |
| Graft failure for rejection (n) | 0                  | 0                |
| Patient death (n) | 1 (brain stem infarction) | 1 (aspiration)  |
| Serum creatinine after 3 months (μmol/l) | 103±32            | 102±38          |
| Adverse events (%) |                  |                  |
| CMV               | 2 (3.6%)          | 6 (9.8%)        |
| Pneumonitis/UTI   | 12 (21.4%)        | 17 (27.9%)       |
| Septicemia        | 3 (5.4%)          | 1 (1.6%)        |
| Pneumonia         | 1 (1.8%)          | 3 (4.9%)        |
| Herpes simplex    | 8 (14.3%)         | 6 (9.8%)        |
| Herpes zoster     | 3 (5.4%)          | 3 (4.9%)        |
| Wound infection   | 1 (1.8%)          | 6 (9.8%)        |
| Malignancy        | 0                  | 0                |
| Posttransplant diabetes mellitus | 4 (7.1%)        | 1 (1.6%)        |

Basiliximab or daclizumab with this triple therapy represent safe and efficient immunosuppression strategy, demonstrated with low incidence of early acute rejection episodes, excellent allograft function and acceptable adverse event profile.

PO-256

MYCOPHENOLIC ACID CLINICAL PHARMACOKINETICS INFLUENCED BY A CYCLOSPORINE C2 BASED IMMUNOSUPPRESSIVE REGIMEN IN RENAL ALLOGRAFT RECIPIENTS

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The variability in mycophenolic acid (MPA) clinical pharmacokinetics was investigated in this observational study. We performed repeated measurements of MPA and MPA-glucuronide (MPAG) trough concentrations during the first three months post-transplant in 69 renal allograft recipients receiving standard immunosuppression (mycophenolate mofetil (MMF), cyclosporine (CsA) and steroids).

The patient population was divided according to C2 concentration during the first week post-transplant; within range (1600-2000μg/l), n=26 or below range, n=43. Median MPA total concentration was 0.9μg/ml in patients within and 1.2μg/ml in patients below range (p=0.19). The incidence of acute rejection in any patient of the two groups. In conclusion, in RTx recipients with allograft nephropathy, the latter appeared 6.8 months after transplantation.

PO-257

PROTEINURIA IN RENAL TRANSPLANT RECIPIENTS (RTx) AFTER CONVERSION TO EVEROLIMUS OR SIROLIMUS FOR ALLOGRAFT NEPHROPATHY

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The aim of this study was to evaluate the appearance of proteinuria after conversion of calcineurin inhibitors (CI) to either Everolimus or Sirolimus. Two groups of patients were included: the first group 8 RTx recipients on Methyldprednisolone (MP), Cyclosporine (CsA)/Tacrolimus (TAC) and Mycophenolate Mofetil (MMF), 47.6±2.4 months post-Tx with creatinine(sCr) 2.2±0.3μg/ml were converted to MP, MMF and Everolimus, because of allograft nephropathy. The initial dose of Everolimus was 6mg/day, the maintenance 6.5±3.4mg/day, and the levels were 8±2.1±2.9μg/ml sCr. The proteinuria increased 1.2±0.8 (0.5-2) months after conversion. The incidence of acute rejection in any patient of the two groups. In conclusion, in RTx recipients with allograft nephropathy discontinuation of CI and conversion to Everolimus or Sirolimus is safe. However in the majority of these patients significant proteinuria develops, with undefined impact on graft survival for the time being.

PO-258

MMF SUBSTITUTION FOR CSA IN CHRONIC ALLOGRAFT DYSFUNCTION: 2-YEAR FOLLOW-UP OF A MULTI-CENTER RANDOMIZED CONTROLLED STUDY

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The commonest cause of late renal transplant loss is chronic allograft dysfunction (CAD), characterized by progressively increasing serum creatinine ('creeping creatinine'). A 143-patient multi-center randomized controlled study demonstrated benefit to renal function of adding mycophenolate mofetil (MMF) followed by CsA withdrawal in patients with CAD. In the MMF group, renal function stabilized or improved in 58% of patients (defined by flat or positive slope of the reciprocal creatinine plot) against 32% in the CsA group (p=0.006). 103 patients completed the one-year core study and 79 entered a 4-year, observational, follow-up study (MMF group N=41, CsA group N=38). Interim data from 2 years follow-up show that improvement in renal function demonstrated in the core study is maintained. The difference increases in per-protocol analysis of patients who remain CNI-free in the MMF group, and who continue CNIs in the CsA group. There was no late acute rejection. Three deaths occurred in the MMF group (lymphoma, sepsis), and two in the CsA group (sepsis). Graft loss due to CAD occurred in 11 patients, 7 in the MMF group and 4 in the CsA group. These data are consistent with other recent studies and demonstrate that substitution of CsA with MMF in patients with CAD results in improvement or stabilization of renal function that is maintained over 2 years.

PO-259

CONVERSION FROM MYCOPHENOLATE MOFETIL TO ENTERIC-COATED MYCOPHENOLATE SODIUM IN MAINTENANCE RENAL TRANSPLANT PATIENTS: RESULTS OF A PROSPECTIVE INTERNATIONAL MULTI-CENTER TRIAL

Frank Pietruck1, Barbara Suwaleck2, Katrin Ivens3, Wolfgang Arns4, Karl Lhotta5, Bernard Bourbignon6, Wolfgang Fischer7, Björn Nashan8. For the ERL2405-DE02 Study Group, Dept. of Nephrology, 1University Hospital Essen, 2University of Münster, 3University of Düsseldorf, Germany; 4Merheim Medical Center, Cologne, Germany; 5University of Innsbruck, Austria; 6University Hospital Brest, France; 7Novartis Pharma GmbH, Nürnberg, Germany; 8Dept. of Surgery, Dalhousie University, Halifax, Canada.

Enteric-coated mycophenolate sodium (EC-MPS, myfortic®) and mycophenolate mofetil (MMF, CellCept®) are comparable regarding efficacy and safety. We investigated safety and tolerability of converting maintenance renal transplant patients from MMF to EC-MPS.
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**PO-260**  
**SIRILOMUS ATTENUATES CHRONIC ALLOGRAFT NEPHROPATHY IN AN EXPERIMENTAL RAT KIDNEY TRANSPLANTATION MODEL**

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**Background:** Chronic allograft nephropathy (CAN) is the primary reason for late allograft loss in transplantation. It is an irreversible fibrogenic process leading eventually to the loss of the graft. The use of calcineurin inhibitors (CNI) is suggested to be a risk factor for CAN. Thus, CNI-free immunosuppressive protocols are needed to improve long-term graft outcome. Sirolimus (SRL) affects the immune response by inhibiting post-receptor interleukin-2 signaling. Safety profile of SRL is different from that of CNI. Here we investigated the long-term effects of SRL on kidney allografts and fibrogenic growth factor expression and compared it to cyclosporine A (CsA).

**Methods:** Kidney transplantsations were performed from DA to WF rats and syngeneic controls were done between DA rats. Allograft recipients were immunosuppressed with SRL 2 mg/kg p.o. or CsA 1.5 mg/kg s.c. SRL-treated animals were also treated with CsA 1.5 mg/kg s.c. for 0-7 days post-transplantation. Serum creatinine levels were measured once a week. Grafts were harvested on day 90 for histology and immunohistochemistry. Histology was scored according to Chronic Allograft Damage Index (CADI).

**Results:** No signs of CAN were seen in syngeneic grafts. CADI 0.0±0.2 (mean+S.E.M.). In CsA-treated allografts intense chronic changes were seen, CADI 3.0±1.0. SRL ameliorated significantly CAN compared to CsA, CADI 3.0±0.5, *p*<0.05. Creatinine values of SRL-treated allografts were lower compared to CsA-treated allografts being nearly similar to syngeneic grafts. SRL decreased markedly fibrogenic PDGF expression compared to CsA.

**Conclusions:** Our results demonstrate that SRL attenuates CAN and restores kidney function. SRL seems to be less fibrogenic via decreased growth factor induction. Based on our findings SRL is a promising therapy for CAN.

**PO-261**  
**BAYES ESTIMATES OF EXPOSURE AFTER THREE POINT MONITORING OF MYCOPHENOLATE MOFETIL (MMF) IN RENAL TRANSPLANTATION COMBINATION TREATMENT CONFIRM THE NEED FOR MMF DOSE REDUCTION**

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**Purpose:** To use a prospective population pharmacokinetic (PK) method, and Bayesian estimates of the AUC, to optimize mycophenolate mofetil (MMF) dosing in maintenance combination therapy after renal transplantation.

**Methods:** 27 stable adult (19/8 male/female) renal transplant recipients (mean age 41.5 ± 8.8 kg) had MMF administered with methylprednisolone and sirolimus, cyclosporine or tacrolimus. 111 blood samples were analyzed from troughs (C0), 30 min (C30) and 2 h (C2) postdose. Non-linear mixed effects (NONMEM) was used to build population PK simulating a two-compartment oral absorption model, followed by Bayes estimation of individual patient PK parameters. Systemic clearance, CL, was used to titrate the dose for a target AUC (range) for MMF of 50 mg h/L (40–60 mg h/L).

**Results:** Administered doses were 731.7 ± 130.0 mg b.i.d., and AUC0-12 of 63 (15.8–160.4) mg h/L. The bioavailability (F)–scaled NONMEM-FOCE population PK parameters for MMF were (true value, interindividual CV%): for C0: 13.2 ± 2.2 mg/L, interindividual variation, V=208 L, absorption rate constant, ka=2.2 h⁻¹, and time delay, Tlag=0.35 h. The C0 and the C2 appear valid surrogates of the AUC, although the C0 appears less robust.

**Conclusion:** Reduction of the standard MMF dose appears necessary in combination immunosuppression post renal transplantation. TDM with Bayes AUC estimation (e.g. using C2 or C0+C2) is preferable.

**PO-262**  
**CALCINEURIN INHIBITOR FREE IMMUNOSUPPRESSION IN KIDNEY TRANSPLANTATION FROM DONORS AGED 65 YEARS OR MORE**

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**Introduction:** Ageing affects particularly the kidney and increases its susceptibility to nephotoxicity of calcineurin inhibitors (CNI). We herein compare the efficacy and safety profiles of a CNI-free (CNI-F) and a CNI-based (CNI-B) regimen in kidney transplantation (KTx) from elderly donors.

**Methods:** From January 1999 to February 2005, 91 cadaveric KTxs were performed from donors aged 65 years or more. Twelve recipients, enrolled in other investigational studies, were not considered. The remaining 79 patients were analysed retrospectively. Twenty recipients (25.3%), (6 single-KTxs and 14 dual-KTxs), were managed according to a CNI-F regimen based on induction with basiliximab and steroids, plus maintenance with low dose steroids, mycophenolate-mofetil and rapamycin (introduced 7 days after KTx and adjusted to maintain a trough level of 10-15 ng/dl). The remaining 59 patients (44 single-KTxs and 15 dual-KTxs) were managed in a CNI-B regimen, using low dose Neoral® (n=54) or Prograf® (n=5) introduced when creatinine fell below 2.5 mg/dl.

**Results:** Two patients (CNI-B) died perioperatively. Delayed kidney graft function occurred in 25 patients (CNI-Bvs CNI-F; *p*=0.02). Overall, acute rejection rate was 7.6% (10.1% CNI-Bvs 0% CNI-F). One-year mean creatinine level was 1.2 mg/dl (range 0.9–2.0 mg/dl) in CNI-F vs. 1.6 mg/dl (range 0.3–4.0 mg/dl) in CNI-B (*p*=0.01). Treatment with statins was required only in CNI-F (*n=*13; 65.0%) (*p*=0.0001). Four-year patient and graft survival rates were both 100% in CNI-F and 88.1% and 80.3% in CNI-B, respectively.

**Conclusions:** Our data show that CNI-F immunosuppression is a valid alternative to CNI-B regimens in KTx from elderly donors.

**PO-263**  
**RISKS AND BENEFITS OF IV-Ig COMBINED WITH QUADRI ThERAPY IN HIGH IMMUNOLOGICAL RISK KIDNEY TRANSPLANT RECIPIENTS**

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IV-Is have been used with some success in the treatment of acute humoral rejection. We report the prophylactic use of IV-Igs in renal transplant recipients at high immunological risk.

**Patients and methods:** 13 recipients aged 45 (26-69) were transplanted with a first (n = 7), a second (n = 5) or a third (n = 1) cadaveric kidney. All were highly sensitized with either an historical positive cross-match (n = 11) or a current PRA > 80% (n = 2). Treatment included prophylactic IV-Ig (15mg/kg/D from D0 to D4, repeated on D21, D42, D63) with low dose heparine and a quadritherapy combining basiliximab (n=3) or ATG (n=10), steroids, ciclosporine and MMF.

**Results:** After a mean follow-up of 7.9 months, patient and renal survival were 100% and serum creatinine was 160 (99 – 252 micromol/l. Five cases of severe haemorrhage occurred. DGF was observed in 3 pts (23%). Clinically and biopsy proven acute rejection (AR) occurred in 4 pts (31%), with a favourable outcome in all. The 3-month routine biopsy (n = 11) revealed grade 1 acute rejection in 3 cases and borderline lesions in 1, allograft glomerulopathy (n = 3) or glomerulitis (n = 2).

**Conclusion:** prophylactic IV-Ig with quadratherapy is associated with excellent short-term results in patients at high immunological risk but due to the high incidence of rejection lesions on routine renal biopsies, concerns remain for the long term outcome.

**PO-264**  
**EVEROLIMUS (E) WITH LOW DOSE CsA IN KIDNEY TRANSPLANTATION: 24-MONTHS ANALYSIS**

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Efficacy and safety of the proliferation signal inhibitor everolimus (CERTICAN®) plus low CsA (NEORAL®) exposure and steroids was evaluated in this randomized, open-label, multicenter trial.
237 patients (ITT-population) entered the 1-year core trial on 1.5 or 3 mg E (N=112 and N=125). 167 patients (76 and 91) still on study drug after 1 year entered the extension (EXT-population) and 143 (60%) completed 24 month on study drug. E target C2-levels were ≥3 ng/ml, and CsA target C2-levels (mg/L) were 1200 (week 0-4), 800 (week 5-8), 600 (week 9-12) and 400 (month 4-24). Efficacy failure rates (BPAR, graft loss, death or loss to follow-up) for the 1.5 and 3 mg group were 30% and 27% (p=NS) for the ITT-population and 16% and 17% (p=NS) for the EXT-Population. Median on-treatment creatinine clearance (Cockcroft-Gault) was 68 and 61 ml/min at 24 months (69 and 62 ml/min at 12 months) in the ITT-Population. Frequent AE's (≥20%) were hypercholesterolemia, anemia, peripheral edema, hypertension. Rates of CMV-infection, (0.9% and 4.0%), malignancies (1.8% and 2.4%) and MACE (3.6% and 3.2%) were low. Good clinical outcomes, particularly stable renal function and efficacy were observed up to 24 months. Therefore, E plus low CsA exposure is safe and effective for longer term management of kidney transplant patients.

PO-265 DIURNAL VARIATION IN CYCLOSPORIN LEVELS
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Objectives: Cyclosporin (CsA), as an immunosuppressant, is currently used in 2 divided doses per day. Trough (C0) or peak (C2) levels are being monitored as tool to dose Cyclosporin (CsA), to achieve the therapeutic window for immunosuppression while moderating side effects. This study was conducted to determine the extent diurnal variability in C2 and C0 levels.

Methods: In total 208 samples were collected from patients (n=52), with 4 blood samples being taken from each patient (C0 and C2 after the morning and evening doses of CsA - C0am, C2am, C0pm and C2pm respectively). Liquid chromatography tandem mass spectrometry (LC-MS/MS) (Quatro micro tandem mass spectrometer, Micromass, Manchester, UK) was used for measurement of CsA levels (expressed in nanograms/L).

Results: Median values of C0am and C0pm were 188±113 and 206±99 respectively. Median values for C2am and C2pm were 782±382 and 624±303 respectively. Diurnal variation for C0 (DVC0) was calculated as C0am - C0pm and for C2 (DVC2) as C2am - C2pm. The median for DVC0am was 230 and 259 ±329 respectively. None of the patients had DVC0 >250. However, 50% (n=28) had DVC2 > 250 and 32% (n=17) had DVC2 > 500. Patients tended to have a higher C2 after the morning dose [63% (n=33)].

Conclusions: There is a greater diurnal variation in C2 than in C0. Thus if C2 is used to dose CsA, patients showing significant variation in C2 would be exposed to lower daily doses of CsA and thus pre-dispose them to acute rejection.

PO-266 A RANDOMIZED STUDY TO COMPARE IMMUNOSUPPRESSION BASED ON BASILIXIMAB INDUCTION AND LOW INITIAL DOSES OR DELAYED NEORAL IN KIDNEY TRANSPLANT RECIPIENTS AT HIGH RISK FOR DELAYED GRAFT FUNCTION
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This multicenter, prospective, randomized study evaluates the efficacy of basiliximab induction, MMF 1g/day, steroids and 3 patterns of Neoral initiation in renal transplant (RT) recipients at high risk for delayed graft function (DGF): donor age >60 years, creatinine >2mg/dL, cerebrovascular disease as cause of death and/or cold ischemia time >24h. Patients received: G1) early CsA (24 h, post-RT) at 3 mg/kg/d (C2:800 ng/ml); G2) early CsA at 5 mg/kg/d (C2:1200 ng/ml); G3) delayed CsA (days 7-10 post-RT) at 5 mg/kg/d. 117 patients were randomized: 38 in G1; 40 in G2; and 39 in G3. Similar percent of patients had DGF (at least 1 hemodialysis post-RT): 32%, 40% and 50%. 6-month acute rejection was higher in G3 (delayed cyclosporine) vs G1 (25% vs 5.3%, p<0.05), with significant differences between G3 and G2 (15%), 6-month graft survival (89.5%, 95%, 83.3%), patient survival (92%, 93%, 93%) and serum creatinine were similar. Induction treatment with basiliximab in RT at high risk for DGF and three patterns of Neoral initiation, MMF and steroids showed excellent 6-month renal function and graft survival. Delayed Neoral initiation did not evidence a quicker improvement of DGF. Early low Neoral initiation achieved extremely low rate of acute rejection with significant differences when compared with delayed Neoral initiation.

PO-267 MYCOPHENOLATE MOFETIL MONOTHERAPY IN LONG-TERM LIVER TRANSPLANT RECIPIENTS WITH CALCINEURIN INHIBITOR-INDUCED CHRONIC RENAL DYSFUNCTION
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Background: Mycophenolate mofetil monotherapy have been recently proposed for liver transplant recipients with adverse events (nephrotoxicity, hyper tension) related to calcineurin inhibitors (CNI). We reports 70 cases of conversion for nephrotoxicity.

Methods: From 1986 to September 2004, 883 patients underwent OLT. We analyze 70 adult recipients (7.9%) that were converted from CNI to MMF monotherapy, these showed stable liver function and absence of AR at least 15 months before to start MMF monotherapy.

Results: There were 51 males and 19 females, mean age of 50.8 ± 9.6 years, and the time elapsed from OLT to onset of MMF monotherapy was 85.1 ± 46.4 months (182-205). Mean follow-up after monotherapy was 19.3 ± 13 months (0.3-52). Other side effects associated were: hypertension in 18 patients, and diabetes in 7. Excluding 4 patients who underwent hemodialysis, mean creatinine improved significantly from baseline values (1.69 ± 0.41 mg/dl) to the last outpatient visit (1.55 ± 0.53 mg/dl; P<0.05), as the same manner that creatinine clearance (baseline of 51.54 ± 16.4 ml/min vs last outpatient visit of 58.1 ± 19.3 ml/min; P<0.001). AR rate was present in 5, and we recorded 22 adverse effects (31.4%) related with MMF monotherapy.

Conclusions: Conversion from CNI to MMF monotherapy in liver transplant recipients with chronic renal dysfunction is a good practice, the renal function improves, the acute rejection rate is low, and adverse events are well tolerated.

PO-268 A LARGE 12 MONTHS STUDY OF ENTERIC-COATED MYCOPHENOLATE SODIUM (EC-MPS) IN COMBINATION WITH NEORAL AND STEROIDS IN DE NOVO KIDNEY TRANSPLANT RECIPIENTS
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In pivotal trials EC-MPS (myfortic®) has shown to be therapeutically equivalent to MMF (Cellcept®). However dose reductions (DR) or interruptions (DI) during MMF treatment are common and may increase the risk of acute rejection. 456 patients, aged 47.4 ± 12.6 years were enrolled in 5 countries and 39 sites throughout Europe and the US. All patients received EC-MPS, Neoral, anti IL2 induction + steroids. 26 patients (5.7%) didn't complete due to either withdrawal of consent(3), administrative problems(8), Lost to Follow up (4) or death (11).

Up to week 4 94% of the patients received the daily target myfortic® dose of 1440 mg or higher. At month 3/6/12 still 85%/82%/81% of the patients reached this target dose.

Overall, 99.6% of the patients presented adverse events (Aes) or infections, 47.6% haematological, 77.8% GI disorders.[table 1] After 12 months 29% of the patients with a DI or DR experienced a BPAR compared to 20% of those without DR/DI.

Conclusions: EC-MPS demonstrated good tolerability in the novo renal transplant recipients. Few GI events led to DR/DI, whereas the main reasons were hematological side effects. DR/DI have a negative impact on the outcome of patients in terms of rejection.
TO SWITCH OR NOT TO SWITCH: INDICATIONS AND BENEFITS OF CONVERSION FROM CYCLOSPORIN A TO TACROLIMUS OR VICE VERSA

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Background: The aim of this cross-sectional study was to analyze the indications for change from cyclosporine A (CyA) to tacrolimus (Tac) or vice versa in adult liver transplant recipients.

Methods: Indications, outcome and side effects of conversion from CyA to Tac or vice versa were retrospectively studied in 140 consecutive adult liver transplant recipients receiving calcineurin inhibitor (CNI)-based immunosuppression between 1995 and 2003 at the University Hospital Zürich.

Results: CyA was initially given in 82 (59%) patients, and 58 (41%) patients received Tac. 22 patients (26.9%) were subsequently converted from CyA to Tac (median conversion time 42 days (7-1193 days)), and 7 patients (12%) were converted from Tac to CyA (median conversion time 23 days (8-413 days)). Main reasons for CNI conversion were acute rejection (44%), duc-topicen chronic rejection (17%), nephrotoxicity (10%) and cholesterol (10%). Patients after CNI conversion had a trend (p=0.17) to higher survival rates of 93% as compared no non-converted patients (88%). Acute rejection was the major reason for CNI conversion irrespective of the primarily used drug, and occurred more often in patients who underwent CNI conversion (p=0.03). There was a trend to continued Tac medication despite of acute rejection. Other side effects did not reach statistical significance due to the small patient numbers.

Conclusion: Although no general recommendations exist for CNI conversion after liver transplantation, 1) CNI switch mostly improved the pathology leading to conversion, and 2) conversion was beneficial independently of initial CyA or Tac medication. Therefore, in case of severe side effects or repeated rejections, conversion should be considered since it demonstrated individual benefit.

CNI CONVERSION AFTER KIDNEY TRANSPLANTATION: INDICATIONS AND OUTCOME

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Background: The study was aimed to analyze indications and outcome for conversion from cyclosporine A (CyA) to Tacrolimus (Tac) or vice versa in kidney transplant recipients.

Methods: In this cross-sectional study, 246 adult kidney recipients between 2000 and 2003 at the University Hospital Zürich were retrospectively analyzed. Patients undergoing > one conversion and/or receiving rapamycin were excluded.

Results: Out of 238 recipients analyzed, 218 patients (91.6%) initially received CyA. 20 patients (8.4%) received Tac. Conversion from CyA to Tac was done in 26 patients (8.0%), mainly for acute graft rejection. Other reasons for conversion were hypertrichosis, CMV infection, GI problems, anuria, compliance problems, lumbalgia and a non-rejection related creatinine rise. One patient was converted from Tac to CyA for GI problems. Median conversion time from CyA to Tac was 23 days (6-138 days), conversion from Tac to CyA was done after 275 days. In the conversion group, 15 patients (55.5%) received a living-related organ as compared with the non-converted group (70 patients, 33.2%). Acute rejection was more frequent in converted (66.6%) than in non-converted patients (7%).

Conclusions: The interim analysis shows an acute rejection rate similar to those previously described, a good renal function evolution and an excellent safety profile for Myfortic® with no withdrawals for gastrointestinal toxicity.

PREVENTION OF ACUTE REJECTION IN DE NOVO KIDNEY TRANSPLANTATION IN A PROSPECTIVE, MULTICENTER, RANDOMIZED, OPEN-LABEL STUDY OF MYFORTIC® WITH STEROID WITHDRAWAL VS MYFORTIC® WITH STANDARD STEROID REGIMEN

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The enterico-coated mycophenolate sodium (EC-MPS, Myfortic®) which releases MPA on the small intestine instead of stomach may allow safe steroid withdrawal 6 months post-transplantation. The present study was designed to evaluate feasibility of steroid withdrawal in the context of a Myfortic®, Sandimmun Neoral (cyclosporine) and steroids immunosuppression in de novo renal transplant recipients.

This is a one-year follow-up prospective, multicenter, randomized, open-label study with two parallel groups (steroid withdrawal at 6 months post-transplant or standard steroid regimen).

A 3-months interim analysis including data from all patients (n=115) has been performed (table shows). 24.3% patients presented treatment failure, defined as biopsy-confirmed acute rejection, graft loss or death. Biopsy-confirmed acute rejection rate was 19.1%. There were 5 cases of graft loss and one death. Serum creatinine at 3 months was 1.9±0.8mg/dl (mean±SD). Treatment withdrawal due to side effects was observed in 7 patients, mainly because of cytomegalovirus infection (4 patients) or cyclosporine toxicity (2 patients). No patient dropped the study for gastrointestinal toxicity, previously reported with mycophenolates.

Treatment failure, biopsy-confirmed acute rejection, graft loss, death or loss to follow-up at 3 months

|                | n  | %     | 95% CI |
|----------------|----|-------|--------|
| Treatment failure | 28 | 24.3  | (16.5-32.2) |
| Biopsy-confirmed acute rejection | 22 | 19.1  | (11.9-28.3) |
| Graft loss        | 5  | 4.3   | (0.6-8.1)  |
| Death            | 1  | 0.9   | (0-2.8)    |
| Lost to follow-up| 4  | 3.5   | (0.1-6.8)  |

Conclusions: The interim analysis shows an acute rejection rate similar to those previously described, a good renal function evolution and an excellent safety profile for Myfortic®, with no withdrawals for gastrointestinal toxicity.

SWITCH FROM MYCOPHENOLATE MOFETIL (MMF) TO MYCOPHENOLATE SODIUM ENTERIC COATED (MPS-EC) IN TRANSPLANT RENAL RECIPIENTS IS AN ALTERNATIVE IN SERIOUS GASTROINTESTINAL INTOLERANCE

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Large clinical trials in the last decade demonstrated that mycophenolate mofetil (MMF) in combination with corticosteroids and a calcineurin inhibitor was superior to azathioprine in preventing acute rejection in organ transplantation. The most commonly observed adverse events associated with MMF are gastrointestinal (GI) effects (nausea, vomiting, diarrhea, constipation, dyspepsia). Patients experiencing GI or other adverse events usually respond to dose reduction. However, frequent dose changes have been associated with poorer outcomes, including a higher incidence of graft loss. Mycophenolate sodium enteric coated (MPS-EC) in theory improved GI tolerability. In human trials, the safety profile of MMF and MPS-EC and the incidence of GI intolerance were similar.

No data is available in the evolution of patients switched from MMF to MPS-EC in serious GI intolerance.

Patients: 12 patients, 7 male, 5 female, age 47.97±7.1 years, mismatch 3.09±2.19, serum creatinine 177±53 mmol/l, creatinine 177±53 mmol/l, haemoglobin 11±2.3 vs 12±3±2.3%, platelets 268,000±12000 vs 220000±74000/mm3, and weight 74±12±20 vs 74±7±20 kg.

No GI adverse events were observed in the 9 switched patients.

Conclusion: The switch from MMF to MPS-EC equivalent doses in a targeted population of renal transplant recipients, with severe GI adverse effects results in better tolerance of immunosuppressive regime.
PO-273 STEROID-FREE REGIMEN VERSUS STANDARD TREATMENT IN LIVER TRANSPLANT RECIPIENTS
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**Objective:** Evaluate a steroid-free regimen versus standard treatment in liver Tx.

**Methods:** First liver allograft recipients received: Group A (n = 78) Daclizumab 2 mg/kg 6 hours after surgery and 1 mg/kg on the 7th day post-transplantation, MMF 2 mg/day. Aimed FK trough level: 5-15 ng/ml during the first month after transplantation and 4-8 ng/ml onwards. Group B (n = 79): Steroids 15-20 mg/day during the first week and decrease to withdrawal between Weeks 12-24. Aimed trough level of FK: 5-15 ng/ml. Primary end point was acute rejection at 6 months.

**Results:** 157 patients participated in the study. Patients were mainly male and most frequent primary indication for transplantation was alcohol cirrhosis. Nine patients (11.5%) from group A and 21 (26.6%) from group B suffered from acute rejection (p = 0.017) at end point. There was 1 severe acute rejection (group B). Three additional acute rejection episodes (2 in group A, 1 in group B) occurred between month 6 and 12 (no fixed treatment per protocol). There were no differences between groups regarding patient and graft survival, opportunistic infections and HCV recurrence. Significantly differences were found in favour of the steroid-free regimen in the new onset DM rate and cholesterol levels from 3 to 5 months.

**Conclusions:** The steroid-free regimen with Daclizumab, Mycophenolate Mofetil and Tacrolimus is significantly more effective than standard treatment with similar infection rate and better cardiovascular risk profile.

PO-274 SELECTIVE CO-STIMULATION BLOCKADE WITH BELATACEPT (LEA29Y) RESULTS IN DECREASED INCIDENCE OF CHRONIC ALLOGRAFT NEPHROPATHY IN RECIPIENTS OF SUBOPTIMAL RENAL ALLOGRAFTS, COMPARED WITH CYCLOSPORINE

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Certain factors are associated with increased risk for chronic allograft nephropathy (CAN). Such factors include advanced donor age, prolonged cold ischemia time (CIT), and early graft dysfunction. Calcineurin nephrotoxicity can complicate these risks. We report 12 month results comparing cyclosporine A (CsA) with belatacept (LEA29Y), a selective co-stimulation blocker, in recipients of donor kidneys with these risk factors.

**Methods:** Renal allograft recipients were randomized 1:1:1 to belatacept more (N=74; M), less (N=71; L), intensive regimens or CsA (N=73) (total=218). All regimens included basiliximab induction, and maintenance therapy with MMF/corticosteroids. Assessment included death graft loss, acute rejection (AR), biopsy-proven chronic allograft nephropathy (CAN) and measured GFR (iohexol clearance). Results are reported for groups with initial dysfunction (Group 1, N=94;218: delayed graft function, dialysis within 7 days of transplant; slow graft function, serum creatinine ≥3.0 mg/dl at post-transplant day 7) and suboptimal donors (Group 2, N = 43;218: donor age≥60 or CIT≥24 h).

**Results:** CAN was less frequent in both belatacept groups vs. CsA at 12 month graft function, dialysis within 7 days of transplantation and ≤8 and 12 µg/dl. Data collected included side effects, ACR rates, HCC recurrence and outcome.

**Conclusions:** The median FU was of 28.5±12.5 months. SRL was discontinued in 3 (21%) patients due to severe anemia (month 24), pneumonia (month 5) and biliary complications (month 29), HCC recurrence (bone metastasis) was seen in 2 (14%) patients at 6 and 2 month post LTx (overall survival of 24 m for both). SRL-related side effects were: n=7 (50%) mouth ulceras, n=5 (36%) increased serum creatinine, n=2 (14%) wound dehiscence, n=2 (14%) pneumonia, n=1 (7%) severe anemia. ACR rates before and after conversion were of 28.6% and 7% respectively. Three-years overall and disease-free survival are of 85% and 81% respectively.

**Conclusions:** Early SRL monotherapy switch is well tolerated allowing low ACR. Preliminary results shows a trend for low HCC recurrence in recipients beyond standard criteria. Further controlled studies are mandatory to confirm these results.

PO-277 AN ANALYSIS OF HIV TRANSPLANTED PATIENTS AND THE INTERACTION OF IMMUNOSUPPRESSANT MEDICATION WITH PROTEASE INHIBITORS

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HIV infected patients have an improved prognosis since the introduction of highly active anti-retroviral therapy (HAART). This population is increasingly being considered for renal transplantation. A total of five HIV infected patients have received renal transplants at our center and 15 patients are listed. 2 of the 5 have had a significant interaction between their calcineurin inhibitor (CNI) and protease inhibitor resulting in elevated CNI trough levels.

**Methods/materials:** We analyzed the following data in the 2 patients: type and dosage of CNI, CNI trough levels, type of protease inhibitor, and HIV viral load.

**Results:** Protease inhibitors and CNI are metabolized via CYP3A4 and transported by the P-glycoprotein system, resulting in a potential interaction when used together. This interaction resulted in a significant elevation of CNI trough levels in 2 of 5 HIV infected patients.1 patient was on FK506 and the other on cyclosporine. Protease inhibitor levels were not measured. The first individual was not able to tolerate FTY720 due to side effects. FK506 trough levels were reduced to 0.5 mg/day every three days (0.007/mg/kg every three days). The second individual was able to tolerate FTY720 and the trough levels were reduced to 0.5mg/kg.
did not achieve steady-state until the cyclosporine dose was reduced to 25mg every other day (~3 mg/kg every other day). Aside from slow graft function, no significant side effects attributable to CNI toxicity were observed. HIV viral loads remained undetectable at last follow-up.

Conclusion: Significant drug interactions between CNI and protease inhibitors can occur in transplanted HIV infected patients on HAART. CNI trough levels need to monitored closely post-transplant.

**PO-278**

THE INFLUENCE OF TACROLIMUS (TAC) AND MOFETIL MYCOPHENOLATE (MMP) ON IMMUNE REJECTION IN LIVER TRANSPLANT RECIPIENTS

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Estimation of anti-CMV-IgM-index is considered as screening tool of CMV infection. The aim of study was: the examination how the therapeutic use of Tac and MMP influences serum anti-CMV-IgM-index in renal graft recipients. The study group consisted of 79 patients transplanted between April 1998 and Jan. 2005, suffering from CMV disease (pp65 positive) who were treated as following: Azathioprine (Aza)+Cyclosporine (CyA)+Prednisone (Pr) 44 patients (43±12 yrs); MMP+CyA+Pr 20 patients (44±14 yrs); Tac+MMP+Pr 15 patients (37±12 yrs). 11 of 15 Tac+MMP+Pr patients and 20 of 44 Aza+CyA+Pr patients at the 1-st month after transpl. received methyl-prednisolone therapy due to acute rejection. The anti-CMV-IgM-index in Aza-CyA+Pr was not higher than in MMP+CyA+Pr (2.07±1.8 vs 1.63±1.6, p=0.08). The anti-CMV-IgM-index in Aza+CyA+Pr was marginally higher than in Tac+MMP+Pr (2.07±1.8 vs 1.29±1.25, p=0.08). There was no difference in anti-CMV-IgM-index between MMP+CyA+Pr and Tac+MMP+Pr. Using fixed nonlinear regression we found that age at the time of transplantation was an independent confounding factor negatively correlated with anti-CMV-IgM-index (B = -0.2, p=0.029). Taking the age into consideration we were also able to point out the relative influence of the type of IS therapy on anti-CMV-IgM-indexes: immunosuppression including MMP: B = -0.21, p=0.039; immunosuppression including Tac: B = -0.22, p=0.016; MMP+CyA+Pr: B = -0.21, p=0.022. We found no influence of CyA precisely and as a constituent of CyA+Aza+Pr therapy.

Conclusion: Immunosuppression including MMP and/or T results in diminution of CyA precisely and as a constituent of CyA+Aza+Pr therapy. We found no influence of CyA precisely and as a constituent of CyA+Aza+Pr therapy.

**PO-279**

USE OF IV MMF IN LIVE DONOR LIVER TRANSPLANTATION (LTX) TO PRESERVE RENAL FUNCTION

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MMF is an effective immunosuppressant after LTX. It has no nephrotoxicity.

Aim: Examine the role of peri operative IV MMF and low dose tacrolimus on renal function, rejection, patient and graft survival in live donor LTx.

Material & Method: 29 LTx patients received IV MMF for 3 to 5 days with delayed low dose tacrolimus and standard steroid taper. Liver biopsies were performed as clinically indicated and scored as per Banff's criteria. All patients were followed for a mean period of 13 months.

Results: Renal function remained stable in the 1st month after LTx. One patient (3.4%) required short-term hemodialysis 9 days after LTx.

Rejection. Out of 17 biopsies performed, 3 biopsies from 2 patients (6.9%) showed mild acute rejection.

Patient survival. 4 patients died at 2, 5, 8, 18 months post LTx from Sepsis (n=3) & Recurrent HCC (n=1).

Graft survival. No graft was lost for immunological reasons.

Conclusion: IV MMF with low dose tacrolimus is well tolerated, preserves renal function and achieves 93% freedom from rejection.

**PO-280**

IL-2 RECEPTOR ANTAGONIST (BT563/BB10) VS. ANTHYMOCYTE GLOBULIN AS INDUCTION THERAPY AFTER HEART TRANSPLANTATION: 10-YEARS RESULTS OF A PROSPECTIVE RANDOMIZED TRIAL

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Allotransplant-activated T-cells express the high-affinity interleukin-2 receptor (IL2R). The aim of the study was to compare the clinical efficacy of a IL-2RA vs. polyclonal rabbit antithymocyte globulin (ATG) as induction therapy in cardiac transplantation.

40 patients heart transplant recipients were randomly assigned to receive either BT563/BB10 or rabbit antithymocyte globulin as induction therapy and underwent the same triple immunosuppression thereafter. 10-years-surveillance for rejection, infection, allograft vasculopathy, and tumorgenicity was performed. Allograft rejection and vasculopathy were assessed by biopsies and coronary angiographies respectively. Screening for infections included blood, urine or tracheobronchial cultures and serology. BT563/BB10 bioavailability was assessed by murine and human anti-mouse antibodies. Peripheral T lymphocytes and subsets were determined by FACS analysis.

10 years survival and tumorgenicity were comparable between the two groups (50% for the IL2RA group and 30% for the ATG group, p=NS). Actuarial incidence of severe rejection was significantly higher in the IL2RA group (55 vs. 10.5% 10 years postoperatively, p=0.0007, 50 vs. 0% during the first postoperative months, p=0.0001). Patients of the ATG group presented a higher viral infection incidence 1 and 3 months postoperatively (0 vs. 40% and 20 vs. 40%, p=0.001 and p=0.035 respectively). Freedom from allograft vasculopathy was higher in the ATG group (40 vs 20%, p=0.031).

BT563/BB10 is less effective as ATG for prevention of acute allograft rejection after cardiac transplantation which reflects a higher incidence of allograft vasculopathy in the long run. Clinically relevant infections or tumorgenicity were not increased by the use of ATG.
PO-282 SINGLE CENTER EXPERIENCE WITH STEROID AVOIDANCE AFTER RENAL TRANSPLANTATION UTILIZING THYMOCYTOBLIN® INDUCTION IN CONCERT WITH TACROLISMO AND MYCOPHENOLATE MOFETIL (MMF) OR SIROLISMO

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Evaluation of Impact of Steroid avoidance 3 days post transplant utilizing Thymoglobulin, on Cardiovascular Disease, PTDM, Bone disease, BMI, Cosmetic/mood changes, rejection, infection, malignancies, patient and graft survival.

Methods/Materials: Caucasian, PRA<20, 1st transplant, [-] CDC X match. High risk patients excluded. Thymoglobulin® 6 mg/kg over 3 days, Tacrolimus, Mycophenolate Mofetil. Sirolimus arm: Levels 10 for 90 days, 5 thereafter.

Results: Study began in March 2003. 84 enrolled, 71 active, 13 off protocol. 71 actively enrolled, 23 > 1 year, 37 > 6 months, 45 > 3 months. Mean age 52 years, 3/84 [4%] developed Acute rejection. 2 Antibody mediated rejections. 82/94 grafts functioning 1 death. In 45 patients followed for >3 months mean GFR: 65 ml/min. △ BMI 2.4 compared to 7 observed in steroid treated group. Hypertension treatment in 8% [4/45] no meds, 65% [29/45] 1 med, 27% [12/45] 2 meds, 0% [0/45] 3 meds. 36 non-diabetics and 8 diabetics. 35/36 non diabetic patients had normal glucose and HbA1C, 136 needed an oral hypoglycemic agent. Satisfaction with facial appearances, hirsutism, body image, skin health reported. No myocardial events or arrhythmias [n=71] MMF treated patients [n=63] # Hs050a/HL0 Cholesterol [Pre/Post]: 2, LDL Cholesterol ##Hs050-12. Sirolimus treated patients [n=8] treated with Lipid lowering agents.

Patients and Methods: Twenty patients additionally received OKT3 as an adjuvant immunosuppressive drug that play an important role in transplant.

Conclusion: In low risk group of renal transplant patients early steroid withdrawal can be successfully accomplished utilizing lymphocyte depleting agent [Thymoglobulin®].

PO-284 EFFECTS OF THALIDOMIDE, CYCLOSPORINE, AND DICLOFENAC ON SKIN ALLOGRAFT SURVIVAL IN RABBITS

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The present study evaluated the effects of thalidomide, cyclosporine, and diclofenac on skin allograft survival in 42 rabbits divided into the following groups (n = 6): group 1, autograft control; group 2, allograft control; group 3, allografts under thalidomide (100 mg/kg/d); group 4, allografts under sodium diclofenac (2 mg/kg/d); group 5, allografts under cyclosporine (10 mg/kg/d); group 6, allografts under cyclosporine (5 mg/kg/d) plus thalidomide (100 mg/kg/d). The drugs were given via the oro-gastric tube the day before transplantation and daily during the postoperative period. Total circular skin grafts from the ear were exchanged between Carthorina and White New Zealand rabbits. Cyclosporine (10 mg/kg/d) increased allograft survival, an effect that was comparable to cyclosporine (5 mg/kg/d) plus thalidomide (100 mg/kg/d). Thalidomide and diclofenac given alone had minimal significantly effects on the mean survival of skin allografts. The number of eosinophils around the necrotic skin was higher in the diclofenac group. The group receiving cyclosporine combined with thalidomide displayed the lowest number of eosinophils surrounding the allograft. In conclusion, the combination of thalidomide and cyclosporine in subtherapeutic doses may be useful for the treatment of skin allografts.

PO-285 ASSESSMENT OF CYTOKINE EXPRESSION TO PREDICT IMMUNOSUPPRESSION OF EVEROLISMO

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Purpose: The potential of T helper 1 and 2 cytokine expression in the immune response is well known. However, most of the earlier studies only analyze the effect of cytokine expression. Therefore, in this study we measure the expression of several cytokines of CD4+ and CD8+ T cells in peripheral blood of human heart transplant (HTx) recipients to predict immunosuppression of Everolimus (ERL) and to compare with the immunosuppressive effect of calcineurin-inhibitors (CNI) CsA and tacrolimus (TRL).

Methods: Blood from 8 HTx recipients was collected at morning trough values before and after conversion from CNI to ERL, because of severe renal dysfunction. 24-hours after the last CNI dose patients were treated with a fixed dosing regime of 0.75 mg/BID ERL on days 1 to 3. All patients received mycophe-
To compare effectiveness and safety profile of a single-dose versus a multiple-dose ATG-induction after HTx used in two centers by retrospective analysis in comparable cohorts.

2 groups of heart recipients were included: Gr.I, 84 patients (age 53±13) transplanted 01/92–12/98 received 5.8±0.8 doses of ATG; Gr.II,104 patients (age 52±12) transplanted 05/95–12/98 received a single dose ATG. All patients received CyA, azathioprine/MMF, steroids and CMV Ig prophylaxis as well as preemptive iv. ganciclovir. Surveillance was achieved by regular endomyocardial biopsy and echocardiography, coronary angiography at 1 year post HTx, thereafter as indicated.

Follow-up in Gr.I was 8.4±3.6, in Gr.II 6.7±2.4 years. Freedom from acute rejection (AR) at 1 month/1 year was 86.7/76.2% in Gr.I vs. 86.5/65.5% in Gr.II, respectively (p=n.s.). Death due to AR occurred in 8/84 patients in Gr.I and in 1/104 in Gr.II. Survival at 1 month, 1 and 5 years was 83.0, 72.6 and 63.1% in Gr.I vs. 87.2, 81.5 and 75.1% in Gr.II, respectively (p=n.s.). Freedom from graft vasculopathy at 6 years was 77.4% in Gr.I vs. 85.6% in Gr.II (p=n.s.), Incidence of malignoma at 146 and 3.6±10.7% in Gr.I vs. 0.3±8.8% in Gr.II (p=0.05 at 6 years). No malignoma was diagnosed in either group beyond 6 years post HTx.

AR incidence & survival is similar in both groups. Malignoma incidence, however, is significantly lower at a follow-up of up to 9 years in patients that received only a single dose of ATG.

Conclusion:

Rutizumab and high dose sirolimus along with splenic radiation and DFP showed better results with almost rejection free transplantation. Further study is needed to see the long term results using this protocol.

**PO-291 MORBIDITY RATES WITH REDUCED MMF DOSAGE – A SINGLE CENTRE EXPERIENCE**

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**Objective:** Mycophenolate Mofetil (MMF) is a key component of the available immunosuppressant regimen for transplantation. Traditionally a dose of 1g bd is utilised, with the incidence of side effects, most notably GI, being well known to transplant teams. The aim of this study was to assess the incidence of side effects and rejection rates with reduced dosing of MMF compared to standard regimens.

**Methods:** Case notes of 117 renal transplants performed at the Leicester General Hospital from 2002-2004 were reviewed retrospectively, and the incidence of side effects and rejection rates compared for MMF dosing at 1g bd (n=96) and 500mg bd (n=27).

**Results:** All patients received triple therapy with MMF, steroids and calcineurin inhibitor or sirolimus. The incidence of side effects were all higher at 1g bd. Symptoms overall were ameliorated in 34% of patients when the MMF was reduced to 500mg bd. The incidence of acute rejection was similar in both groups, with 16(19%) patients receiving 1g bd or higher, and 6(22%) patients receiving 500mg bd. Of these, 9(16%) and 3(6%) had drug levels below the target range for this department at the time of rejection.

**Conclusion:** The balance between adequate immunosuppression, side effects and the risk of rejection is a constant dilemma faced by transplant surgeons. This study shows a reduced side effect profile with similar rejection rates when using a lower dose regime of MMF. This may have implications for future immunosuppressive protocols.

**PO-292 THE EFFECT OF CSA, FK506 AND MMF ON THE EXPRESSION OF INDUCIBLE CELL ADHESION MOLECULES (ICAMS), TRANSPLANT VASCULOPATHY AND LEUKOCYTE INFILTRATION**

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ICAMs play a critical role in mediating allograft rejection, leading to transendothelial migration into the myocardium. We investigated the effect of CSA, FK506 and MMF on ICAM-1, VCAM-1, PECAM-1 and P-Selectin expression, the resulting leucocyte infiltration and neointimal proliferation of arteries after cardiac an transplantation in rats.

After transplantation animals (Lewis to Fisher) were divided into 4 groups: CSA 3mg/kg/d (n=74), FK506 40mg/kg/d (n=86) and Control (no therapy, n=74). 3-4 animals of each group were sacrificed in intervals of 1-4 days up to day 60. Using immunohistochemistry we investigated quantity, intensity and geometric distribution of ICAM-1, VCAM-1, PECAM and P-Selectin staining. We analysed the accumulation of leucocytes (CD4, CD8, CD11a, VL4A) in the perivascular space (pvs) of arteries. TVP in coronary arteries was expressed as mean vessel occlusion (mo).

In controls staining parameters of ICAMs, leucocyte accumulation and mo rapidly increased and were reduced by all drugs. We found significant correlations between staining parameters, infiltration of leucocytes and mo. MMF was superior to CSA and FK506 in reducing TVP, leucocyte attachment, infiltration and ICAMs expression, except VCAM-1 expression and VL4A infiltration being significantly higher in MMF treated animals. Only difference between the calcineurin inhibitors was further reduction of VCAM-1 expression and VL4A leucocyte infiltration by FK506. Although MMF had no significant effects on VCAM-1/VLA4 expression, it reduced the development of TVP significantly compared to calcineurin inhibitors. This effect was due to the reduction of ICAM-1, PECAM-1 and P-Selectin expression that correlates with the infiltration of leucocytes into the pvs of arteries.

**PO-289 PREVENTING CARDIAC ALLOGRAFT VASCULOPATHY: LONG-TERM BENEFICIAL EFFECTS OF MYCOPHENOLATE MOFETIL**

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**Purpose:** The impact analyses of the immunosuppressive combinations including cyclosporin A (CsA), azathioprine (Aza), tacrolimus (TAC), and MMF on the time of onset, extent, and progression of CAV.

**Methods:** 273 consecutive heart transplant recipients (1995-2002, mean age 51.2 ± 12.2 years, mean follow-up 6.8 ± 1.9 years) received coronary angiography each year. The onset of CAV was analyzed by means of Kaplan-Meier estimates and the log rank test for four treatment combinations namely CsA/Aza (n=47, 17.2%), CsA/MMF (n=26, 9.5%), TAC/Aza (n=62, 22.7%), and TAC/MMF (n=138, 50.5%).

**Results:** Freedom from CAV at 5 years was 47% with CsA/Aza, 66% with CsA/MMF, 60% with TAC/Aza, and 70% with TAC/MMF. The TAC/MMF group showed a significantly lower incidence of CAV than the CsA/Aza group (log rank 7.58, p=0.0059). CsA (n=73) was compared to TAC (n=200) and MMF (n=164) to Aza (n=109); freedom from CAV was 51.2% in CsA patients versus 66.1% in TAC patients (log rank 5.7, p=0.017) and 54.6% in Aza patients versus 67% in MMF patients (log rank 4.36, p=0.037) after 5 years.

**Conclusion:** The choice of immunosuppression has an impact on the incidence of CAV. In terms of prevention of CAV, MMF is superior to Aza in either combination. TAC is superior to CsA as a primary immunosuppressant with regard to both onset and severity of CAV. For prevention of CAV, the best combination of the analyzed immunosuppressants is TAC/MMF. Less rejection episodes in the MMF groups may have contributed to these results.

**PO-288 REDUCTION OF LONG-TERM MALIGNOMA INCIDENCE BY SINGLE DOSE ATG-INDUCTION AFTER HEART TRANSPLANTATION (HTx): A TWO CENTER STUDY**

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0.1mg/kg/d and sirolimus at 3mg per day and discontinued from day four. Gp II received Tacrolimus 0.1mg/kg/d, MMF 1.5mg/d and prednisolone. Acute rejection was seen in 2 patients(6.2%) in Gp I compared to 9(21.4%) in Gp II. Hyperacute rejection needing graft nephrectomy was seen in two patients in Gp II and nil in Gp I. Infection episodes were same in both groups. In Gp I patients the first day urine output was 20±6.4 L and serum creatinine 1.9±1.2mg/dl and 1.3±0.8 on day two compared to 9±4.5 litres urine output in day one and creatinine of 2.8±2.1mg/dl on day one and 2.2±1.3 on day two in Gp II patients. All cases of acute rejection were reversed in both groups with pulse Methyl prednisolone and/or inj Iorid. Follow up preoid ranged from six months to one year. Post Transplant diabetes Mellitus was seen in three patients in Gp I compared to six in Gp II.

Conclusion: Rutizumab and high dose sirolimus alongwith splenic radiation and DFP showed better results with almost rejection free transplantation. Further study is needed to see the long term results using this protocol.

**PO-290 PRETRANSPLANT IMMUNE CONDITIONING REGIMEN: NEW ROLE FOR RUTIZUMAB AND HIGH DOSE SIROLIMUS**

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Prospective clinical study was done to assess the benefits of using rituximab and high dose sirolimus alongwith splenic radiation and double filtration plasmapheresis as pretransplant immune conditioning regimen. 32 patients(16 of each) that had severe immune preconditioning that included splenic radiation, single dose Rituximab and 10mg/d Sirolimus starting form minus two days and Double Filtration Plasmapheresis(DFP). 42 patients(GpII) matched for age sex and disease were put on DFP. Splenic radiation and single dose Zenapax as pretransplant immunosuppressants. Post Transplant Gp I received MMF 1mg per Day, prednisolone and tacrolimus started form day three at
IMPACT OF MYCOPHENOLATE MOPHETIL THERAPY ON PLASMA LEVELS OF SOLUBLE ADHESION MOLECULES IN ORTHOTOPIC HEART TRANSPLANT RECIPIENTS

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Introduction: Plasma levels of soluble forms of adhesion molecules are reported to be elevated in heart transplant (HTx) recipients. Adhesion molecules are believed to play an important role in pathogenesis of coronary graft vasculopathy. Mycophenolate mophetil (MMF) is capable to reduce endothelial expression of adhesion molecules in vitro experiment. Current study was designed to test the impact of MMF administration on plasma levels of sICAM-1 and s-P-selectin in HTx recipients.

Methods: Thirty-six HTx recipients were divided early after OHTx into two groups according to immunosuppressive therapy (IS) used. Group No. 1 consisted of 17 patients (males 71%, females 29%, age 47.5±6.9 years) treated by CsA+azathioprine (AZA)+prednisone. The remaining 19 HTx recipients (males 95%, females 5%, age 50.3±11.05 years) treated by CsA+AZA+Prednisone formed group No. 2. sICAM-1 and s-P-selectin plasma levels were determined in both studied groups using ELISA method after one year of therapy. Control group consisted of 40 healthy individuals (30 males, 10 females, age 52±1.5 years).

Results: sICAM-1 and s-P-selectin plasma levels were found elevated in HTx recipients when compared to control group (sICAM-1: p=0.0002, sP-selectin: p=0.0002). No differences in sICAM-1 and s-P-selectin plasma levels were observed between studied subgroups of HTx recipients (sICAM-1: p=0.58, s-P-selectin: p=0.29).

Conclusions: MMF included IS therapy does not significantly influence sICAM-1 and s-P-selectin plasma levels in recipients one year after HTx in compare to classical IS therapy - CsA+AZA+Pred.

SIROLIMUS RESCUE TREATMENT IN CALCINEURIN-INHIBITED NEPHROTOXICITY AFTER KIDNEY TRANSPLANTATION

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Although calcineurin-inhibitors have played a major role in improvement of survival rate of kidney transplant grafts, their nephrotoxicity still continues to be a major problem. Discontinuation of calcineurin-inhibitors permits a decrease or stabilization of nephrotoxic effects. From April 2003 to October 2004, immunosuppressive regimen of the 25 patients was converted to sirolimus because of the chronic allograft nephropa thy due to calcineurin-inhibitors. The mean age was 30.6 years and 5 were women, 20 were men. Six of 25 patients transplanted from cadaveric donors. The range of switch was from 3 to 170 months. Kidney biopsy was performed in 15 patients. Sirolimus was given at a dose of 5 mg/day after withdrawal of calcineurin-inhibitors and the dose was adjusted according to whole blood levels of 12-20 mg/dl. At baseline and at 1, 3, 6 and 12 months after conversion serum creatinine and lipid levels were measured. The mean serum creatinine dropped significantly from 3.3±1.21 to 2.85±0.97 one month after the switch (p<0.05). There are two biopsy proven acute rejection episode after the switch. Cholesterol and triglycerides elevations were insignificant. But four patients have to use anti-hippertensive drug after the switch. Also one other patient had to use anti-lipidemic drug due to elevated blood pressure. In one patient, 3 month after conversion pulmonary tuberculosis and in the other patient seven month after conversion disseminated herpes virus infection developed. Graft survival at 3rd, 6th and 12th month after the switch were 96, 87 and 62% respectively.

We think that sirolimus is an effective alternative for patients in whom calcineurin-inhibitors toxicity has developed.

DE NOVO TUMORS AND LYMPHOPROLIFERATIONS (PTLD) AFTER LIVER TRANSPLANTATION

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De novo malignancies represent a major cause of morbidity after organ transplantation. Specific risks remain to be established. Since 1988, 1618 liver transplantations were performed in 1474 patients. Until 1992, immunosuppression consisted of cyclosporine A, azathioprine, steroids and antithymocyte globuline (ATG). Afterwards, this standard was changed to tacrolimus and steroids. However, most patients entered one of 16 immunosuppressive trials. De novo malignancies were included in i.e. also high grade dysplasia (e.g. uterine cervical intraepithelial neoplasia; CIN). 115 de novo malignancies were detected (112 patients; 7.6%). The risk to develop any type of de novo tumor depended on the time of follow-up (5 years: 5.4%, 10 years: 18.1%; p<0.005) and PTLD (t21=21; 1.4% were most common. Other common tumors were oropharyngeal and lung cancer (each n=13; 0.9%), and CIN (n=11; 0.7%). No single drug could be identified to significantly increase the tumor risk. However, an early randomized trial (follow-up > 12 years) had compared the 2 standard protocols and now revealed a significantly increased risk in the quadruple arm when compared to the tacrolimus dual regimen (17 of 60 pts. vs. 6 of 61 pts.; p=0.03).

In conclusion, the assessment of risks of immunosuppressive drugs as well as the recognition of risks in cases of immunosuppression discontinuation is recommended because relevant follow-up periods may take more than a decade. A signifi-
PO-298 HUMORAL MECHANISMS OF REJECTION AND ISCHEMIC INJURY IN KIDNEY TRANSPLANTATION
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Humoral mechanisms of rejection after kidney transplantation (TX) can be identified through the detection of diffuse complement C4d deposits in peritubular capillaries (PTC) in graft biopsies and/or donor-specific antibodies (DSA) in serum samples. It has been hypothesized that ischemic injury in the graft may facilitate humoral responses. Kidney grafts from non-heart-beating donors (NHBD) present more often and severe ischemia lesions than grafts from heart-beating or living donors.

Methods: A review of 22 kidney TX from NHBD performed from December 2002 to November 2004 out of a total of 273 TX, corresponding post-TX graft biopsies with histological findings, frozen tissue for the detection of C4d in PTC (three-step immunofluorescence technique with an antibody for clone 10-11, Biogenesis, Sandown, NH) and post-TX DSA data, when available.

Results: 9 recipients of NHBD TX underwent 12 biopsies for severe delayed graft function (> over 15 days or with scan deterioration). All showed acute tubular necrosis, but one also presented IA Banff acute rejection and one had neutrophils in PTC. These 12 biopsies of 9 patients did not have diffuse C4d deposits in PTC. Serum samples of 7/8 patients were available: negative in DSA flow XM (n=4) and PRA<0% (n=3).

Throughout the same period, we diagnosed acute humoral rejection in 13 patients -with acute renal dysfunction, C4d and DSA after TX- and have detected C4d in 8 biopsies of a subgroup of 32 performed more than six months after TX.

Conclusions: Severe ischemic injury does not necessarily determine the activation of humoral mechanisms of rejection mediated through DSA. Therefore, C4d is extremely interesting for the identification of humoral rejection in any clinical setting.

PO-299 SAFE CONVERSION TO MYCOPHENOLATE MOFHETIL IN STABLE LIVER TRANSPLANTED PATIENTS WITH TOXICITY SECONDARY TO ANTICALCINEURINICS
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Aim: To analyze our results obtained with conversion to MMF in stable liver transplant (LT) patients presenting adverse events (AE) related to anticalcineurins (ACN).

Methods: From 1991 to 2002, 323 patients surviving more than 1 year were transplanted in our center. Conversion to MMF was performed in 56 LT: 24 (43%) to MMF in monotherapy and 32 (57%) to MMF + low doses of ACN. Patients converted to MMF, presented more severe preconversion chronic renal failure (CRF). Follow-up post-transplant varied from 1 to 11 years. Indications for conversion were basically CRF. The mean time between LT and AE onset was 39 months (r:2-101). Follow-up post-conversion was 25 months (r:2-96).

Results: Renal function improved significantly for the totality of patients, during the first 3 months postconversion and this amelioration was maintained but without further improvement. Eleven (19.6%) patients presented acute rejection (2 severe) after conversion. The two severe rejections (requiring steroid boluses) appeared in the MMF group, and 1 finally died. In the remaining patients, rejection was treated increasing (4) or reintroducing (5) ACN. Hypertension improved in 8 (14%) out of 41 patients affected; delipidemia improved in 4 (7%) out of 15 and DM in 1 (2%) out of 16.

Conclusions: MMF is useful as conversion therapy in stable LT patients with CRF due to ACN. When AE due to ACN appear, we propose an early conversion to MMF + low doses of ACN as first step. If patient remains stable and AE persists, conversion to MMF-monotherapy is advisable.

PO-300 PET-CT IN STAGING AND FOLLOW-UP OF POST TRANSPLANT LYMPHOPROLIFERATIVE DISORDER FOLLOWING ADULT LIVER TRANSPLANTATION
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Introduction: Post transplant lymphoproliferative disorder (PTLD) is a rare but serious complication of immunosuppression (IS) after transplantation. Positron emission tomography (PET) has been proven to be not only highly accurate in diagnosis and re-staging of lymphomas but also a strong prognostic factor in the early course of treatment. However only very little is reported about PET-CT in patients with PTLD.

Aim: To analyze the use of PET-CT in the management of our patients with PTLD after liver transplantation (LT).

Material and Methods: Between 1995 and 2004, 4 out of 154 (2.5%) patients after LT developed PTLD at our institution. Diagnosis was confirmed with a biopsy and staging scan performed with CT scan and bone marrow biopsy. PET-CT was used depending on availability and clinical necessity. Treatment included reduced IS, anti-CD20 antibody and chemotherapy.

Results: The PET-CT was used in 1/4 patient for staging revealing a positive additional lesion in the right lobe which was confirmed with a biopsy. In all patients a negative PET-CT showed tumor response with complete remission after treatment. During long term follow up a CT showed suspicion of tumor progression in two patients, both lesions were PET-posit. Histology confirmed PTLD in one patient with a pharyngeal lesion. In the other patient with bilateral lung lesions however, the open lung biopsy showed chronic inflammation (false positive result).

Conclusion: PET-CT is a very sensitive tool in the staging and follow-up of PTLD after LT. However, as false positive findings occur, biopsy remains compulsory for diagnosis. Further studies are needed before implementing PET-CT in the routine clinical use.

PO-301 PRETRANSPLANT sCD30 AND TNF-α AS PREDICTING VALUE OF ACUTE KIDNEY REJECTION
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Aims: The proinflammatory cytokine tumor necrosis factor-alpha (TNF-α) has been implicated in the pathogenesis of acute rejection (AR) while recent studies suggest that serum level of soluble CD30 (sCD30), as a marker for the activation state of Th2-type cytokine, is a useful predictor of graft outcome. The aim of this study was to determine whether TNF-α and sCD30 influence the incidence and severity of AR in the first six months following kidney transplantation.

Methods: Pretransplant sera of 79 deceased-donor kidney recipients were retrospectively tested for serum level of TNF-α and sCD30 using commercially available ELISA kits. Inclusion criteria were first graft patients with cyclosporine-based immunosuppression, alive with functioning graft and at least one year follow up. The rejection episodes were defined clinically and classified as steroid-resistant or responsive.

Results: The incidence of AR was 18% in-group of recipients with high level TNF-α and 24% was free of rejection. With respect to the sCD30, incidence of AR was significantly correlated (p=0.00001, Fishers Exact). Than recipient cytokines were analyzed together, the sCD30 producer had worse prognosis, 47% with episode of AR versus high level of TNF-25% at level of significance (p=0.004, Fishers Exact). However sCD30 positive/high TNF-α recipients had more severe and two or more AR episodes.

Conclusion: Our data indicate that sCD30 is an important marker of AR following kidney transplantation. However it is still useful to combine few immunological parameters which may have clinical role in identifying patients at risk of multiple and severe rejections.

PO-302 IMMUNOLOGICAL AND NON IMMUNOLOGICAL FACTORS IN PREDICTING CHRONIC KIDNEY REJECTION
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Chronic allograft dysfunction, which is the common cause of allograft failure, is in part caused by ongoing immune response. To prevent the significant degree of graft loss attributable to chronic kidney failure, we have to be able to identify patients at risk during the posttransplant period and monitor them. The prospective study of possible risk factors for chronic rejection (CR) based on three years follows up is the aim in this work. 315 primary kidney recipients whose graft survived more than one year were followed for a mean of 3.7 years. Kidney recipients with exhibiting a humoral response to the allo- graft demonstrate lower graft survival and increased risk for the development CR. 37.8% recipients had MHC-reactive alloantibodies 35.2% failure among posttransplant positive patients (p=0.00002) statistically significant. The risk of CR was independent of serum and number of acute rejection within first six months. The increase in serum creatinine level (SCR) occurred in different time following the MHC- alloantibodies. Our study includes a multivariate analysis of the risk to onset of first symptoms of CR, comparing the relative importance of immunological and non-immunological factors.
CLINICAL EXPERIENCE OF RAPAMYCIN AS A RESCUE THERAPY IN CHRONIC ALLOGRAFT NEPHROPATHY

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Purpose: NICE guidelines on renal transplantation suggest that rapamycin should be considered in patients with proven intolerance to calcineurin inhibitors. The Tricontinental study demonstrated that early withdrawal of cyclosporin and maintenance with rapamycin improved graft function. This retrospective study analysed the effects of rapamycin as rescue therapy whilst withdrawing calcineurin inhibitors in renal transplant recipients primarily presenting with chronic allograft nephropathy.

Methods: Data on 16 renal transplant recipients was collected. Comparison of biochemical parameters at 3, 6 and 12 months was made with Wilcoxon rank test. GFR was calculated using the Cockcroft-Gault formula.

Results: 38% of patients were black and 62% were white. 31% were male with mean age of 49 years. 88% had cadaveric transplants. Rapamycin therapy was started 61(2-202) months after transplantation. Follow-up was 16(3-34) months.

Mean creatinine and GFR before rapamycin switch were 231±1 mol/l and 38±3mls/min respectively. In 5 patients creatinine improved with a mean change of 67±2 mol/l, 7 patients had stable renal function, and in 4 patients creatinine deteriorated with a mean change of 75±2 mol/l at the end of follow-up. In the latter group, creatinine was >250±5 mol/l before rapamycin switch. However, creatinine and GFR did not differ significantly at 3, 6 or 12 months (212±5 mol/l P=0.215, 216±5 mol/l P=0.311, 223±5 mol/l P=0.314, 42±5mls/min P=0.234, 45±5mls/min P=0.560, 35±5mls/min P=0.484) respectively.

Subgroup analysis of patients with creatinine >250±5 mol/l before rapamycin switch showed improved renal function at these 3 timepoints but was only significant at 3 and 6 months (155±5 mol/l P=0.047, 149±5 mol/l P=0.038, 167±5 mol/l P=0.076).

Conclusion: This study suggests that there is limited benefit in using rapamycin as a rescue therapy in chronic allograft nephropathy, particularly in patients with creatinines of >250±5 mol/l. 

RECOMMENDATION ON THE USE OF SIROLIMUS AFTER LIVER TRANSPLANTATION – EVIDENCE BASED GUIDELINES FROM A CONSENSUS CONFERENCE

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Sirolimus is an m-TOR inhibitor without renal side effects and potentially protects against the development of malignancy. On the background of the current information available, the potential role of Sirolimus in liver transplantation was assessed by leading representatives of transplant centers in Germany, Austria and Switzerland. The consensus gives recommendations on the Use of Sirolimus as primary/secondary immunosuppressant and precisely stresses factors like underlying disease, HCC etc. Further aspects are initial and maintenance dosage with partial and complete CNI withdrawal as well as trough levels (initial and maintenance) in such situations. Finally the management of undesirable drug effects are discussed.

VARIABLES AFFECTING SIROLIMUS BIOAVAILABILITY IMMEDIATELY AFTER RENAL TRANSPLANTATION: GENETIC POLYMORPHISMS (MDR1 AND CYP450 3A4 AND 3A5) AND DRUG INTERACTIONS

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Introduction:

MDR1 and CYP3A are important rate limiting factors of SRL bioavailability. We have very scarce information about the relation of SRL bioavailability with MDR1 or CYP single-nucleotide polymorphisms (SNP) or with administration of different drugs that affect MDR1 function.

Materials and Methods: All renal transplant patients treated with sirolimus without calcineurin inhibitors were included (n=46). During first month after transplantation creatinine, analytical parameters, acute rejection, drugs known to affect SRL pharmacokinetics or MDR1 function, and dose and blood trough concentration of SRL were recorded. SRL concentration/dose(C/D) ratios were calculated at 2 points; 1) almost after 6 SRL daily doses; 2) month one. SNP of MDR1 (C1236T, G2677T/A, C3435T), CYP3A4*1B and CYP3A5*3 were identified by real time PCR. The frequencies of SNP were compared to 67 controls.

Results: Genotype frequencies were comparable between patients and controls. There was no significant difference between SRL C/D ratio of the CYP3A5 and MDR1 genotypes. There was a statistical trend ( p=0.07) towards lower SRL C/D ratio in the groups with CYP3A4*1B SNP. Amlodipine and atorvastatin increased the SRL C/D ratio at the first month after transplantation (p=0.02).

Conclusion: Treatment with drugs that affect MDR1 function alter SRL bioavailability. Carriers of CYP3A4*1B SNP probably require more doses to achieve enough SRL blood levels. Possibly due to the low number of patients we couldn’t detect a relation between SRL bioavailability and MDR1 and CYP3A5 SNP.

DACLIZUMAB AND ALEMTUZUMAB AS INDUCTION AGENTS IN ADULT INTESTINAL AND MULTIVISCERAL TRANSPLANTATION: A COMPARISON OF TWO DIFFERENT REGIMENS

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Purpose: Induction therapy has been adopted for intestinal transplant in order to reduce acute cellular rejection (ACR) episodes during first period. We compared retrospectively two groups of patients during first month, randomly allocated with daclizumab (Zenapax®) and alemtuzumab (Campath®-1H®).

Methods: We transplanted 27 patients in a 4 years period: 23 were suitable for comparison.Eighteen received an isolated intestinal graft, 5 a multivisceral (2 with liver). Alemtuzumab was administered to 12 patients at dose of 0.3 mg/kg before transplant, after reperfusion, at day 3, at day 7; maintenance was based on Tacrolimus (Prograf®) without steroids. Eleven recipients received Daclizumab at dose of 2 mg/kg every week (ill 3rd month) and 1 mg/kg every two weeks (up to 6th month); maintenance was based on Tacrolimus and steroids. Rejections and infections were considered.

Results: After a mean follow-up period of 1050 days we experienced 2.0 rejection episodes per patient in daclizumab recipients while after 477 days we found 2.1 rejection episodes per patient for alemtuzumab recipients. During first month, 5 daclizumab recipients (43%) experienced 6 ACRs of mild degree, treated with steroids; seven patients (63%) developed an infection requiring treatment. We found 3 ACRs in both alemtuzumab recipients (16%), 2 with moderate degree,treated with steroids; 9 patients (75%) required treatment for infection.

Discussion and Conclusion: Alemtuzumab seems to offer a better immunosuppression against ACRs during first month. Infection rate is considerably high in both protocols.
PO-307 LATE REJECTION EPISODES AND GRAFT SURVIVAL UNDER SIROLIMUS TREATMENT AFTER ADULT INTESTINAL AND MULTIVISCERAL TRANSPLANTATION

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Purpose: Efficacy of Sirolimus (Rapamycin) as primary immunosuppression with Tacrolimus has been proven in first period after intestinal transplantation. We focused on its prolonged effect on rejections and graft survival as adjuvant therapy.

Methods: Twenty isolated intestinal recipients and 5 multiislercal (2 with liver) were considered: fifteen were started on Sirolimus because of nephrotoxicity (8), rejection (7), and diabetes (2). Sirolimus was administered with a 5 mg/m2 loading dose, followed by a 2 mg/m2 maintenance dose to keep a level of 10 mg/ml. Eight recipients discontinued Sirolimus because of recovered nephrotoxicity (2), sepsis (2), mictotoxicity (2), PTLD (1) and response to rejection (1). Primary immunosuppression was based on Tacrolimus.

Results: Sirolimus group was followed-up for a mean period of 941 days: patients experienced 8 ACR’s (0.3 ACRs/patient/year) with a mean follow-up of 524 days, while when Sirolimus was discontinued 26 ACRs were found (1.5 ACRs/patient/year) during a mean follow-up period of 415 days. Ten recipients did not receive Sirolimus (control group) and experienced 19 treated ACRs (1.7 ACRs/patient/year) during a mean follow-up period of 404 days. Cumulative 3 years graft survival was 93.4% in Sirolimus group and 70% in control group.

Discussion and Conclusion: Sirolimus may be useful as adjunct to Tacrolimus when nephrotoxicity or rejection are present: during prolonged treatment we showed decreased number of ACRs and increased graft survival. Adverse events may prevent its use as maintenance therapy.

PO-308 SAFE CONVERSION TO A GENERIC CYCLOSPORINE (CICLOHEXAL) IN STABLE RENAL TRANSPLANT PATIENTS

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The cost of immunosuppression following renal transplantation remains prohibitive. The cost of the generic cyclosporine (CicloHexal) has resulted in a significant cost-saving. The aim of this study was to investigate the impact of converting stable renal transplant patients to generic cyclosporine. Stable renal transplant recipients being followed in the Renal Unit at Groote Schuur Hospital were included in the study. The patients were converted from the conventional cyclosporine to the generic cyclosporine (CicloHexal). The patients also received Azathioprine and prednisone. The cyclosporine dose, cyclosporine trough level, and serum creatinine, for the three-month period prior to conversion and the three-month and the three-month period postconversion were recorded

There were 332 patients being followed-up. Only 75 patients were on cyclosporine and were included in the study. The dose of cyclosporine prior to conversion was exactly the same as the dose post-conversion. The mean cyclosporine trough level prior to conversion was 127 + 7ng/ml compared to a level of 130+9ng/ml following conversion. The mean serum creatinine was 136+6 prior to conversion and 132+5.

In conclusion, patients can be safely converted to the generic cyclosporine without changing the dose and without the need for additional monitoring. This is associated with a significant cost-saving.

PO-310 PANCREATECTOMY WITH ISLET AUTOTRANSPLANTATION FOR THE TREATMENT OF CHRONIC PANCREATITIS

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Pancreatectomy may lead to the decreasing of endocrine pancreatic function with consequent metabolic and nutritional disorders. The opportunity to perform an islet autotransplant provides the potential to prevent the onset of diabetes. Our aim was to study the short and long-term results of pancreatectomy together with islet autotransplantation of chronic pancreatitis.

Pancreatectomy together with islet autotransplantation in conjunction with a glucocorticoid-free immunosuppressive regimen consisting of sirolimus and tacrolimus has been offered since 1999. Islets were isolated by ductal perfusion with cold, purified collagenase, digested and purified in xenoprotein-free medium, and transplanted immediately by means of a portal embolization. The follow-up times range from 6 months to 4 years. The data presented here include the annual postoperative oral glucose tolerance test and glycosylated hemoglobin results, together with insulin and opiate requirements.

Seven male and 8 female patients (median age 42, range 25-63) have been transplanted. The principal indications for surgery were abdominal pain refractory to medical therapy (33%), biliary stenosis (27%), pancreatic pseudocyst (27%), suspicion of malignant neoplasm (13%). A median of 130108 (24491, 165538) islet equivalent (IEQ) were transplanted, which related to 2025 (311-23218) IEQ per kilogram of body weight. At 2 years posttransplant, six patients had a median glycosylated hemoglobin of 6.5% (5.4-19.2%), fasting C-peptide of 0.69 ng/mL (0.28-2.61 ng/mL), and required a median of 14 (0-43) units of insulin per day. At 4 years, these figures were 12% (7.1-15.1%), 2.3 ng/mL (1.2-3.6 ng/ml) and 68 U/day (10-89 U/day), respectively.

Islet autotransplantation offers a valuable addition to the pancreatectomy for the treatment of chronic pancreatitis.
The pancreas was procured from a Maastricht category human islets allotransplantation. 21 type 1 diabetic patients who underwent islet transplantation alone following ethanol injection without provoking liver or renal failure. Higher dose of STZ (150 mg/kg) uniformly provoked in both species, liver steatosis (AST/ALT > 6 mg/dl). In pigs, the use of high STZ dose (150mg/kg), produced an increase of FBG after 1 week, but a significant reduction of FBG occurred 4 weeks after STZ treatment (297±193 mg/dl to 187±161 mg/dl after week and 4weeks, respectively, p<0.05). In pancreas, a significant correction of IVGTG correlated with an increase of insulin production (p<0.005) and a hypertrophy of immature beta cells (120±12 vs. 98±7 µm² for STZ 4w. vs. tw., respectively, p<0.05) were observed in pigs 4 weeks after STZ. In contrast to rats/primates, a very weak GLUT2 staining was observed in pig livers and kidneys.

Conclusion: The low expression of GLUT2 and the higher proportion of immature beta cell clusters in pigs could explain why this animal is more resistant to the STZ activity.

**PO-312 TRANSPANTATION OF HUMAN ISLETS FROM A NON-HEART BEATING DONOR (NHBD)**

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Purpose: This work demonstrates the possibility of using NHBD pancreas for human islets allotransplantation.

Methods/Materials: The pancreas was procured from a Maastricht category 3 NHBD (48 yrs old female; BMI=23.4; Glucose=162 mg/dl; Amylase=124 IU/l; Lipase=316 IU/l). Cold perfusion was started through an aortic catheter after 7 min of cardiac arrest and islet isolation after 125 min of UW preservation (total CT). Islets preparation was performed with UltraPure® in a polynitrophenyl chamber. Purity of preparation, islets yield/integrity/viability/functionality were assessed and compared with 15 isolations of brain dead human donors (HBD). Islets were infused in a type 1 diabetic patient (C-peptide: 0.16 pmol/ml, insulin requirement 11.1U/kg/day and HbA1C<6%) already transplanted with a kidney and under IS therapy (Tac. MMF ST).

Results: After digestion, 428,600 IEQ (9,317 IEQ/g of digested tissue) was obtained from the NHBD pancreas in comparison with 221,885 ± 72,647 IEQ (5520 ± 2663 IEQ/g) from 15 HBD pancreases. After purification, 228,100 IEQ (65% purity, 82% of islets viability) were transplanted into the recipient liver. During the first 9 months after transplantation, a 41% reduction of daily insulin (0.64 U/kg/day) was observed but after 14 months, it dropped down to 23% reduction of daily insulin associated with a C-peptide >0.5 and HbA1C in 7.2. Additionally, no hypoglycaemia occurred during the follow-up period.

Conclusion: This case report demonstrated that sufficient mass islets obtained from a NHBD can improve quality of life in a type 1 diabetic patient.

**PO-313 ADVERSE EVENTS AFTER ISLET TRANSPLANTATION ALONE: 2 CASES OF ACUTE CARDIOMYOPATHY**

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The use of a steroid free immunosuppressive regimen, daclizumab, sirolimus and tacrolimus (Edmonton Protocol=EP), has been one of the most important changes in islet transplantation. The risk/benefit ratio remains a major concern of this tryp (150,000–500,000 IEQ). We describe 2 cases of acute cardiomyopathy among 21 type 1 diabetic patients who underwent islet transplantation alone following the EP. Case 1: 15 months after the 1st infusion fever and pharyngitis occurred; 1 month later, right ventricular dilatation was observed at echocardiography; the patient underwent cardiac MRI, that showed left ventricular focal late enhancement; ventriculography, that confirmed ventricular dilatation; endomyocardial biopsy that was representative of myocarditis, with fibrosis and focal signs of activity, while PCR viral screening was negative. No cardiological therapy was needed. Case 2: 6 weeks after the 1st infusion fever, rhinitis and progressive fatigue occurred. Within one month signs of acute dilated cardiomyopathy were observed. Echocardiography showed left ventricular dilatation (ejection fraction <15%), cardiac MRI showed left ventricular dilatation but no signs of late enhancement, ventriculography confirmed ventricular dilatation; endomyocardial biopsy of the right ventricular chamber was negative for myocarditis. Diuretic, angiotensin-converting enzyme and digoxin were required. In conclusion: even if there is not a direct correlation between the immunosuppression and the evidence of acute cardiomyopathy, it is important to consider this complication in the evaluation of risk/benefit ratio after islet transplantation alone.

**PO-314 HISTOLOGICAL ANALYSIS OF POST-PRESERVATION NATIVE PANCREATIC TISSUE BEFORE AND AFTER COLD STORAGE. A RETROSPECTIVE STUDY**

Tércio Genzini, Marcelo P. de Miranda, Fábio Crescentini, Dino Martini, Nam J. Kim, George Joppert, Kauê Serdeira, Fernando H. Lojudice, Patricia B. Santos, Leticia Labriola, Freddy G. Eliaschewitz, Anna C. Goldberg, Mary C. Sogayar. HEPATO, São Paulo, SP, Brazil; NUCEL, USP, SP, Brazil.

Appropriate cold storage solution and short cold ischemia have been crucial to the success of islet isolation. Histological changes due to storage solutions and the acceptable cold ischemia time have not been clearly defined. This study analyzed histological changes in pancreatic tissue according to the storage solution and the mean preservation time. Pancreas biopsies were obtained from 36 preserved human pancreas grafts, before and after cold storage. Two groups were established according to storage solution: University of Winsconsin (UW) n=18 and Eurocollins (EC) n=18. Histological aspects like necrosis, inflammation, fibrosis, acinar structure, pancreatic ductal system and islet morphology were analyzed. Donor parameters, such as age, BMI, ICU days, cardiorespiratory arrest, cardio-active drugs, cause of death, serum amylases and glucose levels were also examined. Univariate test (Pearson or Fischer p<0.05) and T Student test were applied. Statistical significant (p<0.05) changes were found in islet morphology, with increased vacuole formation (p=0.019) in EC storage. Increased edema (p=0.090), acinar structure damage, such as detracellulization (p=0.015), vacuoles (p=0.028) and degranulation (p=0.002), were significant with the UW solution. However, no significant differences were found between the two groups. In conclusion, UW seems to be less detrimental for islet integrity than EC but structural parenchyma damage can be observed with increased cold storage time.

Support: FAPESP, CNPq, FINEP and PRP-USP.

**PO-315 CAN MORPHOMETRIC PARAMETERS OF POST-PRESERVATION PANCREATIC BIOPSYES PREDICT SUCCESSFUL HUMAN ISLET ISOLATION OUTCOME?**

Tércio Genzini, Marcelo P. de Miranda, Fábio Crescentini, Dino Martini, Nam J. Kim, Kauê Serdeira, Fábio C.M. Torricelli, Fernando H. Lojudice, Patricia B. Santos, Carolina A. Guzzi, Johnny C. Ferretti, Carla L. Fortuna, Ana C. Sogayar. HEPATO, São Paulo, SP, Brazil; NUCEL, USP, SP, Brazil.

Islet transplantation is an attractive procedure that is still under development, yet major problems are related to cost and unpredictable outcome. Parameters allowing prediction of islet isolation yield would be helpful to improve the success rate and to lower the cost of this procedure. The purpose of this retrospective study was to analyze whether successful islet isolation conditions might be predicted from morphological aspects of preserved pancreatic tissue. 38 biopsies were obtained systematically after pancreas preservation. The samples were processed for light microscopy and analyzed for the following morphometric criteria: islet shape, delamination and number of islets per defined area (10 fields, magnification x10) and presence of adipose conjunctive tissue.

Numerical values were attributed to subjective criteria and correlated to purified islet equivalents (Total IEO and IEG) pancreatic cell) for statistical analysis. Successful islet isolation events were considered when the yield was >10,000 IEOs. Multivariate statistical regression (Logistic Regression) was applied to analyze the results. According to our study, islet number (p = 0.008), islet shape (p = 0.01) and islet delamination (p = 0.007) are shown to be significant (p<0.05) values to predict the success of islet isolation. We conclude that analysis of morphometric aspects of pancreatic biopsies under light microscopy may be helpful to predict the probability of successful islet isolation.

Support: FAPESP, CNPq, FINEP and PRP-USP.
**PO-316** OCCURRENCE OF STEATOSIS AFTER INTRA-HEPATIC ISLET AUTO- AND ALLOTRANSPLANTATION

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**Purpose:** The aim of the present study was to analyze liver parenchyma of patients previously transplanted with islet auto- and allografts.

**Patients and Methods:** Patients were divided as Group 1 (allograft) and Group 2 (autograft). Islet function was assessed by daily insulin requirement, fasting and stimulated C-peptide, HbA1c at time of imaging. All patients were investigated by abdominal ultrasound and MRI.

**Results:** In Gr.1, steatosis was observed on MRI in 3/16 patients, and in Gr.2, in 3/6 patients. In Gr.1, patients with steatosis had higher basal (476 vs. 289 pmol/L, p < 0.05) and stimulated C-peptide (1210 vs 548 pmol/L, p < 0.05), longer duration of insulin independence (20 vs 10.7 months, NS), and lower total daily insulin requirement (11 vs 28 units, NS). In Gr.2, there was no significant difference between patients with or without steatosis.

**Conclusion:** Hepatic steatosis can be associated with both islet auto- and allografts. In islet allograft recipients, steatosis was clearly correlated to a better graft function, and confirms the hypothesis that local insulin release might induce lipid accumulation in hepatocytes.

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**PO-317** IS IL-1β IMPORTANT IN PANCREATIC ISLET CELL TRANSPLANTATION?

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**Aim:** Determination of glyceremia and IL-1β levels which impairs early islet graft immunogenicity.

**Methods:** 8 groups with 6 Wistar albino rats were established: Group 1 [allo-graft non-diabetic, untreated]; Group 2 [allograft non-diabetic, cyclosporine-A (CyA) treated]; Group 3 [allograft diabetic, CyA]; Group 4 [allograft diabetic CyA]. Groups 5, 6, 7 and 8 were xenograft with same sequence. Diabetes was induced by single dose Streptozotocin (STZ). CyA was injected at days -1, 0, +1 and +2. For transplantation, 85±0.150 allogeneic islets from 3 donors and approximately 1500 human xenogeneic islets were given intraperitoneally. Serum IL-1β levels at day 1, +1 and +2 were assayed by ELISA, glyceremia was determined from tail vein.

**Results:** Statistical significance was observed in IL-1β levels in following conditions: at day +1, between groups 1-8 (p < 0.002), 2-6 (p < 0.016), at day +2, between groups 1-2 (p < 0.005), 2-6 (p < 0.025), 2-8 (p < 0.001). For glyceremia there was difference between groups 1-8, 2-8 (p < 0.001) at day +1 and 1-8, 2-4 (p < 0.001) and 2-8 (p < 0.0001) at day +2.

**DISCUSSION:** Our findings show IL-1β level increases, glyceremia decreases at day +1 whereas profile is opposite at day +2. Considering groups 1, 2 and 4, immunosuppression doesn’t affect this situation at peri-transplant period. In conclusion, cytokine monitoring and immunosuppressive agent selection should be taken into consideration to prevent graft rejections in early period.

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**PO-318** MINI LIVE DONOR NEPHRECTOMY USING LAPAROSCOPIC INSTRUMENTS – REPORT OF 84 CASES

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We describe an open technique of living donor nephrectomy via small incision using laparoscopic instruments, the ETS-FLEX Vascular Cutter which allows a fast AND secure division of the renal vessels and ureter and perfect haemosta-sis.Donors had an MRA, the left side was chosen. The patient is positioned on the right lateral decubitus. The table is flexed. The patient is secured with a de-flatable beanbag and adhesive tape. A 7±1mm Loin incision is made anterior to the 11th rib. When positioned on a vessel, the Vascular Cutter applies three staple lines proximally and three distally and divides the vessel between them. The distal end of the Vascular Cutter can be rotated to fit on a vessel regard-less of the angle. After the vessels and ureter are dissected-free the vascular staplers are applied. The kidney is flushed after removal of the staple lines. Between Oct. 2000 and Nov. 2004 we performed, 84 LDN using this technique, 55 females, 29 males age 21-67 years (mean 46). The warm ischemia time (mean ± SD) 65 ± 15 seconds. The operative time (mean ± SD) 66 ± 10 minutes. All grafts were successfully revascularised with 100% patient and graft survival (1- 48 months follow up). Patient stay in the hospital (mean ± SD) 3±1 days. LDN is associated with low morbidity. Using the vascular staples reduces sig-nificantly the warm ischemia and total operative time and allows a safe removal of the kidney via small incision, especially when there is more than one renal artery or vein and also allows early discharge from the hospital.

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**PO-319** HIGH RATE OF PRIMARY FUCTION IN CADAVERIC KIDNEY IN A CENTER WITH THE FIRST 40 CADAVERIC EXPERIENCE

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**Introduction & Objective:** Renal graft function and survival are influenced by various factors. One of the factors related to cadaveric grafts is cold ischemia. Cadaveric renal transplantation is usually associated with delayed function (DFG) due to prolonged cold ischemia time (CIT).

**Material & Methods:** In this study we present the results of the first 40 cadav-eric grafts at our locally procured center. DFG was defined as the requirement for hemodialysis for two or more sessions.

**Results:** The 40 recipients included 22 women of mean (± SD) recipient age 33.3±11.55 years. And 18 men of mean (± SD) recipient age 27.61±11 years, with colds ischemia > 2 hours. All kidney were successfully implanted, there were no graft loss due to surgical complications. Primary renal function was observed in 38 recipients. Graft loss was occurred in 3 cases due to acute hyper rejection in 2 cases and accelerated rejection in 1 case. There was no delayed graft function. One recipient died 32 hours after transplant from heart failure. **Conclusion:** Primary function is highly desirable in cadaveric kidney recip-i ents. Short CIT due to local procurement of organ may have contributed to the high primary function seen in our center.

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**PO-320** MAJOR VASCULAR AND UROLOGIC COMPLICATIONS OF RENAL TRANSPLANTATION: RESULTS FROM A SINGLE CENTER IN IRAN

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**Introduction & Objective:** The objective of this research is to identify and determine the major vascular and urologic complications in kidney transplant-ation recipients at our center.

**Material & METHODS:** Records of 786 patients subjected to renal transplan-tation were retrospectively reviewed to analyze the major postoperative com-plications. The complications were grouped as vascular and urologic.

**Results:** Six (0.76%) recipients developed vascular complications. Renal vein thrombosis (2 patients 0.25%) and stenosis kinking of renal artery (2 patients 0.25%) was the most common followed by 1 patient 0.125% and iliac vein laceration and uncontrollable bleeding lead to death of diabetic, fatty woman recipient (1 patient 0.125%). Thirty three recipients developed urologic complications. In decreasing order frequency, there were seventeen (2.18%) cases of urine leakage of which only 5 cases responded to conservative management. Six (0.76%) urinary obstruc-tion due to ureteral stricture, six (0.76%) distal ureteral necrosis, and 4 (0.5%) patients developed renal calcual.

**Conclusion:** The complication rates in our kidney transplantation are low, and considered acceptable. These results reflect our center’s focus on thorough preoperative evaluation, meticulous surgical technique, intensive postopera-tive care, and prompt diagnosis and appropriate treatment of complications.

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**PO-321** APPLICATION OF AN ARTIFICIAL NEURAL NETWORK MODEL TO PREDICT DELAYED GRAFT FUNCTION IN PAEDIATRIC KIDNEY RECIPIENTS

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Although conventional multivariate models allowed to identify risk factors for
Prospective comparison of post-operative pain risk factors for malignancies in renal transplant patients, even though it is infrequent and has not been proved. The difficulty to evaluate malignancy in APKD makes the diagnosis all the more challenging [1]. As there is no data to support prophylactic nephrectomy, these patient should be closely monitored and any suspicion of malignancy should be evaluated with imaging modalities.

Conclusion: Due to this difficulty in diagnosis in the transplant patients and owing to the need for immunosuppression, nephrectomy should be considered early if malignancy is suspected [2].

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**PO-324 ROLE OF NITRIC OXIDE IN RENAL ISCHEMIC PRECONDITIONING**

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Introduction: Ischemic preconditioning (IPC), a phenomenon consisting of ischemia and reperfusion periods which renders an organ tolerant to subsequent prolonged ischemia. This study was designed to explore the involvement of nitric oxide (NO) in the protection afforded by molsidomine in renal ischemic preconditioning.

Methods: Ischemic acute renal failure (ARF) was induced by occlusion of the left renal artery and vein for 45 minutes followed by reperfusion, two weeks after contralateral nephrectomy. IPC, which consists of three cycles of 2-min ischemia followed by 5-min reperfusion, was performed prior to 45-min ischemia. Molsidomine was given thirty minutes before the surgical procedures.

Results: IPC as well as animals treated with molsidomine, significantly improved the renal function and histological renal damage such as tubular necrosis, haeiline casts and medullary congestion. NO metabolites (NOx) production in the kidney after 45-minute ischemia was markedly increased in preconditioned as well as molsidomine treated rats compared with animals not treated with IPC and molsidomine. The improvement in renal dysfunction in IPC as well as molsidomine treated animals was abolished by pretreatment with L-NAME, a non specific NOS inhibitor.

Conclusions: This study demonstrates the contributory role of nitric oxide in the protection afforded by molsidomine in renal ischemic preconditioning.

**PO-325 DIFFERENCES IN HUMORAL IMMUNITY BETWEEN A NON-REJECTION GROUP AND A REJECTION GROUP AFTER ABO-INCOMPATIBLE RENAL TRANSPLANTATION**

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Background: Renal transplantation across the blood barrier is a unique model for investigating the humoral response to different carbohydrate antigens. However, in such a renal transplantation, the characteristics of B cells as well as of the antibodies produced by B cells are less well defined.

Methods: In the present study we investigated B cell subsets, i.e., the CD5 (+) B-1 and CD5 (-) B-2 cell T-dependent activation occurs only in group 2. The antibody subclasses analysis showed mild elevation of IgG2 and IgM in group 1 as opposed to remarkable elevation of IgG2, IgM and IgG1 in group 2.

Conclusions: The results of this study suggested that CD5 (+) B-1 cell T-independent activation usually occurs soon after ABO-incompatible renal transplantation, but that CD5 (-) B-2 cell T-dependent activation occurs only in patients who experience graft rejection.

**PO-326 RISK FACTORS FOR MALIGNANCIES IN RENAL TRANSPLANT RECIPIENTS**

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Background. Malignancies continue to be an important cause of morbidity and mortality after renal transplantation. Unfortunately, risk factors for malignancies have not been well defined regarding new immunosuppressive agent such as tacrolimus, mycophenolate mofetil and basiliximab.
BONE RESORPTION IS INCREASED IN KIDNEY RECIPIENTS

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Bone metabolism disturbances occur in the majority of kidney transplant recipients. Bone metabolism was evaluated using noninvasive parameters in 49 kidney transplant recipients (23 male, 26 female), aged 21-64 years, with good and stable renal function (creatinine clearance > 65 mL/min.). Bone mineral density (BMD) was estimated in the lumbar spine, femoral neck and distal third of the radius using dual energy absorptiometry (DEXA). 0.25-181 months after transplantation. The control DEXA was performed 11-57 months after the first (if the first DEXA was made >6 months posttransplant, N=16, the control DEXA was made after 11-14 months). The BMD changes (delta BMD) were calculated per 12 month period. The relationship of bone metabolism disturbances and BMD changes was investigated. The following serum parameters were estimated: IPTH, total alkaline phosphatase, crosslaps, Ca, Pi. IPTH values were above the upper reference range in 24%, Ca in 47%, alkaline phosphatase in 14%, and crosslaps in 65% of patients. Crosslap values were significantly higher in patients in whom the estimations were performed during the first posttransplant year. IPTH serum values correlated significantly positively with Ca and alkaline phosphatase, and negatively with Pi. Alkaline phosphatase correlated significantly positively with crosslaps. Crosslaps correlated significantly and negatively with posttransplant period duration as well as with delta BMD for the lumbar spine, femoral neck, and distal radius. Bone resorption was increased in most kidney transplant recipients, and was higher during the first posttransplant year. Bone resorption may not have been increased solely due to PTH, other factors also seemed to play a role. Increased bone resorption resulted in the bone loss in kidney transplant recipients.

ASSESSMENT OF QUALITY OF LIFE IN 50 PATIENTS UNDER HEMODIALYSIS AND FOLLOWING KIDNEY TRANSPLANT

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Introduction & Objectives: According to modern standards, a life-saving intervention such as kidney transplantation (KTx) is expected to do more than merely prolong life. In order to be considered worth the risks, effort, time, and expertise involved, KTx must also contribute to the overall health of the patient. This overall health is referred to by some as quality of life. Material & Methods: The current study used a self-rating questionnaire to evaluate the quality of life in 50 hemodialysis patients (68 males & 32 females, average age: 31 years) with KTx. Mean duration of hemodialysis was 3 years and mean postoperative time was 2.4 years when tested. No patients was tested less than 3 months following transplant. 55% of patients were between 1.1-4 mg/dl and 3% had 2.5-2.9 mg/dl. A five point scale was used to evaluate the patients’ status in regard to these factors. Life quality was graded as either very good, good, medium, different, or disabled.

Results: In more than 80% of patients there was an improvement in several dimensions of quality of life following KTx. KTx is not only a life-saving intervention; it also increases the quality of life of the patient and can be considered cost-effective for the patient and the society.

Conclusions: KTx has positive effect on several dimensions of quality of life. Quality of life has been associated with overall well-being, low levels of dys-functional stress, and physical as well as psychological health. Renal transplantation can thus be considered accost-effectif intervention both in saving lives and in improving the quality of life.
tion were performed in Mashhad University of Medical Sciences. In this study 100 renal transplant recipients who had a complete file and an address were selected. They were 18-61 years with mean age of 33 years. They had hemodialysis for at least six months and the most of them had hemodialysis for seven years. Evaluation of patients before and after renal transplantation was standardized, and included a medical history, physical examination, routine biochemical and hematological studies, and sexual function.

**Results:** Potency: Before chronic renal failure: After chronic renal failure: After renal transplant
86 cases good 30 cases good 76 good
12 moderate 52 moderate 18 moderate
2 cases poor 8 cases poor 6 poor
Good means: full erection for intercourse
Moderate means: Semierrection but enough for intercourse.
Poor means: Semierrection but not enough for intercourse or no erection.
Lidibo: Before chronic renal failure: After chronic renal failure: After renal transplant
88 good 22 good 80 cases good
10 moderate 52 moderate 16 moderate
2 poor 26 poor 4 poor

**Conclusion:** Kidney transplantation not only improve the quality of life and health of patients with chronic renal failure but also improve libido, potency and fertility.

**PO-332 RENAL TRANSPLANTATION IN OLDER ADULTS: IS GRAFT SURVIVAL AFFECT BY AGE?**

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**Background:** End-stage renal disease (ESRD) increases with advancing age and renal transplantation should be considered in ESRD patients older than 50 years. There is a paucity of data on long patient and graft survival in this population.

**Materials and Methods:** From Nov.1983 to Sep. 2004, 485 renal transplantations were performed at Ghaem medical center (Iran). The following data were analyzed and compared between the patients >50 years old (group I) and < 50 years old (group II): actuarial patient and graft survival, serum creatinine and blood pressure at 1.35 and 7 years.

**Results:** Patient survival at 1, 3, 5, and 7 years was 72%, 58%, 41%, and 41% for group I, and 95%, 86%, 86% and 86% for group II respectively. Graft survival at 1, 3, 5, and 7 years was 72%, 58%, 41%, and 41% for group I, and 95%, 85%, 85%, and 85% for group II respectively.

**Conclusion:** Renal transplantation should be considered in patients older than 50 years of age, since graft survival is excellent in this population, and early mortality and complications in this group has no difference comparing with younger recipients. Although these patients have a shorter life expectancy, they benefit from renal transplantation similarly to younger kidney transplant recipients.

**PO-333 UNCOMMON SIDE EFFECT OF MMF IN RENAL TRANSPLANT RECIPIENTS**

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**Purpose:** We assessed MMF related hepatotoxicity in renal transplant recipients.

**Methods/Materials:** A total of 124 renal transplantation recipients (RTRs) were evaluated for elevated liver enzymes associated with MMF and 79 patients were enrolled to the study. Patients were used MMF 2g/day. The patients who had progressive increase in liver enzymes after renal transplantation and their AST, ALT, GGT, ALP, bilirubin levels, hepatitisB, hepatitisC, CMV, abdominal ultrasonography, duration of hepatotoxicity and decreased dosage or withdrawal of MMF were recorded.

**Results:** Of the 79 patients, 11 patients (13.9%) had progressive increase in liver enzymes. The median (min-max) age of the patients with MMF hepatotoxicity was 39.00 (19-54) and 72.7% of them were male. None of the patients had hepatitis B, CMV infection or other possible causes for elevated liver enzymes and their abdominal ultrasonography were normal. High liver enzyme levels were regressed after the withdrawal (n=6) or reduce dosage (n=5) of MMF. The median increase of the increase in liver enzymes was 28.00 (4-70) days, and after reduced % 50 or withdrawal of MMF, returned to normal values in 16.00 (4-210) days. The median levels of ALT in waiting list (I), before (II) and after (III) reduction dosage or withdrawal of MMF are 22.0 (3-222), 222.0 (51-508) and 33.0 (21-64) U/L respectively (p I-II=0.004, p I-II=0.013 and p II-III= 0.005). There were no differences for ALP, GGT, total bilirubin and direct bilirubin levels.

**Conclusion:** If hepatotoxicity related with MMF is not considered especially in the early period of renal transplantation, resolution of hepatotoxicity can be required long term.

**PO-334 INCREASED RISK OF CHOLELITHIASIS IN THE SAME PATIENTS AFTER RENAL TRANSPLANTATION ACCORDING TO DIALYSIS PERIOD**

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**Purpose:** There is no consensus on incidence and management of cholelithi-asis (CI) in renal transplant recipients (RTR). We assessed CI and its complications in RTR before and after transplantation.

**Methods/Materials:** Body mass index (BMI), serum biochemistry, abdominal ultrasonography and complications of CI, duration of end stage renal disease, renal transplantation and immunosuppressive drugs were evaluated. A total of 53 patients (M/F; 31/22) were evaluated and the mean age of the patients was 34.11 ± 9.42 years. Before transplantation, 47 of 53 patients were on hemodialysis. The duration of hemodialysis, peritoneal dialysis and transplantation were 22.0 ± 1.97, 1.32 ± 0.74 years and 44.72 ± 33.68 months, respectively.

**Results:** Before transplantation, one patient (1.9%) and after transplantation 6 patients (11.3%) had CI. None of the patients had history of cholecystectomy before transplantation and one patient had cholecystectomy due to pancreatitis after transplantation. Five of 6 patients who had CI were on cyclosporine therapy and one patient was on tacrolimus therapy. Before and after transplantation, total cholesterol (p=0.043), HDL-cholesterol (p=0.000), calcium (0.045), BMI(p=0.007) were significantly different from each other and borderline differences for CI.

**Conclusion:** The incidence of CI increased from 1.9% to 11.3% in RTR, complication of CI was detected only in one patient. The incidence of CI is higher in RTR than pre-transplant patients. Our study was different from the others because pre and post transplant patients were the same patients. The most important factors for development of CI was the usage of cyclosporine and exposed time of cyclosporine.

**PO-335 LEUCOCYTE DEPLETION SIGNIFICANTLY IMPROVES RENAL FUNCTION DURING REPERFUSION USING AN ISOLATED HAEMOPERFUSED PORCINE KIDNEY MODEL**

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**Purpose:** Ischaemia reperfusion injury is an important early pathophysiological process following renal transplantation. White cells, in particular polymorphs, are thought to play a pivotal role in ischaemia reperfusion injury. This study aims to demonstrate the effect of circulating white cells in early graft injury using an isolated haemoperfused porcine kidney model.

**Methods:** Porcine kidneys were perfused with normothermic 37°C oxygenated autologous blood for six hours on an isolated organ perfusion system after two hours cold storage in a hyperosmolar citrate solution. The system was designed using cardiopulmonary bypass technology and perfusion commenced with a circulating creatinine concentration of 1000μmol/L, to assess renal function. In group A (n=4) a leucocyte filter was included in the circuit and in group B (n=4) non-filtered blood was used. Physiological and biochemical parameters were measured throughout the six hour perfusion period.

**Results:** Group A demonstrated significantly improved parameters of renal function when compared to group B as shown in the table. Values are the mean ± SD

| Functional Parameters | Group A | Group B | P Value |
|-----------------------|---------|---------|---------|
| % Creatinine Fall      | 95.2±4  | 67.1±10.2| 0.03    |
| Creatinine Clearance ml/min/100g | 43.7±14 | 5.5±1.7 | 0.03    |
| Urine output ml/h     | 148.5±18| 40.5±4.4 | 0.002   |
| 0' rBC lysis ml/min   | 41.2±7.1| 23.7±6.9 | 0.03    |
| Renal blood flow ml/min/100g | 59.8±4.4 | 34.4±6.6 | 0.03    |
| Renal Vascular Resistance mmHg/ml/min | 0.43±0.9 | 0.81±0.2 | 0.03    |

**Conclusions:** The depletion of leucocytes in blood used to perfuse kidneys significantly improves early graft function indicating an important role for white cells in ischaemia reperfusion injury.
DAILY BLOOD PRESSURE CONTROL IS NOT SUFFICIENT TO REGRESS CARDIAC HYPERTROPHY AND DYSFUNCTION: A BI-VENTRICULAR TISSUE DOPPLER ECHOCARDIOGRAPHIC STUDY

Erkan Demir, Mustafa Balal, Saime Paydas, Ugur Erken.

Purpose: We assessed the relationship between the levels of 24 hours blood pressure and left ventricular mass index and bi-ventricular tissue Doppler echocardiographic measurements in renal transplant recipients, dialysis patients and healthy volunteers.

Methods/Materials: We evaluated 32 nondiabetic renal transplant recipients (G1), 18 hemodialysis patients (GII) and 19 healthy volunteers (GIIL). Results: There were no differences for age, gender, day-time blood pressures and loads among the groups. The mean night-time systolic-diastolic blood pressures (SBP-DBP) in GI, GII and GIIL were 119.77±17.41-77.34±14.46, 120.23±25.53-76.17±18.77; 99.90±9.30-64.35±8.77 mmHg respectively, (PI-I=1.0, PI-II=0.000, PI-III=0.013- PI-II=0.99, PI-III=0.001, PI-III=0.06). The mean night-time SBP load were 4.92±2.77, 6.10±1.81, 6.0% respectively, (PI-II=0.94, PI-III=0.003, PI-II=0.001). The mean night-time DBP load were 7.78±1.83, 8.02±1.28, 2.40±0.50% respectively, (PI-I=1.0, PI-II=0.009, PI-III=0.021). The mean levels of left ventricular mass index (LVMI) were 115.81±28.07, 128.06±65.72 and 85.05±13.01 mm²/g respectively, (PI-I=0.85, PI-III=0.000, PII-III=0.049). The mean levels of left ventricular Em/Am by tissue Doppler echocardiography were 1.13±0.40, 0.90±0.29, 1.59±0.38 respectively, (PI-II=0.127, PI-II=0.000, PI-III=0.000). The mean levels of right ventricular-Em/Am by tissue Doppler echocardiography were 0.89±0.37, 0.88±0.26, 1.31±0.19 respectively, (PI-I=0.99, PI-II=0.000, PI-III=0.001).

Conclusion: After renal transplantation, LVMI and bi-ventricular diastolic dysfunction were not regressed. Even tough, day-time blood pressures and loads were similar in three groups, in RTx night-time blood pressures and loads were significantly higher than healthy volunteers and similar to dialysis patients. We can say that well controlled day-time blood pressure and load is not sufficient to decrease cardiovascular risk in RTx. Also, it is important to control of night-time blood pressure and night-time DBP load.

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THE ADDITION OF MYCOPHENOLATE AND/OR BASILIXIMAB TO CALCINEURIN-INHIBITOR IMMUNOSUPPRESSION REDUCES THE HIGH RISK OF ACUTE REJECTION IN LIVE DONOR TRANSPLANTS

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Purpose: Live donor (LD) kidneys transplants, particularly from unrelated donors can be associated with poor HLA-matching and high risk of acute rejection. We wanted to assess the impact of the addition of MMF →-a humanised IL-2 monoclonal antibody (basiliximab) to standard calcineurin inhibitor-based therapy on acute rejection in LDs.

Methods: A consecutive series of 93 LD transplants (10 unrelated donors) were treated with stimulated immunosuppression consisting of a calcineurin inhibitor and prednisolone (CNI+P; n=54) or with tacrolimus and prednisolone in combination with MMF + basiliximab for patients with 1 or more HLADR mismatches. The two study groups were well matched for rejection risk factors including recipient age (32 ± 12 vs 36 ± 11 yrs; NS) and total HLA match (21 ± 12 vs 23 ± 11 mismatch; NS). Overall rejection rates were 30/54 (56%) in the CNI+P group and 12/41 (29%) in the IL-2+MMF group (RR=1.986, P=0.0129 Fisher’s exact). Steroid resistant rejection was higher in the CNI+P group (8/54 vs 3/41, RR=1.38, NS). For patients with 1 or more HLADR mismatch, rejection rates were higher with CNI+P (25/39 (64%) vs 10/29 (34%) P=0.027).

Conclusion: CNI-based immunosuppression in LD transplantation is associated with high rates of acute rejection. Addition of MMF + basiliximab significantly reduces frequency of acute rejection even in poorly matched grafts. This approach may form the basis for a new treatment paradigm in immunosuppression for high-risk LD.

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RENAral TRANSPLANTATION IN BOURNEVILLE-PRINGLE DISEASE: CASE REPORTS

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The Bourneville-Pringle disease, or tuberous sclerosis (TSC), is a rare (1-3/100 000) genetic disorder, located on the 9th or 16th chromosome. Major characteristic features are: facial cutan angiofibromas, renal angiomyolipomas, and cortical tubers in brain, and cardiac rhabdomyomas. 2/3 of the patients are women, renal involvement is about 60%, and 1-15% of them are candidate to have chronic renal failure.

Patients: 1. 26y female patient was admitted in the status of haemorrhage shock. By the laparotomy a ruptured, angiomyolipomatoid left kidney (7500g) was removed; she needed 4 blood transfusion. Bournville-Pringle disease, with all known signs, was diagnosed. Two years later, in 2001, pre-emptive ca- daver kidney transplantation, than three months later right kidney nephrectomy was performed, but she needed reoperation due to bleeding. She is keeping well now. 2. 43y female patient was transplanted in 1998, already binephrectomised because of angiomyolipomas. In 2003 we had to perform a left forearm amputa- tion due to a cystic, untreatable bleeding degeneration. She needed thoraco-otomy because of intathoracic haemorrhage, with unknown origin. After that small intestin resection was performed for a bleeding, metastasing epitheloid angiosarcoma; she needed →11 l blood transfusion. A couple of weeks later she died due to tumorous propagation.

Summary: Our patients fulfill all criteria of TSC. The speciality of our first case was the largest removed kidney, we know from the literature. The second case showed 6 years posttransplant a malignant small intestine tumour, which can occur as minor sign. Both patients needed reoperations, and massive transfusions due to bleedings. Transplantation is a favourable therapeutic modality for TSC, but requires close follow up for malignancy.

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PO-340

QUANTIFICATION OF INTERSTITIAL FIBROSIS IN RENAL ALLOGRAFTS BY QUANTITATIVE IMAGE ANALYSIS IS MORE RELIABLE THAN BY SEMI-QUANTITATIVE METHOD

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Purpose: Interstitial fibrosis is currently assessed by semi-quantitative analysis. Subjective interpretation of the pathologist is the main limiting factor of such method. We have developed a new objective method to quantify interstitial fibrosis by computerised colour image analysis and have compared this method to the semi-quantitative one in renal transplant biopsies.

Methods: 40 Masson's trichrome stained biopsies from transplant kidney, both, stained and imaged and analysed by a new program of colour segmentation image analysis. These results were compared with those obtained by two experts in renal pathology, a non renal expert pathologist and two nephrologists who have assessed interstitial fibrosis according to the criteria defined by the Banff 1997 classification. Statistical analysis used a kappa's test for groups comparison.
Results: The intra and inter-observer reproducibility of the automatic method was excellent and characterized by standard errors of 0.07% and 0.09% respectively. The inter-observer concordance using the semi-quantitative method was low. Kappa values between the two renal pathologists were 55% and between clinicians and pathologists 53% to 62%. Kappa values between expert pathologists and quantitative analysis were 33% to 35% and between clinicians and automatic method 41% to 46%.

Conclusion: The automatic colour segmentation image analysis is a more reliable and reproducible method than the semi-quantitative one to evaluate renal interstitial fibrosis. This new tool will be of considerable interest in the study of chronic allograft nephropathy.

PO-341 RISK FACTORS AND OUTCOME OF FOCAL AND SEGMENTAL GLomerulOSCLEROSIS RECURRENCE IN ADULT RECIPIENTS
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Purpose: Recurrence of nephrotic syndrome after renal transplantation for primary focal segmental glomerulosclerosis (FSGS) is a frequent and still unpredictable complication but clear risk factors for recurrence have not yet been identified.

Methods: Here, we report in a retrospective study the clinical course, risk factors and outcome of recurrence of thirty five renal transplantations performed in 33 adult recipients with end stage renal disease (ESRD) secondary to FSGS.

Results: Recurrence of FSGS occurred in 12 grafts (34%). Recurrence was observed during the first month after renal transplantation in 8 patients. A significantly higher number of patients in the group with recurrence (R group) compared with the group without recurrence (NR group) received Cyclosporine before transplantation (83.3% vs. 43.5%, p < 0.02). Donors in R group were significantly older than in the non NR group (42.8 years vs. 35 years, p < 0.05). A higher number of patients from the R group required post transplantation dialysis (33.3% vs 17.4%, p = 0.002). Acute rejection occurred more frequently in patients from the NR group compared with the R group, although the difference was not significant. Among the 9 patients treated with plasma exchange, graft loss related to recurrence occurred in 6 cases. The 5 year-graft survival was significantly lower in patients with recurrence compared with patients without recurrence (57% vs. 82%, p <0.001).

Conclusion: The 5-year graft donor age is a reliable risk factor for recurrence in adult recipients and suggests for the first time an opposite relation between recurrence and acute rejections.

PO-342 REQUIREMENTS AND CONSEQUENCES FOR LIVING KIDNEY DONOR SCREENING
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Background: In our centre the proportion of living donor kidney transplants has increased to 60%. For that purpose we screened hundreds of apparently healthy individuals for kidney donation. We wondered how many of these potential kidney donors eventually became actual donors and what the main reasons were for not donating.

Methods: We performed a medical status data survey of all 421 potential kidney donors that approached our outpatient clinic between January 2000 and January 2003. Results: 256/394 (65%) completed screenings resulted in 236 performed and 20 planned donations; 27 screenings are pending. 138/394 (35%) screenings did not result in nephrectomy; 30/138 (22%) times for immunological reasons, while in 41/138 (30%) cases acceptor factors and in 67/138 (49%) cases donor factors precluded donation. Acceptor factors included 14 deceased donor kidney transplants, 18 delisted or died on the waitlist, 5 had psychological problems with living donation, 3 still too good for transplantation and 1 acceptor changed to another hospital. Donor factors included 20 times withdrawal of consent and 3 times other relatives that preferentially donated. There were 44 medical contra indications: 12 cardiovascular and 10 neurological problems, 6 fibromuscular dysplasias of the a. renalis, 4 malignancies, 4 hepatitis/liver disease, 4 diabetes, 3 hematomal disorders and 1 patient with schizofrenia.

Conclusion: In a routine living kidney transplantation program, 35% of the donor screening procedures did not result in donation, while 11% of the potential donors had clinical contra indications. This implies that to perform 100 living donations it is necessary to screen 155 apparently healthy individuals with the consequence of diagnosing 17 of them as patients.

PO-343 LONG-TERM RESULTS AFTER BALLOON DILATATION OF URERETAL STRICTURES
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Balloon dilatation (BD) is the procedure of choice for ureteral strictures after kidney transplantation (KTx). We sought to determine the long-term outcome of BD among our patients.

Patients & Methods: A retrospective survey of patients who underwent KTx between 1997-2003 was done using our database. Risk factors for development of a ureteral stricture were assessed using uni- and multivariate analy- sis. The efficacy of BD was determined by freedom from ureteral stent with a stable allograft function. Median follow-up was 50.5 months.

Results: The overall incidence of ureteral strictures was 4.8% (26/540 patients); 80% were distinct and involved the distal ureter. There was no correlation between ureteral strictures and donor or recipient age, ureteral anastomosis technique and use of ureteral stents. A higher incidence of strictures was found in living donor vs. deceased donor KTx (p=0.026). The mean number of BD per patient was 1.85 and the overall success rate was 55.5%. Higher suc- cess rate was observed when therapy was instituted <3 months, 63.3% vs. >3 months, 42.8%, after transplant (p=ns). Surgical repair of ureteral strictures as a primary treatment option was successful in 7 patients and in another 6 of 7 patients who failed BD. Mean hospital stay in patients who underwent BD was 35.5 days vs. 26 days in those who underwent surgical repair.

Conclusions: Balloon dilatation as a treatment of ureteral strictures after transplant might be effective for distinct stricture which diagnosed <3 months post- transplant. In all other cases surgical repair should be instituted early to save costs and preserve graft function.

PO-344 URINE CYTOLOGY AS A USEFUL SCREENING METHOD FOR POLYOMA VIRUS Nephropathy in renal transplant PATIENTS, A SINGLE CENTER EXPERIENCE
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Polyoma virus nephropathy (PVN) occurs in 2% to 4% of renal transplant recipients. In this study our goal was to determine the incidence of polyoma virus infection in transplant patients, on the basis of age, sex, creatinim level and post transplantation period. During this study 1086 urine samples were collected from 362 patients, these samples were centrifuged and stained with papricanius staining method. All of these slides were examined and classified as negative or positive (> 1 decocells/sample). Among 1086 urine cytologies from 241 men and 121 women, decoc cells were identified in 26.6% (96) of patients, 29.9% (72) males and 20% (24) females. The incidence of decoc cells (26.6%) and its increased prevalence in men was coincident with the previous reports. Increased incidence of decoc cells was noted with prolonged transplantation period (P>0.05), this was also consistent with the studies done earlier. But no significant relation was detected between older age and positive urine cytology, which was different from the previous studies that showed increased incidence of decoc cells in older age groups. The patients with positive urine cytology for the decoc cells had more abnormal plasma creatinin(26%) as compared to the patients with negative urine cytology(13.5%), it was also similar to the studies done earlier. Identification of cells with viral inclusions (decoc cells) can help with the diagnosis of viral replication or active infection, so it is suggested that routine urine cytology to be used as screening method for the detection of polyoma virus infection.

PO-345 THE INFLUENCE OF RENAL HEPATOCYTE GROWTH FACTOR (HGF) EXPRESSION ON EARLY AND LATE GRAFT OUTCOME OF PATIENTS WITH ACUTE REJECTION
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Purpose: Our aim is to examine the influence of renal HGF expression on renal graft outcome in case of acute rejection (AR).

Methods: For this purpose biopsies of 72 patients were included in the study. Out of 72, 63 patients had AR (Group 1).Remaining 9 patients had normal renal biopsy and used as control (group 2). For HGF immunostaining Renal (Glomerular, tubular and interstitial) HGF expression was graded semiquan- tatively. The influence of renal HGF expression on the development of interstitial fibrosis (IF) and graft loss during 36 months after AR episode was evaluated. Additionally, influence of renal HGF expression on graft function in the first 6 months after AR episode was studied.
DOES COLCHICINE HAVE AN ANTIFIBROTIC EFFECT ON THE DEVELOPMENT OF INTERSTITIAL FIBROSIS IN RENAL ALLOGRAFTS OF RECIPIENTS WITH FAMILIAL MEDITERRANEAN FEVER (FMF)?
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Purpose: Colchicine has been reported to inhibit collagen deposition by suppressing fibroblast growth factors such as TGF-beta. We hypothesized that because the patient's amyloid deposition, colchicine may prevent the development of interstitial fibrosis (IF) in amyloidosis patients.

Methods: For this purpose we design a study to evaluate the influence of colchicine therapy on the development of IF in 25 FMF patients (Group 1). For control group 25 non-amyloidotic patients that did not received colchicine therapy was included in the study (Group 2). Patients were carefully matched for risk factors predisposing to IF. The incidence of recurrence and the development of IF in the 1st, 2nd and 3rd year posttransplantation were evaluated from the follow-up biopsies of all cases.

Results: Only 4 patients showed amyloid recurrence in renal allograft. The development of IF was 44% (11/25) in group 1 patients and 80% (20/25) in group 2 patients during 36 months (p<0.01). The incidence of the development of IF in the 1st, 2nd and 3rd years posttransplantation was found statistically higher in group 2 recipients when compared with group 1 recipients (p<0.01).

The overall 1-, 2- and 3-year graft survival rates for the group 1 recipients were 96%, 92%, and 80%, respectively. The corresponding graft survival rates were 96%, 88%, and 60% for group 2 recipients respectively.

Conclusion: Our results support the thesis that colchicine therapy may have a beneficial effect on preventing the development of renal interstitial fibrosis.

DEVELOPMENT OF ULTRASOUND KIDNEY TRANSPLANT GLOMERULOGRAM AND ITS APPLICATION TO GLOMERULAR HEMODYNAMIC STUDY
Takahiro Akiyama1, Tsukasa Nishioka1, Tetsuro Nagano1, Tomomasa Yamamoto1, Atsusi Onoue2, 1Department of Urology, Kinki University Sakai Hospital, Sakai, Osaka, Japan; 2Division of Ultrasound, Chouji Clinic, Sakai, Osaka, Japan.

Purpose: We tried to establish kidney transplant glomerulogram using ultrasound enhancing agents and to evaluate glomerular hemodynamic changes in various abnormal conditions of the graft by this method.

Methods/Materials: After intravenous injection of enhancing agents Levovist1, the intensity of ultrasound signals obtained from microbubbles in the graft subcapsular ROI including amounts of glomeruli were counted sequentially by Advance Dynamic Flow (ADF). Thus, time intensity curve (TIC) of the signal and its parameters such as T max, T 1/2, delta T and lmax were gained. Ultrasound glomerulogram will reflect the hemodynamics in the transplant glomeruli themselves. Twenty-five kidney transplant recipients were examined. TIC parameters were compared to carotidcinin inhibitor (CNI) trough levels. Changes of TIC before and after the administration of AT1 receptor blockers (ARB) were also observed in 6 patients.

Results: T max and S-Cr values in 9 patients with low CNI trough level (CVA below 70 ng/ml, TAC below 7 ng/ml) are correlated significantly (P<0.0003), whereas no correlations were seen in 12 patients with high CNI level (n.s.). This might demonstrate that same alteration constriction in various degree will occur in high CNI group, so glomerular blood flows were not correlated with graft function. T max and T 1/2 in all of 6 patients decreased significantly after administration of candesartan. This will suggest afterload & efferent arteriolar dilating effect, glomerular tension lowering effect and renal protection effect of ARB.

Conclusion: Ultrasound glomerulogram may be a sensitive and noninvasive tool to evaluate glomerular hemodynamics for analyzing CNI nephrotoxity and mechanism of effect of vasoactive agents ARB.

EFFICACY AND SAFETY OF VALENDAFIN IN RENAL TRANSPLANT RECIPIENTS WITH ERECTILE DYSFUNCTION
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Purpose: Erectile dysfunction (ED) profoundly affects the quality of life. The prevalence of ED in renal transplant recipients (RTRs) is reported as high as 50%-60%. We evaluated the efficacy and safety of vardenafil in RTRs with ED. Also, the effect of vardenafil on graft function and interactions between cyclosporine/tacrolimus were investigated.

Methods: Eighteen RTRs with ED and serum creatinine < 2 mg/dl were treated with vardenafil. ED was assessed using the self-administered International Index of Erectile Function (IIEF), ED was diagnosed by using penile colour-Doppler ultrasonography and intracavernosal injection. Vardenafil efficacy was assessed by re-administering the IIEF questionnaire after 4 weeks of therapy. Serum creatinine levels, creatinine clearances and cyclosporine/tacrolimus concentrations were measured before and after vardenafil therapy. Eighteen RTRs without ED served as control.

Results: The IIEF scores improved from 13.16±3.41 to 26.38±5.26 in vardenafil treated RTRs with ED and IIEF score increased at least 9 points for each patient. There were no changes in renal function and cyclosporine/tacrolimus concentrations. Side effects were observed in 3 (17%) patients (headache in 2 patients, palpitation in 1 patient).

Conclusion: To our best knowledge, vardenafil has not been evaluated in RTRs with ED until now. Our study demonstrates that ED improved with vardenafil in RTRs with ED. For 4 weeks vardenafil therapy was side effect free. Renal function test did not change. Also, the dose changing in immunosuppressive drugs were not required for optimal serum levels during 4 weeks of vardenafil therapy.

ENDOTHELIAL DYSFUNCTION BEFORE AND AFTER KIDNEY TRANSPLANTATION
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Cerebrovascular disease (CVD) accounts for increased mortality in chronic renal failure (CRF), decreasing after renal transplant (RT). Endothelial dysfunction plays a role in CV morbidity-mortality.

Aim: To evaluate changes in endothelial dysfunction after RT

Methods: We enrol CRF patients studied for living RT and 8-10 months post-RT with biochemical markers, noninvasive pulse wave, noninvasive plethysmography (forearm reactive hyperemia); wire myography (endothelium-dependent and independent responses); and confocal microscopy of resistance arteries from abdominal fat. Non parametric analysis has been used for comparisons of continuous variables and analysis of variance for repeated measures for curves.

Results: 8 patients have completed studies: 7 female/1 male, 31-62 years; 4 first and 4 re-TR; 4 pre and 4 in dialysis. We found significant improvement in renal function (post-RT creatinine clearance=70-72 vs 50-60, hemoglobin, homocystein, uric acid, triglicerides, apolipoprotein and blood pressure<0.05). But we found no significant differences in endothelial function: biochemical markers (GMPc =11.2±14.4 vs 54±1.93, endothelin=6.2±1.4 vs 6.9±2.6 pmol/l, nitrires=53.4±7.3 vs 46±1.73 mmol/l, slementum=72.6±9.2 vs 69±3.8 µg/l), noninvasive pulse wave (oscillatory compliance = 4.1±1.9 vs 4.6±1.1/mHgX100), noninvasive plethysmography (218±114 vs 236±120 with no difference in curves) and wire myography (maximum response to Ach=73.2±22.3 vs 63.6±16.2 and nitropressuse 95±6.2±3 vs 93.4±3.6% with no difference in curves). Confocal microscopy demonstrated endothelium with a non-significant increased density of cells(450± 160 vs 631± 70 EC/mm²) and slight improvement in nuclear morphology.

Conclusion: This study does not find significant changes in endothelial dysfunction 8-12 months after successful RT.

THE IMPACT OF CYTOMEGALOVIRUS DISEASE AND ASYMPTOMATIC INFECTION ON ACUTE RENAL ALLOGRAFT REJECTION
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Purpose: The aim of the study was to determine the impact of CMV disease and asymptomatic infection on biopsy-proven acute rejection (AR) during 12 months post-RTx.

Methods: A total of 108 consecutive RTx recipients at risk for CMV (donor and/or recipient CMV seropositive) were included in the study and followed...
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RENAL TRANSPLANTATION (RT) IN DIALYSIS PATIENTS WITH THE HISTORY OF CORONARY ARTERY BYPASS GRAFTING (CABG) – A SINGLE CENTRE EXPERIENCE

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Pre-transplant cardiovascular disease (CVD) is a major risk factor for post-transplant CVD. Therefore, prior to RT, it is mandatory to diagnose and treat coronary artery disease (CAD). The objective for this study was to define results of RT in patients with CABG performed prior to RT. 6 hemodialysis and 4 peritoneal dialysis treated patients (9M, 1M), aged 54 ± 9.5 years received RT (second RT in 2). Mean number of mismatches was 3.1 (range 1-4). Median total ischemic time was 9.7 ± 5.5 hours. MMF (8/10) or AZA (2/10) and CyA (8/10) or TAC (2/10) were used. 4 cases of acute tubular necrosis and 2 cases of acute rejection were diagnosed. Urinary tract infections and necrosis of the ureter were the most common early complications. In one diabetic patient an asymptomatic increase of cardiac enzymes without alteration in ECG or cardiac US was observed on the third day after RT (during his first failed RT he experienced 2 or more acute rejections (0.42 ± 0.84 g/day, P=0.03).

Case 3 finally recovered and returned on hemodialysis.

PO-352

RENAL TRANSPLANTATION (RT) IN DIALYSIS PATIENTS AFTER CARDIAC VALVE REPLACEMENT – CASE REPORTS

Alicja Dęb ska-Slizien, Slawomir Lizakowski, Andreż L. Chamięnia, Anna Milecka, Maria Dudziak, Jan Rogowski, Zbigniew Sledzinski, Bolesław Rutkowski, Nephrology, Transplantology and Internal Medicine, Medical University of Gdańsk, Poland.

Prior to transplantation, it is mandatory to diagnose and treat not only coronary artery disease, but also heart failure due to valvular disease or cardiomyopathy. The objective for this study was to define results of RT in patients after the replacement of cardiac valves. The period on waiting list lasted between 12 to 102 months (mean 48 months). The period on waiting list lasted between 12 to 102 months (mean 48 months). The modality of dialysis peritoneal with 5/10, hemodialysis with 6/10 patients. The type of valve aortic with 3/10, aortic mitral with 2/10, aortic mitral with 2/10. Age/gender 53/m 51/m 50/m. The warm ischemia time was 1.72 ± 0.27 g/dl, respectively. Mean observation period after CABG and RT is now 55 (10-131) and 21.8 months (2-62) respectively. During this long-term observation only one patient developed the mentioned above cardiologic problem.

CABG treated dialysis patients have excellent outcome after RT. The cardio-surgical intervention in dialysis patients with CAD may create a chance for RT and improved quality of life.

PO-353

IS EARLY PROTEINURIA AN INTEGRATOR OF ENTERIC-COATED MYCOPHENOLATE SODIUM (EC-MPS) EFFICACY? 

Anna Milecka, Maria Dudziak, Jan Rogowski, Zbigniew Sledzinski, Alicja Debska-Slizien, Slawomir Lizakowski, Andrzej L. Chamienia, Alicja Debska-Slizien, Slawomir Lizakowski, Andrzej L. Chamienia.

In case 2 acute tubular necrosis (ATN) and in case 3 both ATN and acute rejection, and the mean creatinine level were 120 ± 31 µmol/l and 36.4% and 35.2% patients had proteinuria, respectively. Proteinuria at 3 months and 6 months was more abundant in patients who experienced 2 or more acute rejections (0.42 ± 0.84 g/day, P=0.03).

Conclusions: Early proteinuria may be an integrator of pre-transplant renal lesions, ischemia-reperfusion injury and immunologic aggression. The effect of lowering early proteinuria on long-term graft function should be tested.

PO-354

ENTERIC-COATED MYCOPHENOLATE SODIUM (EC-MPS) SAFE ALTERNATIVE TO MYCOPHENOLATE MOFETIL IN LONG-TERM STABLE MAINTENANCE RENAL TRANSPLANT RECIPIENTS

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Introduction: Mycophenolic acid (MPA) in the form of Mycophenolate Mofetil (MMF) is a successful strategy in renal transplantation, combined with calcineurin inhibitors and corticosteroids. EC-MPS was developed as an alternative, advanced formulation of MPA. The aim of this study was to evaluate the long-term safety of this formulation in maintenance patients converted to EC-MPS.

Materials and Methods: Patients who completed a 1 year, double-blind/placebo-controlled multicenter, parallel-group study of safety, tolerability, and efficacy of EC-MPS compared with MMF as part of a triple immunosuppressive therapy regimen with Neoral® and steroids in maintenance renal transplant patients were followed for 2 years. Patients initially randomized to MMF (1000mg bid) were converted to EC-MPS (720 mg bid) after 1 yr. A total of 260 patients, who completed the core study, entered the extension (130 Ex-MMF; 130 EC-MPS; Month 12 cohort). Long-term data were available for 195 patient (98 Ex-MMF; 97 EC-MPS; Month 24 cohort).

Results: Compliance to treatment was high. Patients in both groups received >85% of their planned daily dose of EC-MPS throughout extension. The conversion to EC-MPS was not associated with an increased risk for efficacy or safety related events. The incidence of severe events was low and comparable between groups, patient and graft survival were high. No major differences between both cohorts for any specific AE leading to discontinuation were noted.

PO-355

IS EARLY PROTEINURIA AN INTEGRATOR OF IMMUNOLOGIC AND NON-IMMUNOLOGIC AGRESSION IN KIDNEY TRANSPLANTATION?

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Purpose: Pre-transplant renal lesions, ischemia/reperfusion injury and acute rejections constitute the main causes for long-term graft loss. It would be interesting to have an early marker of the consequences of these parameters on the kidney. Proteinuria could be such a marker.

Methods: 484 consecutive renal allograft recipients treated with the same immunosuppressive regimen were evaluated at 1 and 3 months after transplantation, and were followed up in our institution (median follow-up: 7.2 years (range: 0.4-15.4 years)).

Results: Mean recipient age was 44.4 ± 13.6 (62% male, 98.3% Caucasians). Cyclosporine combined with azathioprine (56.6%) or with MMF (23.4%) was preferentially used. At 1 and 3 months, creatinine was 153 ± 103 and 136 ± 65 µmol/l, and 36.4% and 35.2% patients had proteinuria, respectively. Proteinuria at 3 months and 6 months was more abundant in patients who experienced 2 or more acute rejections (0.42 ± 0.86 vs 0.18 ± 0.39 g/day, P<0.02; 0.44 ± 0.90 vs 0.23 ± 0.84 g/day, P<0.03).

Conclusions: Early proteinuria may be an integrator of pre-transplant renal lesions, ischemia-reperfusion injury and immunologic aggression. The effect of lowering early proteinuria on long-term graft function should be tested.

Detergents of proteinuria

Proteinuria At 1 month At 3 months

| Proteinuria | Odds Ratio | 95% CI | P | Odds Ratio | 95% CI | P |
|-------------|------------|--------|---|------------|--------|---|
| Donor age > 60 | 4.43 | 1.61-14.13 | 0.003 | 4.70 | 2.10-14.65 | 0.002 |
| Donor cardiovascular death | 1.98 | 1.20-3.14 | 0.002 | 1.72 | 1.39-3.67 | 0.01 |
| Warm ischemia time > 60 min | 2.23 | 1.39-3.66 | 0.001 | 1.66 | 1.00-2.62 | 0.04 |
| Cold ischemia time > 24 hrs | 1.77 | 1.17-2.73 | 0.006 | 1.77 | 1.16-2.75 | 0.008 |
| Delayed graft function | 1.21 | 0.97-1.51 | 0.09 | 1.20 | 0.96-1.51 | 0.11 |

Conclusions: Early proteinuria may be an integrator of pre-transplant renal lesions, ischemia/reperfusion injury and immunologic aggression. The effect of lowering early proteinuria on long-term graft function should be tested.
Renal Function in Renal or Liver Transplant Recipients after Conversion from a Calcineurin Inhibitor to Sirolimus

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Aims: Two 6-month pilot studies were conducted in renal (n=17) or liver (n=15) transplant recipients to assess whether moderate renal insufficiency to evaluate renal function after conversion from calcineurin inhibitor (CI) to sirolimus (SRL)-based immunosuppression.

Methods: After a SRL loading dose, the daily dose was individualized to achieve whole blood trough levels of 10-22 ng/mL. CI was abruptly discontinued.

Results: There were no statistically significant changes in serum creatinine from baseline to 6 months post conversion. Mean serum creatinine improved from 219.9 ± 201.4 µmol/L at 3 months to 208.4 ± 200.4 µmol/L at 6 months in transplant recipients. Renal function improved (decrease of >5% in serum creatinine) in 40% of patients, remained stable in 22% and further deteriorated (increase of >5% in serum creatinine) in 38% of patients. All patients survived and all grafts were functioning at the end of the study. There was one acute rejection episode in each study and these were successfully reverted. The most commonly reported adverse events were anemia, acne, diarrhea, and hyperlipidemia.

Conclusions: Renal function remained stable, with a tendency towards improvement, after abrupt conversion from CI to SRL-based therapy in renal or liver transplant recipients with moderate renal insufficiency.

Caspase-7 and 3 May Act in Association in Long-Term Rat Renal Ischaemia/Reperfusion (IR) Injury and Divergent Effects of Immunosuppressants

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We have previously explored possible mechanisms of long-term renal IR injury and immunosuppression with focus on apoptosis and inflammation in a rat model. Here, we further explored the involvement of caspase-7 and 3.

Methods: I (45 minutes)/R (16 weeks) and unilateral nephrectomy were induced. Cyclosporine (CsA; 10 mg/kg), tacrolimus (Tac; 0.2 mg/kg), rapamycin (Rap; 1 mg/kg) or mycophenolate mofetil (MMF; 10 mg/kg) was administered daily for 16 weeks. The effects of IR and immunosuppression on kidneys were evaluated by caspase-7 protein expression, active caspase-3 distribution, tubulointerstitial damage and fibrosis.

Results: 28 kDa active caspase-7 was increased by IR and CsA, and decreased by Tac and Rap and MMF in contrast to the controls (p<0.05). Another finding was a numerical, however not statistically significant, increase in mean GFR from 26.8 to 33.2 mL/min/1.73 m² at 6 months among liver transplant recipients. Renal function improved (decrease of >5% in serum creatinine) in 40% of patients, remained stable in 22% and further deteriorated (increase of >5% in serum creatinine) in 38% of patients. All patients survived and all grafts were functioning at the end of the study. There was one acute rejection episode in each study and these were successfully reverted. The most commonly reported adverse events were anemia, acne, diarrhea, and hyperlipidemia.

Conclusions: Renal function remained stable, with a tendency towards improvement, after abrupt conversion from CI to SRL-based therapy in renal or liver transplant recipients with moderate renal insufficiency.

Merkel-Cell Carcinoma in Renal Transplant Recipient

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Merkel-cell carcinoma (MCC) is a rare form of skin cancer of neuroendocrine origin that is considered to be the most aggressive cutaneous malignancy. The exact aetiology of MCC is unknown, but it is postulated to be related to the sunlight exposure. Rare occurrence resulted in lack of consensus regarding the optimal therapeutic approach.

A 57-year-old male was started on haemodialysis in 1998 because of end-stage renal disease caused by IgA nephropathy. He received an allograft in April 2002 and was treated with cyclosporine, mycophenolate mofetil and apoptosis and inflammation, and the progression of tubulointerstitial injury and fibrosis, and the divergent effects of immunosuppression in this model.

Renal Transplantation in Patients with Balkan Endemic Nephropathy

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Endemic nephropathy (EN) is a chronic tubulointerstitial disease of unknown aetiology prevalent in Croatia, Romania, Bulgaria and countries of former Yugoslavia along the tributaries of the river Danube. Its diagnosis is made by excluding other possible reasons for renal failure in people living in endemic area.

Endemic nephropathy accounts for 1.4% of ESRD patients in Croatia in general, and is found in almost 30% of patients in the affected regions. People living in endemic areas, have 20-fold increased incidence of upper urothelial carcinomas when compared with the controls from other parts of Croatia.

In our centre, kidney transplantation had been performed in 9 patients with EN. One patient was transplanted in each of years 1997, 1998 and 1999, four patients in 2002 and two patients in 2003. Number of HLA mismatches ranged from 1 to 4. All patients established good graft function. Male patient who was transplanted in 1997, died 2 years after transplantation. He developed painless, faint microhaematuria without deterioration of the graft function. Cancer of the pelvis of own kidney was disseminated at the time of diagnosis. One patient had permanent microhaematuria and mild proteinuria. He performs urinary cytology every six months. Other patients have excellent graft function with no signs of malignant disease.

Our results demonstrate that patients with EN can be safely transplanted. However, increased incidence of upper urothelial carcinomas in this population accompanied with immunosuppressive treatment demand regular screening.

This is the first report on outcome of patients with Balkan endemic nephropathy after renal transplantation. Reports from other affected countries would improve our understanding of this particular disease.
stereoids. Graft function was optimal, without episodes of acute rejection. A red intradural painless nodule was observed in the left preauricular region in September 2004. Immunohistohchemical staining showed perinuclear express-
ion of cytokeratin 20 and the presence of neuroendocrine markers of neuro-
specific enolase and chromogranin proving the diagnosis of Merkel-cell carci-
noma. Radical resection with a median margin of 2 cm was necessary. Tu-
mour was localised at the time of diagnosis as demonstrated with the sentinel lymph node dissection. The patient received adjuvant radiotherapy in the total dose of 55 Gy in 20 cycles. Immunosuppressive therapy has been reduced. Merkel-cell carcinoma is a rare aggressive cancer that may be misdiagnosed as the indolent skin disease. In immunocompromised host it occurs more often, in younger patients, and probably behaves more aggressively than in general population. For this reason, transplant recipients should be carefully screened for skin changes at least once a year.

**PO-360 OBSTURCIVE ACUTE RENAL FAILURE DUE TO FUNGAL BEZOAORS IN A KIDNEY GRAFT RECIPIENT**

Wissal Sahout, Habbib Skhiri, Sandra Mabret, Khaled Gaha, Ahmed Letalef, Sabra Aloui, Ameer Fih, Samia Bouraoui, Nasr Ben Dhiba, Abdellatif Achour, Mezri Elmay. Nephrology, Monastir Hospital, Monastir, Tunisia.

Severe fungal infections remain a substantial cause of morbidity and mortality among kidney graft recipients. Fungal bezoars of the urinary tract can obstruct the excretry system leading to oligoanuria, worsening graft function and consequently graft loss. We report a case of acute renal failure secondary to Candida Tropicalis bezoars of the upper urinary tract in a transplanted kidney. Our patient is a 23 year old girl who underwent kidney transplantation from a living related donor (her brother). She was discharged on triple therapy (Talcroloimus, MMF and Prednisone) and had an eventful post operative course. Two months later, she presented to our unit for oliguria, graft pain and deterioration of renal function with a creatinine level of 8.3 mg/dl. Radiologic exploration of the graft showed a pyelocalicial dilatation upper an echogenic formation of 1.5 cm of diameter. Fungal bezoars were suspected and were confirmed by a positive urine culture for Candida Tropicalis. She subsequently underwent a chireurgical nephrohyposphory with successful debluking bezoars and she received antifungal therapy including Amphotericin B and 5-Fluocyclosin during 21 days. She was successfully recovered. Obstructive acute renal failure due to fungal bezoars is a rare cause of dete-
roration of graft function in kidney transplant patients; thus, we would evoke such hypothesis. Through this observation, we ascertain that anuria could be absent specially when the patient had a residual renal function; on the other hand, we would remark that rejection is not the exclusive cause of acute renal failure in post transplantation period.

**PO-361 METABOLIC CHANGES IN THE KIDNEY GRAFT MONITORED CONTINUOUSLY DURING KIDNEY TRANSPLANTATION IN A PIG MODEL USING MICRORDIALYSIS**

Arianeb Mehrabi1, Arash Kashfi1, Said H. FaniYazdi1, Mehrdad Soleimani1, Oliver Sakowitz2, Hamidreza Fonouni1, Peter Schenmer1, Carsten N. Gut1, Jan Schmidt1, Markus W. Bücher1, Thomas W. Kraus1. 1Department of Surgery, University of Heidelberg, Heidelberg, BW, Germany. 2Department of Neurosurgery, University of Heidelberg, Heidelberg, BW, Germany.

**Purpose:** Microdialysis (MD) provides the opportunity to continuously monitor metabolic changes in tissues of visceral organs. Tissue metabolic changes in are detected earlier with MD than reflected in peripheral blood chemistry. Metabolic changes of different tissues. Our aim was to quantify whether renal arterial blood flow measurement using Doppler flow probes and postoperative pathologic assessment. Glucose, glycere, lactate, and pyruvate concentrations were measured.

**Materials/Methods:** Sixteen landrace pigs were used for eight heterotopic KTXs. MD catheter was inserted into the cortex of donor kidney. MD samples were collected at 30-minute intervals during cold ischemia time (CIT), warm ischemia time (WIT), and kidney graft reperfusion, including the period after arterial thrombosis. Arterial thrombosis was confirmed by intraportal renal blood flow measurement using Doppler flow probes and postoperative pathologic assessment. Glucose, glycere, lactate, and pyruvate concentrations were measured.

**Results:** In CIT, cell activities were minimal with minor cellular damage. After thrombosis, because of ischemia and cellular damage, increments in lactate and lactate/pyruvate ratio were observed, showing the anaerobic metabolism of the graft. Glycere increased after thrombosis, reflecting cellular damage. In contrast, glycere level decreased significantly during thrombosis period.

| Table 1 | Analyzed metabolites | Baseline | CIT | WIT 1 hour after thrombosis | 3 hours after thrombosis | 6 hours after thrombosis |
|---------|----------------------|---------|-----|-----------------------------|--------------------------|-------------------------|
| Glucose (mM/L) | 1.4 | 0.67* | 1.5 | 0.8* | 0.95 | 0.2* |
| Glyceral (µM/L) | 26.9 | 9.7 | 20.7 | 16 | 145.7 | 303.5 |
| Lactate (mM/L) | 0.8 | 0.1 | 1.2 | 1.8 | 1.9 | 2.02 |
| Pyruvate (µM/L) | 52.3 | 3.6 | 57.7 | 31.5 | 17.6 | 7.03 |

Data are shown as mean (p<0.05, change vs. baseline).

**Conclusion:** One hour after renal artery thrombosis, metabolites alterations were observed. In conclusion, MD is a reliable, easy method for detection of re-

**PO-362 EARLY DETECTION OF ARTERIAL THROMBOSIS AFTER EXPERIMENTAL KIDNEY TRANSPANTATION USING MICRORDIALYSIS**

Anash Kashfi1, Arianeb Mehrabi1, Mehrdad Soleimani1, Said H. FaniYazdi1, Oliver Sakowitz2, Peter Schenmer1, Carsten N. Gut1, Thomas W. Kraus1, Markus W. Bücher1, Jan Schmidt1. 1Department of Surgery, University of Heidelberg, Heidelberg, BW, Germany. 2Department of Neurosurgery, University of Heidelberg, Heidelberg, BW, Germany.

**Purpose:** Management of arterial thrombosis, as an important complication of kidney transplantation (KTx), depends on rapid diagnosis, medical and/or surgical intervention. Microdialysis (MD) is a viable device for monitoring the metabolic changes of different tissues. Our aim was to quantify whether renal artery thrombosis can be rapidly and easily detected after porcine KTx with MD.

**Materials/Methods:** Sixteen landrace pigs were used for eight heterotopic KTXs. MD catheter was inserted into the cortex of donor kidney. MD samples were collected at 30-minute intervals during cold ischemia time (CIT), warm ischemia time (WIT), and kidney graft reperfusion, including the period after arterial thrombosis. Arterial thrombosis was confirmed by intraportal renal blood flow measurement using Doppler flow probes and postoperative pathologic assessment. Glucose, glycere, lactate, and pyruvate concentrations were measured.

**Results:** In CIT, cell activities were minimal with minor cellular damage. After thrombosis, because of ischemia and cellular damage, increments in lactate and lactate/pyruvate ratio were observed, showing the anaerobic metabolism of the graft. Glycere increased after thrombosis, reflecting cellular damage. In contrast, glycere level decreased significantly during thrombosis period.

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| Lactate (mM/L) | 0.8 | 0.1 | 1.2 | 1.8 | 1.9 | 2.02 |
| Pyruvate (µM/L) | 52.3 | 3.6 | 57.7 | 31.5 | 17.6 | 7.03 |

Data are shown as mean (p<0.05, change vs. baseline).

**Conclusion:** One hour after renal artery thrombosis, metabolites alterations were observed. In conclusion, MD is a reliable, easy method for detection of re-

**PO-363 CLINICAL SIGNIFICANCE OF QUANTITATIVE POLYMERASE CHAIN REACTION FOR HUMAN PARVOVIRUS B19 INFECTION IN KIDNEY TRANSPLANT RECIPIENTS**

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**Purpose:** Human parvovirus B19 (B19) infection in renal transplant recipients presenting as persistent anemia or pure red cell aplasia (PRCA) has been reported. The aim of this study was to evaluate the incidence and clinical significance of B19 infection.

**Methods:** Five hundred and eighty two samples from one hundred seven-
teen patients who had received a renal transplantation from September 2003 to October 2004 were analyzed retrospectively. B19 DNA was detected with quantitative polymerase chain reaction (PCR) with LightCycler Parvovirus B19 Quantitation Kit.

**Results:** Fifty eight out of 117 renal transplant recipients showed PCR positive at least one time. (49.6%) In 58 patients with PCR positive, 42 patients without- out anemia preoperatively were group I (35.2%) and 16 patients with anemia (hemoglobin <9.0g/dL) preoperatively were group II. (13.7%). In PCR positive patients, a negative correlation was significant between hemoglobin and copy numbers of B19 according to statistical analysis using Pearson Correlations. (p<0.01, group I; r=0.330, group II; r=0.507) In patients whose number of B19 copy was more than 10^6copies/reaction, 5 patients experienced a se-

| Table 1 | Analyzed metabolites | Baseline | CIT | WIT 1 hour after thrombosis | 3 hours after thrombosis | 6 hours after thrombosis |
|---------|----------------------|---------|-----|-----------------------------|--------------------------|-------------------------|
| Glucose (mM/L) | 1.4 | 0.67* | 1.5 | 0.8* | 0.95 | 0.2* |
| Glyceral (µM/L) | 26.9 | 9.7 | 20.7 | 16 | 145.7 | 303.5 |
| Lactate (mM/L) | 0.8 | 0.1 | 1.2 | 1.8 | 1.9 | 2.02 |
| Pyruvate (µM/L) | 52.3 | 3.6 | 57.7 | 31.5 | 17.6 | 7.03 |

Data are shown as mean (p<0.05, change vs. baseline).

**Conclusion:** One hour after renal artery thrombosis, metabolites alterations were observed. In conclusion, MD is a reliable, easy method for detection of re-

**KIDNEY**
**Conclusion:** We figured out that B19 infection in renal transplant recipient was associated with low hemoglobin level. Quantitative measurement of B19 DNA might be a good diagnostic method to predict an occurrence of PRCA and to determine the best time point of IVIG treatment.

**PO-364 EVALUATION OF C2 MONITORING IN CYCLOSPORINE BASED KOREAN RENAL TRANSPLANT PATIENTS**

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**Purpose:** A prospective study to evaluate the value of C2 monitoring in Korean renal transplantation patients.

**Methods:** In 39 patients who underwent living related kidney transplantation, a full 8-point pharmacokinetic measurement of cyclosporine A(CyA) was performed on 2, 3, 7 day following surgery and 5-point of that was performed on 14, 28 day. The AUCₐₕ₋ₜ and AUCₜ₋ₜ were calculated by using the trapezoidal rule. The Pearson correlation coefficient of single time point samples with AUC was evaluated. Association between CyA pharmacokinetic parameters and the occurrence of the rejection within six months was evaluated.

**Results:** Nine patients of 39 had acute rejection and 2 patients had actue tubular necrosis unrelated with cyclosporine toxicity. Cₜ₋ₜ was more correlated with AUC than Cₜ₋ₜ at day 3, 4, 7, 14, 28 posttransplant except for postoperative second day.(Pearson correlation coefficient r, Cₜ₋ₜ versus Cₜ₋ₜ: 0.55, 0.48, 0.81, 0.8 vs 0.54, 0.52, 0.21, 0.19, Cₜ₋ₜ level at day 14 of 0.47). An effect had an effect on the rate of rejection. (Cₜ₋ₜ rejection group versus non rejection group: 602 ± 259 ng/ml versus 880 ± 281 ng/ml, p=0.015). AUC at day 14, 28 posttransplant also affected the rate of rejection. We found no significant differences in C₀ levels between patients with rejection and patients with non-rejection.

**Conclusions:** The 2-hour values of cyclosporine were the better predictors of AUC than trough value of cyclosporine in Korean renal transplant patient. C₂ level seemed to be helpful in identifying patients at risk for rejection.

**PO-365 COMPARISON BETWEEN CYTOMEGALOVIRUS(CMV) ANTIGENEMIA ASSAY AND QUANTITATIVE CMV PCR ASSAY IN RENAL TRANSPLANT RECIPIENTS**

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**Purpose:** The pp65 antigenemia assay has been used for diagnostic purpose of CMV infection. Quantitative CMV PCR assay is currently regarded as an alternative diagnostic approach. This study compared the results of both assays with large series of kidney transplant recipients.

**Methods & Materials:** Among all kidney transplant recipients from August 2003 to January 2005, 1200 blood samples of 1401 recipients were examined with CMV antigenemia assay and quantitative CMV PCR assay simultaneously.

**Results:** The results of a quantitative CMV PCR assay correlated well with the outcomes of a pp65 antigenemia assay. Our previous study showed that CMV antigenemia titer of higher than 50 per 500,000 leukocytes could be used as useful guide to preemptive treatment of CMV infection after kidney transplantation. When CMV antigenemia titer of higher than above was considered as the ‘gold standard’, the optimal cutoff value of quantitative real-time PCR assay for initiating preemptive treatment could be predicted as 30 copies/ul.

Based on this optimal cutoff value of quantitative real-time PCR assay, the sensitivity and specificity of the quantitative CMV PCR assay were 93% and 92%, respectively.

**Conclusion:** The present study suggest the assays as a new standard for quantitative assessment of CMV infection in kidney transplant recipients. But owing to the wide range of quantitative CMV PCR values, the definition of an optimal cutoff value for initiating preemptive treatment of CMV infection will be required for further analysis.

**PO-366 EFFICACY OF BASILIXIMAB FOR RENAL TRANSPLANT RECIPIENTS WITH PERFORMED ANTIBODY**

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Because it is well known that renal transplant recipients with performed antibodies have increased acute rejection (AR) rates, anti-donor-antibody (ADA) and panel-reactive antibody (PRA) are routinely detected before transplantation. To evaluate the efficacy of induction therapy for performed antibody positive recipients, we analyzed the rejection rates and graft survival of the recipients using basiliximab.

We retrospectively analyzed pre PRA and ADA, incidence of AR and patients and graft survival of recipients (n=61) who underwent renal transplantation between December, 2002 and April, 2004. The immunosuppressive therapy consists of basiliximab induction, and cyclosporine (CyA), mycophenolate mofetil (MMF), and methylprednisolone (MP). MP was completely withdrawn on postoperative day 14. The performed antibody was positive in 32% (n=20/61) and among them 3.3% (n=2/61) were ADA T cell positive, 20% (n=12/61) were B cell positive, 17% (n=10/61) were PRA class I positive and 8% (n=5/61) are class II positive. Incidence of acute rejection in all recipients was 22% (n=13/61). In positive performed antibody group incidence was 30% (n=6/20), but humoral rejection was seen in only one recipient.

There were no significant difference in graft function and AR free ratio between positive group and negative group. The presence of performed antibody was not being a risk factor in our protocol. Our immunosuppressive protocol consists of basiliximab, CyA, MMF and MP achieves good results regardless of presence of performed antibody. This examination suggested that basiliximab acted on B cell systems as well as T cell systems and inhibited antibody formation, and as a result, basiliximab inhibited humoral rejection.

**PO-367 MRI RENAL PERFUSION AS A SURROGATE MARKER FOR CHRONIC ALLOGRAFT NEPHROPATHY (CAN)**

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Allograft function monitoring has traditionally relied upon functional markers. Such markers are insensitive and invasive protocol biopsies are advocated for allograft evaluation. This study evaluates the association between renal perfusion measured non-invasively with contrast enhanced MRI (CE-MRI) and histological severity of CAN.

**Methods:** CAN severity was estimated from protocol biopsies using the chronic allograft damage index (CADI) based upon Banff 97 thresholds. We selected four patients considered to have severe CAN (CADI score > 4), and six patients considered to have stable allograft function (CADI ≤ 4). Renal perfusion was estimated using gadolinium-enhanced MRI (mL/min/g). GFR was estimated using the MDRD equation. The association between MRI renal perfusion, GFR and CADI was studied using multiple linear regression where MRI renal perfusion was the dependent variable.

**Results:** Mean (±SD) MRI renal perfusion was 2.23 (±0.37) mL/min/g. Using multiple linear regression there was a significant association between CADI and MRI perfusion but no association between GFR and MRI perfusion. MRI perfusion was significantly lower in the four patients with CADI > 4 (1.94 versus 2.43 mL/min/g, p = 0.03). The effect size for this difference was 'large' (d = 1.7). The R² for the linear regression model after removal of GFR was 0.49.

**Conclusions:** In this pilot study there appears to be an association between CE-MRI renal perfusion and CAN severity. Further studies are needed to confirm this finding and evaluate the role of CE-MRI renal perfusion as a screening test for allograft dysfunction.

**PO-368 DELAYED GRAFT FUNCTION IN LIVE-DONOR RENAL TRANSPLANTS: ANALYSIS OF RISK FACTORS AND IMPACT UPON GRAFT FUNCTION AND SURVIVAL**

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**Purpose:** To address the incidence, risk factors and impact of delayed graft function (DGF) in the live-donor (LD) setting.

**Material & Methods:** Between 1976 and 1999, 1200 consecutive LD renal transplants were performed at a single institute. Group I included 1099 patients (91.6%) with immediate diuresis (within 10 minutes after vascular clamping) whereas group II included 101 (8.4%) with delayed diuresis. Group II were classified into three subgroups according to the onset of diuresis: subgroup Ia (-10 and -60 minutes), Ib (-1 and -24 hours) and Ic (-24 hours).

**Results:** DGF was significantly associated with pediatric recipients and long ischemia time (> 60 minutes) (p = 0.020.001 respectively). Incidence of acute and chronic rejections were significantly higher in group II (p = 0.004 and 0.001 respectively). Mean serum creatinine at 1 year was 1.4 ± 0.5, 1.5 ± 0.7 (p = 0.008). While it was 1.8 ± 1.1, 1.9 ± 1.2 (p = 0.6) at 5 years for both groups respectively. The 1, 5 and 10 years graft survival were 94%, 77% and 53% in group I while they were 80%, 44% and 44% in group II (p = 0.003).

Nevertheless, this significant impact upon survival was not maintained independently on multivariate analysis. There was no significant impact upon long term graft function (p = 0.91) or survival (p = 0.92) among subgroups of group II.
PO-369  A QUALITATIVE PROSPECTIVE PSYCHOLOGICAL STUDY OF END-STAGE RENAL DISEASE PATIENTS AWAITING KIDNEY TRANSPLANTATION

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Purpose: Few studies have concentrated on psychological reactions in the pre-transplantation period. The aim of this IRB-approved prospective study was to analyse specific concerns of end-stage renal disease ESRD patients awaiting renal transplantation (RT).

Methods: Semi-structured interviews were conducted in 28 ESRD patients (age m = 51.9 ± 9.8) before RT and explored their illness experience. Interviews took place at home or in a place selected by the patient. During their selection, the duration was not limited (m = 66.5 ± 31.4 minutes). Interviews were verbatim transcribed. Qualitative thematic analysis was subsequently performed.

Results: Patients (93%) reported loss of freedom. To avoid illness intrusiveness, they reported leading a dual life, trying to display a normal image, while suffering from dialysis related constraints. To cope with illness limitations, 89% scheduled their life carefully and 46% tended to modify medical directives. All patients reported RT as a therapy to recover freedom. Patients reported difficulty in emotional disclosure (100%), feelings of isolation (61%), and of being misunderstood (54%). Negative thoughts (57.1%) were related to their loss of quality of life. Despite emotional fragility, suicidal thoughts were rare (14.3%). Some patients (25%) hid negative feelings to maintain their identity-integrity. A profound sense of personal image of normality was underlined (36%).

Conclusion: Loss of freedom and difficulty in disclosing emotions are frequently found in patients awaiting RT, while suicidal thoughts are rare. Significant individual energy is devoted to handling uncertainty and displaying a personal image of normality. These data provide a basis for exploring optimal psychological support in ESRD patients awaiting RT.

PO-370  STUDY OF LONG-TERM PROTOCOL BIOPSY IN LIVE DONOR RENAL ALLOGRAFT RECIPIENTS: SINGLE CENTRE EXPERIENCE

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Purpose: To evaluate the role of histopathological changes of the transplanted kidney was explored through histological changes of the initial queues of transplantation over a long-term period. We aimed to assess the importance of the long-term basis.

Methods: Protocol biopsies were done for 120 live donor recipients with stable grafts and no-rejection history. Biopsies were performed at intervals of less than 5 years (n = 69) (group 1), from 5-10 years (n = 29) (group 2) and more than 10 years (n = 22) (group 3) post transplant. The histopathological findings using chronic allograft damage index score (CADI) were correlated with different clinical and immunological parameters.

Results: Chronic tubulointerstitial fibrosis was the most prevalent finding being present in 75% of cases. Normal fibrosis were found in 10% of biopsies in group 1 and 2, chronic cyclosporine nephrotoxicity was detected in 5.5% of group 1 and 10.3% of group 2 biopsies (P=0.003). Mean CADI score of glomerulosclerosis, mesangial matrix increase, tubular atrophy and interstitial fibrosis was significantly higher in groups 2 and 3 (P<0.01). Hypertension was significantly correlated with glomerulosclerosis, periglomerular fibrosis and hyalinosis (P<0.05) and diabetes with glomerular basement membrane thickening, intimal proliferation and glomerulosclerosis (P<0.05). Donor age correlated to glomerulosclerosis, tubular atrophy and interstitial fibrosis (P<0.05). Risk factors associated with high CADI score were DR mismatching (P=0.044) and post transplant diabetes (P<0.001).

Conclusion: Protocol biopsy is an important strategy even in the long term. Histopathological findings do exist even with normal renal function and may be predictive for long term graft survival.

PO-371  CHARACTERISTICS OF LONG TERM LIVE DONOR RENAL ALLOGRAFT RECIPIENTS WITH NO REJECTION EPISODES

Tarek M. Abbas 1, Ehab W. Wafa 1, Hussien A. Sheashaa 1, Megahed A. El-Magd 1, Mohamed A. Bakr 1, Mohamed A. Ghoneim 1.

Purpose: Long term renal allograft survival is improving despite the high risk of complications and rejection. We report a group of long term rejection free renal allograft survivors.

Patients and methods: This study included 189 renal allograft recipients who had functioning graft for 10 years or more; out of which 101 patients had no previous rejections (study group) and 88 had previous rejection episodes (control group). The two groups were compared regarding different variables.

Results: The mean age of rejection free patients was 31 years and that of the control group was 28 years (P=0.013). Male recipients constitute 62% of the study group versus 77% of control group (P=0.027). Donor age and gender showed no significant difference. The study group showed significantly fewer ABO (A&B mismatches than control group (P=0.012), DR matching showed no significant difference (P=0.5). Renal allograft function was significantly better in the study group (P<0.001) with significantly lower protein excretion (P=0.001). Long term complications developed in both groups however only hypertension was significantly more common in the control group. Diabetes and infection were more common in the non rejector group but the difference was not significant. Multivariate analysis revealed significant impact of recipient gender, recipient age and development of post transplant hypertension.

PO-372  IS THE SURGEON'S EXPERIENCE A RISK FACTOR FOR POOR SHORT-TERM OUTCOME AFTER CADAVERIC KIDNEY TRANSPLANTATION?

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Purpose: Patient- and organ-related factors influence the short term outcome after cadaveric kidney transplantation. However, little is known about the relevance of surgical aspects like timing and experience.

Methods: We therefore compared 50 kidney transplantations performed by three different surgeons in a 12 month period. One month after kidney transplantation, 28 patients had a good outcome (serum creatinine of <200ng/ml; group A) and 22 had a poor outcome (creatinine >200ng/ml; group B). Patients with good outcome had a shorter time on dialysis prior to transplantation than patients in group B (4.6 years ±0.5 vs. 6.5 years ±0.6, p=0.009).

Results: Both groups had the same median age, Graft-UP matches, panel-reactive antibodies and previous transplantations. Patients with poor outcome had more surgery-associated complications (haemotoma, wound dehiscence, lymphoceles, urinomas) but similar cold ischaemia- and operation times. They had also more acute rejections, CMV infections and less intraoperative urinary output. All three surgeons had comparable rates of primary graft function (54%, 54% and 57% in group A) and procedural complications despite the different frequency of transplantations performed (24, 14 and 11 transplantations). The major difference was found in the time at reperfusion: Half of all patients with poor outcome but only one third of all patients with good outcome were transplanted between 4pm and 8am. Most patients with poor outcome were operated between midnight and 6am. In our study, the occurrence of surgery-associated complications negatively influenced short-term outcome. Timing of transplantation rather than the individual surgeon's experience influenced the frequency of surgery-associated complications and thus short-term outcome of cadaveric kidney transplantation.

PO-373  THE INFLUENCE OF PULSATILE PRESERVATION IN KIDNEY TRANSPLANTATION FROM NON HEART BEATING DONORS

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Purpose: Cold pulsatile perfusion (CPP) may offer improved early function compared with static cold perfusion (SCP) in heart beating cadaveric donors. With an expanding pool of donors we present our preliminary results with the use of CPP and compare them to SCP in preserving kidney grafts retrieved from non heart beating donors.
BK-Virus (BKV) nephropathy is observed in up to 10% of renal transplant recipients. BK-Virus reactivation and BKV-Virus nephropathy in renal transplant recipients may prevent oxidative damage in kidney transplantation. Patients with thymoglobulin induction had an increased antioxidative turnover, reactive oxygen species (ROS) or Prostaglandin D2 (PGD2) activity, TBARS or NO3. Clinically, patients with thymoglobulin induction had a lower microbial translocation rate compared to patients with tacrolimus or azathioprine. There was no difference in PLA2-dependent antioxidative turnover. MDA and 4-HNE were lower in blood from the allograft vein 5 min after reperfusion. There was one death in the 5th postoperative day due to infection. Length of stay was 9 days and mean creatinine at discharge was 334.2 μmol/l. In the second group we had four cases with primary non function (18%) and 15 cases with delayed graft function (83%). The length of stay was 15.3 days and mean creatinine at discharge was 504,1 μmol/l.

**PO-374**

**BK-VIRUS REACTIVATION AND BK-VIRUS NEPHROPATHY IN RENAL TRANSPLANT RECIPIENTS**

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BK-Virus (BKV) nephropathy is observed in up to 10% of renal transplant recipients (RTX). BKV reactivation is a significant inciting event for graft loss. Up to now urine samples of 283 out of 900 patients (pts) were tested by BKV-PCR. In pts with a positive urine BKV-PCR result (>105 copies/ml) plasma was tested for BKV. In case of positive plasma PCR a graft biopsy was performed. Screening was performed 4.5 ys [IQ 1.9-9.9] after RTX. Median age was 56 yrs (44-64); 169 male pts (60%); CsA&4%, Tac29%, Rapa12%, others 3%.

We found BKV replication in urine samples of 53 pts (19%); y post RTX 4.1 [0.9-9.6]. CsA55%, Tac45%, Rapa20%; and blood samples were positive for BKV in 14 pts (4.9%; y post RTX 0.7 [0.4-1.8], CsA21%, Tac65%, Rapa51%; males/females 7.1% vs. 1.8%; p=0.05). Pts age, donor age, CIT, MM, living/cadaveric donor, PRA were comparable between pts with and without positive BKV-PCR. Creatinine (Scr) 12 months before screening was comparable between BKV positive and negative pts (1.5mg/dl [1.3-1.7] vs. 1.4 [1.2-1.7]; p=0.4).

At screening a difference in Scr was evident (BVK positive: 1.95mg/dl [1.79-2.36] vs. BKV negative: 1.5mg/dl [1.2-1.7]; p=0.003).

A graft biopsy was performed in 13 out of 14 plasma BKV-PCR positive pts. Immunohistochemistry (IHC, SV40) was positive in 9 pts (plasma BKV-PCR: 3.5E10 copies/ml [5.5E10-1.0E10]). Viral load was lower in IH negative pts (8.6E10 copies/ml [4.9E10-5.0E10]; p=0.003).

BKV-reactivation in urine was found in 19% of pts. In 5% plasma BKV-PCR was positive whereas RTX-IH was positive in 3%.

**PO-375**

**THYMOLUBIN INDUCTION REDUCES OXIDATIVE STRESS IN CADAVERIC KIDNEY TRANSPLANTATION**

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Thymoglobin induction prevents delayed graft function. We examined if this is associated with reduced oxidative stress.

50 patients underwent cadaveric kidney transplantation. Initial immunosuppression was MMF, CNI and steroids. Additionally, 12 patients received thymoglobin (1.5mg/kg bw) prior to reperfusion. Blood was taken prior to and at reperfusion, as well as 15, 30 minutes and six hours after reperfusion. Blood was taken from the allograft vein 5 minutes after reperfusion. The samples were examined for markers of lipid peroxidation, oxidative stress and antioxidative status.

In patients with thymoglobin induction, the following differences were found: Total glutathione concentration was higher 30 minutes and 6 hours after reperfusion. Antioxidative capacity (Trolox) was higher before reperfusion. Reduced glutathione (GSH) was higher at reperfusion and 5 and 15 minutes thereafter. Molonolialdehyde (MDA) was lower at 15 and 30 minutes and 6 hours after reperfusion. MDA and 4-HNE were lower in blood from the allograft vein 5 minutes after reperfusion. There was no difference in PLA2-dependent antioxidative activity between patients with thymoglobin induction and patients without thymoglobin induction. There was no difference in PLA2-dependent antioxidative activity between patients with thymoglobin induction and patients without thymoglobin induction. Thymoglobin induction did not influence PLA2 or nitrate. Thymoglobin prior to reperfusion improves the antioxidative status and reduces lipid peroxidation in cadaveric kidney transplantation. Thymoglobin may prevent oxidative damage in kidney transplantation.

**PO-376**

**THE THERAPEUTIC EFFICACY OF MYCOPOLENATE MOFETIL IN PATIENTS EXPERIENCING REFRACTORY CHRONIC REJECTION FOLLOWING RENAL TRANSPLANTATION AND SWITCHOVER FROM AZATHIOPRINE OR MIZORIBINE**

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Background: Mycophenolate mofetil (MMF) inhibits not only acute rejection but also chronic rejection (CR) after kidney transplantation. It is also effective in preventing renal graft loss during long-term after transplantation. We therefore replaced azathioprine (Az) or mizoribine (Mz) with MMF in our patients experiencing CR following transplantation. Subjects and methods: We evaluated 15 patients, in whom the immunosuppressant was switched over to MMF within 1 year. Ten patients were treated with MMF in 12 and 3 patients, respectively. The efficacy rating was based on changes in serum creatinine (cr) observed after switchover compared to the pre-switchover baseline. The rating was “improved” if cr improved 20% or more and “unchanged” if changes were 0-20%.

Results: After switchover to MMF, the efficacy rating was effective in 7 and ineffective in 8 (efficiency grade: 46.7%). After switchover to MMF, urinary protein decreased in 10 of the 15 patients (66.7%) but complications occurred in 9 (60%); anemia in 6, infection in 5 and diarrhea in 3.

Conclusion: Switchover was effective in nearly 50% of patients and resulted in a graft survival rate of 66.7%. In particular, urinary protein showed a high improvement rate of 60%. Precautions against anemia are necessary when switching over to MMF.

**PO-377**

**LONG-TERM OUTCOME OF KIDNEY TRANSPLANTATION WITH STEROID WITHDRAWAL**

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We investigated the influence of steroid withdrawal on patient, graft survival, morbidity and graft function in kidney transplantation. Prospective, non-randomized study of 77 patients (23 living, 54 cadaver) with first graft (74 or 3), with kidney or kidney-pancreas (52 kidney, 25 pancreas-kidney) observed 3 years after steroid withdrawal 20.8 month (range 1-153) after transplantation in patients with normal dexamethasone test. 53 patients with steroid discontinuation 3 to 24 mo after transplantation (group 1), 49 patients with prednisone included 6 after transplantation (group 2), similar in age, donor characteristics, cross-match, immunosuppression and closely followed by the same team.

Results: Group 1 patients had more severe background disorders than group 2 (23 versus 5 with > 1 disorder, p= 0.0014, 28 versus 13 with diabetes, p= 0.0078). Group 2 patients stayed longer on dialysis (p= 0.045), had more second grafts (p= 0.0015), more kidney (p= 0.04), less pancreas-kidney transplantation (p= 0.003). In group 2 more early graft dysfunctions (7 vs 1, p= 0.0197), 13 patients (98% vs 93.9%, NS), kidney and pancreas survival were similar. Acute rejection, allo-graft nephropathy were similar. Urinary (p= 0.03), serious (p= 0.03), viral (p= 0.006) complications were lower in group 1. Group 2 had more post-transplant diabetes (p= 0.0058), more onset or aggravation of hypertension (p= 0.0007) and worse control of diabetes (p= 0.0047). Creatinine levels, cholesterol and triglyceride levels (except at 24 mo) were similar. At 3 years, group 1 patients had similar patient and graft survival and graft function and lower rates of infections, diabetes and hypertension.

**PO-378**

**ENALAPRIL ATTENUATES THE PROGRESSION OF CYCLOSPORINE NEPHROPATHY**

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Angiotensin-converting enzyme inhibitors (iACE) have become recognized as agents having renoprotective effect in the treatment of progressive renal diseases including chronic allograft nephropathy (CAN). One of the most frequent morphological findings associated with CAN is interstitial fibrosis and tubular atrophy, being the characteristic feature of chronic Cyclosporine A (CyA) nephrotoxicity. The aim of this study was: to analyse if the efficacy of iACE depends on the genesis of CAN.

The retrospective study included 82 non-diabetic cadaveric kidney graft recipients with biopsy proven CAN. 52 of them (63%) were treated with enalapril.
PO-377
SIROLIMUS AND TACROLIMUS TROUGH CONCENTRATIONS AND DOSE REQUIREMENTS AFTER KIDNEY TRANSPLANTATION IN RELATION TO CYTP3A AND MDRI POLYMORPHISMS AND STEROIDS
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Background: CYP3A5 and MDRI polymorphisms have been shown to influence tacrolimus blood concentrations and dose requirements. The aim is to determine whether these polymorphisms also affect sirolimus trough concentrations and dose requirement after kidney transplantation.

Methods: 85 renal transplant recipients receiving sirolimus were included. Twenty four benefited from a combined sirolimus-tacrolimus regimen. Eighty one patients received steroids. Sirolimus and tacrolimus were adjusted to a target trough concentrations or dose requirement and genetic polymorphisms. Adjusted-prednisolone dose has a significant impact on tacrolimus dose requirements seem not affected by CYP3A5 and MDRI polymorphisms. Genotypes were correlated to the adjusted trough concentrations and dose requirement for both sirolimus and tacrolimus.

Results: There were no significant correlation between adjusted sirolimus trough concentrations or dose requirement and genetic polymorphisms. In a multiple regression model, adjusted-prednisolone dose was involved with a positive or negative effect when considering sirolimus dose requirement or adjusted concentrations, respectively. In the subgroup of patients treated by tacrolimus and sirolimus, adjusted tacrolimus doses were higher in patients carrying at least one CYP3A5 wild allele (0.082±0.002mg/kg vs 0.039±0.016mg/kg for CYP3A5*3/3 patients, p=0.001). Adjusted-prednisolone dose and CYTP3A5 polymorphism explained up to 61% of the variability in tacrolimus dose requirement.

Conclusions: Unlike sirolimus, adjusted sirolimus trough concentrations and dose requirements seem not affected by CYTP3A5 and MDRI polymorphisms. Adjusted-prednisolone dose has a significant impact on tacrolimus and sirolimus dose requirements.

PO-380
THE ROLE OF THE ECHOCARDIOGRAPHY IN ESTIMATION OF LEFT VENTRICULAR (LV) SYSTOLIC AND DIASTOLIC FUNCTION IN CHRONIC RENAL FAILURE (CRF) PATIENTS AFTER KIDNEY TRANSPLANTATION (RT)
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Background: Left ventricular systolic and diastolic dysfunction is well known in the patients with chronic renal failure after kidney transplantation. A change in time of LV function has not been well characterised in that group of patients.

Material: 43 RT patients were prospectively studied by echocardiography (30 months follow-up). They were divided into two groups: one - (1-8 months) and second - (11-146) after RT. The first ECHO examination was performed 3 ± 2 months after RT in group one (11 m, 12 f); and 34.4 ± 29.1 months after RT in group two (9m, 17f). All were followed for 1 year (M12 cohort). Additional data up to 2 years were also available for 94 pts (47 EC-MPS, 47 Ex-MMF-M24 cohorts).

Results: Any severe infection 4(5.7) 3(4.3) 4(8.5) 2(4.3) and any serious infection 12(17.1) 8(11.6) 10(21.3) 8(17.0) were also available for 94 pts (47 EC-MPS, 47 Ex-MMF-M24 cohorts).

Conclusions: There was no apparent unexpected emergent risk associated with long-term EC-MPS treatment or conversion of therapy from MMF to EC-MPS.

Reference: Pelletier, et al., Clin Transplant 2003.

PO-381
LONG-TERM SAFETY AND TOLERABILITY AFTER CONVERSION FROM MYCOPHENOLATE MOFETIL (MMF) TO ENTERIC-COATED MYCOPHENOLENATE SODIUM (EC-MPS, MYCOPRINT) IN STABLE MAINTENANCE RENAL TRANSPLANT RECIPIENTS
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Introduction: MMF is widely used for prevention of acute rejection after transplantation. Discontinuation or dose adjustments of MMF for AEs are a risk factor for increased rejection/decreased graft survival (Pelletier, 2003), EC-MPS was developed in hopes of providing less gastro-intestinal AEs allowing less need for dose adjustments or discontinuations while maintaining a comparable safety and efficacy profile.

Materials and Methods: Maintenance renal transplant patients who completed a randomized, 5-day double-blind, double-dummy multicenter, parallel-group study (core) assessing safety and efficacy of 720 mg bid EC-MPS versus 1000 mg bid MMF administered in combination with Neoral® were followed for 2 years (extension). At end of the core, patients initially receiving MMF were converted to EC-MPS. Those receiving EC-MPS continued receiving EC-MPS. Of the 145 pts who entered core, 139 (69, EC-MPS; 70 Ex-MMF) entered extension. All were followed for 1 year (M12 cohort). Additional data up to 2 years were also available for 94 pts (47 EC-MPS, 47 Ex-MMF-M24 cohorts).

Results: Compliance to treatment was high, and patients on treatment received >90% of their planned daily dose of EC-MPS. As expected, incidence of efficacy-related events was low. The incidence of AEs was comparable between groups, with no major difference between both groups for any specific AE.

Conclusions: There was no apparent unexpected emergent risk associated with long-term EC-MPS treatment or conversion of therapy from MMF to EC-MPS.

Reference: Pelletier, et al., Clin Transplant 2003.

PO-382
CHLAMYDIA PNEUMONIAE INFECTION – AN ADDITIONAL FACTOR FOR CHRONIC ALLOGRAFT DYSFUNCTION
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The study was aimed at evaluating a influence of selected parameters on late kidney transplant graft function. The study was divided into two groups: one - (1-8 months) and second - (11-146) after RT. The first ECHO examination was performed 3 ± 2 months after RT in group one (11 m, 12 f); and 34.4 ± 29.1 months after RT in group two (9m, 17f). All were followed for 1 year (M12 cohort). Additional data up to 2 years were also available for 94 pts (47 EC-MPS, 47 Ex-MMF-M24 cohorts).

Any severe infection 4(5.7) 3(4.3) 4(8.5) 2(4.3) and any serious infection 12(17.1) 8(11.6) 10(21.3) 8(17.0) were also available for 94 pts (47 EC-MPS, 47 Ex-MMF-M24 cohorts).

Conclusions: There was no apparent unexpected emergent risk associated with long-term EC-MPS treatment or conversion of therapy from MMF to EC-MPS.

Reference: Pelletier, et al., Clin Transplant 2003.

(5-10 mg/day). The diagnostics of CAN was based on the Banff criteria. The CyA nephropathy was diagnosed by the presence of nodular arteriolyal- nosis. To estimate the rate of CAN progression the 2-years graft survival since the time of CAN diagnosis was calculated (Kaplan-Meyer method).

According to the morphological features all the recipients were divided into two groups. In the first group 42 recipients with CyA nephropathy were included; 40 recipients with CAN without arteriolalhynosis were included in group 2.

In the first group enalapril attenuated significantly the rate of CAN progression. The 2-years graft survival rate since the time of CAN diagnosis was 87% in enalapril-treated patients (29 pts) and 58% in those (13 pts) who were not treated (p=0.03). But the significant impact of enalapril on the rate of CAN progression in the second group was not found. The 2-years survival rate were 58% (23 pts) and 60% (17 pts) respectively (p=0.9).

Conclusion: Enalapril attenuates the rate of CyA nephropathy progression, but its renoprotective effect is not significant in CAN without arteriolalhynosis.

Any severe infection 4(5.7) 3(4.3) 4(8.5) 2(4.3) and any serious infection 12(17.1) 8(11.6) 10(21.3) 8(17.0) were also available for 94 pts (47 EC-MPS, 47 Ex-MMF-M24 cohorts).

Conclusions: There was no apparent unexpected emergent risk associated with long-term EC-MPS treatment or conversion of therapy from MMF to EC-MPS.

Reference: Pelletier, et al., Clin Transplant 2003.
negative for C.pneumoniae-DNA (22%). CHRF+patients were found to have significantly lower HDL levels (46mg/dl vs. 58mg/dl) and higher triglyceride levels (199mg/dl vs. 152mg/dl). A designed econometric model enabled us to calculate the probability of chronic rejection for a given patient taking into account the most significant risk factors for the development of chronic rejection.

Conclusions: The presence of C.pneumoniae-DNA in peripheral blood leukocytes might be an additional factor for CHRF.

PO-383 ABSTRACT WITHDRAWN

PO-384 PROLONGED WARM ISCHAEMIC TIME LEADS TO SIGNIFICANT IMPAIRMENT OF EARLY GRAFT FUNCTION DURING PERFUSION ON AN ISOLATED HAEMOPERFUSED PORCINE KIDNEY MODEL

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Purpose: Non-heart-beating donor (NHBD) kidneys represent an increasingly important source of renal allografts. However these organs are associated with significantly higher rates of delayed graft function and primary non-function due to the prolonged warm ischaemia sustained during retrieval. The aim of this study was to establish the relationship of warm ischaemia and renal function in a model that is representative of human transplantation.

Method: After two hours of cold storage in a hyperosmolar citrate solution, porcine kidneys were perfused with normothermic 37°C, oxygenated autologous blood on an isolated organ perfusion system. The system was adapted from cardiopulmonary bypass technology and an initial creatinine concentration of 1000mmol/L was added to the blood perfusate to allow the assessment of renal function. Kidneys were divided into four groups (n=5) and were subjected to 5 minutes (controls), 15 minutes, 25 minutes and 40 minutes warm ischaemic time respectively. Physiological and biochemical parameters were measured throughout the 6 hour perfusion period.

Results: Controls kidney demonstrated significantly improved renal function compared to 40 minute WIT kidneys shown in the table below. Fifteen minute and 25 minute WIT kidneys showed impaired function relative to the control group but these differences did not reach significance. All values are the mean ± SD.

| Functional parameters    | Control | 40 min WIT | P Value |
|--------------------------|---------|------------|---------|
| % Creatinine fall        | 72±12.8 | 44±17.3    | 0.03    |
| Creatinine clearance     | 0.8±0.15| 0.3±0.26   | 0.05    |
| Urine output ml/hr       | 78.3±28.3| 23.7±25.2 | 0.03    |
| 02 consumption ml/min    | 30.8±6.9 | 16.8±10.6 | 0.04    |
| Renal blood flow ml/min/100g | 50±11.3 | 27±16.9   | 0.03    |
| Renal vascular resistance mmHg/ml/min | 0.5±0.1 | 0.9±0.25 | 0.02    |

Conclusion: This model demonstrates that kidneys are still viable after 40 minutes warm ischaemia but early function is considerably impaired.

PO-385 TREATMENT OF ADULTS WITH PRIMARY HYPEROXALURIA BY TRANSPLANTATION

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Introduction: Primary hyperoxaluria (PH) is a rare group of genetic disorders causing calculi formation and chronic renal failure (CRF). PH1 results from an absence of glycerate dehydrogenase predominantly in granulocytes. PH3 may reflect increased gut absorption.

Case reports: 1. 23yo male with ESRF due to PH1 underwent split-liver transplantation 02/02 followed by cadaveric renal transplantation 02/04. 2. 43yo. female with PH1 offered combined liver/kidney transplantation but declined because of mortality. Subsequently he had living related kidney transplantation following intensive dialysis. This failed after 13 years. Patient reconsidered when child older and underwent combined cadaveric renal transplantation 11/04. 3. 43yo. male with ESRF secondary to PH2 (undiagnosed) underwent cadaveric renal transplantation 07/01. Graft never functioned and histology confirmed oxalosis. Type 2 diagnosed on biochemical testing. Liver transplantation judged inappropriate. Ongoing workup for living related kidney.

Discussion: Most cases present in childhood with recurrent stones. Rarely late-presenting or missed cases present in adulthood with significant renal impairment. This is likely to be more common in future because of immigration from nations without molecular diagnostics. In such cases prognosis is grave without transplantation. Liver transplantation cures the metabolic disorder in PH1 but not other forms. Where ESRF already present, combined transplantation is indicated. Though not always logistically possible or the patients choice. Renal transplantation requires aggressive pre- dialysis to reduce oxalate levels and primary function/good urine flow rates to prevent tubular calcification.

PO-386 DIABETES MELLITUS AFTER KIDNEY TRANSPLANTATION IN A FRENCH POPULATION: INCIDENCE AND RISK FACTORS

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New onset diabetes is a well known complication after kidney transplantation. However, the incidence and risk factors of post-transplant diabetes mellitus (PTDM) in a French kidney transplant population has not been examined.

Methods: 257 kidney recipients with no diabetes mellitus prior to transplantation were selected for this retrospective study conducted between 2001 and 2003. PTDM was diagnosed according to American Diabetic Association/WHO criteria or the need to start insulin or an oral hypoglycemic agent. The data set included recipient age, gender, race, familial diabetes incidence, BMI and metabolic status before transplantation, HLA mismatches, HCV antibody status, rejection episodes and immunosuppressive medications.

Results: The cumulative incidence of PTDM was 6.3%, 8.5%, and 11% at 3, 12, and 30 months post-transplant, respectively. With actuarial analysis, we identified several risk factors for PTDM including body mass index =<25 kg/m² (log rank: p<0.05), first degree family history of diabetes mellitus (log rank: p<0.05), the use of tacrolimus as the initial immunosuppressive medication instead of ciclosporine (log rank: p<0.01) and pre- transplantation dyslipidemia (log rank: p<0.05). Age >46 and hypertension failed to reach statistical significance (log rank: 0.07 and 0.10) but correlated with other common comorbidities of the metabolic syndrome (i.e. BMI 47.7y (16-78). Our patients all get ulcer prophylaxis. Biopsies were taken from the duodenum, antrum, corpus, and processed for histology, and CMV-PCR.

Results: During a ten year period, 24.4% of all transplanted patients required upper endoscopy. Indication for examination were pain: 44.7%, anaemia: 36.6%, nausea/dyspepsia: 31%. Only 14.7% of the macroscopic findings were negative, but 19% of them showed inflammation by histology. Inflammatory changes were seen in 47.8% of cases, ulcer disease 15%, (in stomach 40, duodenum 25, both 4). GORD was seen in 18.2%. 3 (0.65%) tumours were found, one osophago, one gastric cc, and one MALT lymphoma. Of tested 393 patients 20,6% were Helicobacter pylori positive, 35% were negative for C.pneumoniae-DNA (22%). CHRF+patients were found to have significantly lower HDL levels (46mg/dl vs. 58mg/dl) and higher triglyceride levels (199mg/dl vs. 152mg/dl). A designed econometric model enabled us to calculate the probability of chronic rejection for a given patient taking into account the most significant risk factors for the development of chronic rejection.

Conclusions: This study demonstrates that in a South of Europe kidney transplant population, there is a significant risk of PTDM. Appropriate screening of risk factors before transplantation may allow appropriate management strategies in order to reduce PTDM.

PO-387 UPPER ENDOSCOPY FOR ORGAN TRANSPLANT PATIENTS: SINGLE CENTRE EXPERIENCES

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Introduction: Upper gastrointestinal complications have historically resulted in considerable morbidity and mortality to solid organ transplant recipients. Aim of the study: was to summarize the largest endoscopic database for organ transplanted recipients.

Materials and methods: At our department 1669 kidney, and 218 liver transplantsations were done between 1994 and 2004. At that period we performed 5843 upper endoscopies for 460 patients with significant gastrointestinal complaints. 410 examinations were done for kidney, 48 for liver, 1-1 for heart and SPK recipients. 58% were male, 42% female, mean age 47,7y (16-78). Our patients all get ulcer prophylaxis. Biopsies were taken from the duodenum, antrum, corpus, and processed for histology, and CMV-PCR.

Results: During a ten year period, 24.4% of all transplanted patients required upper endoscopy. Indication for examination were pain: 44.7%, anaemia: 36.6%, nausea/dyspepsia: 31%. Only 14.7% of the macroscopic findings were negative, but 19% of them showed inflammation by histology. Inflammatory changes were seen in 47.8% of cases, ulcer disease 15% (in stomach 40, duodenum 25, both 4). GORD was seen in 18.2%. 3 (0.65%) tumours were found, one osophago, one gastric cc, and one MALT lymphoma. Of tested 393 patients 20,6% were Helicobacter pylori positive, which is one of the relevant population. Of tested 241 patients 48% were positive for Cytomegalovirus-PCR. Of all patients 9,5% suffered from sore.

Conclusions: Gastrointestinal complaints are frequent among transplant patients, and about 25% of them will require upper tract endoscopy. 85% have some kind of objective alterations. It is difficult to distinguish the infection-related from the transplantation related GI complications. Our recommendation is to perform transplant patient’s endoscopy by specialised personnel in transplant centres gastroenterology.
PO-388 DOES IMMUNOSUPPRESSIVE THERAPY AFTER RENAL TRANSPLANTATION INFLUENCE THE PARAMETERS OF OXIDATIVE STRESS?

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Introduction: Different immunosuppressive regimens may affect protein and lipid peroxidation processes and antioxidant status of the patient after renal transplantation.

Methods: The aim of this study was to determine the effect of MMF on the oxidative stress after renal transplantation. We examined the concentration of MDA/4-HNE (malondialdehyde, 4-hydroxynonenal), CG (carbonyl groups) in serum and GSH in erythrocytes. First we compared two groups of patients: with MMF (MMF+, n=16) and without MMF (MMF−, n=33) 6 months after the surgery. The CsA dose did not differ between the two groups. Then we examined the patients (n=18) who were converted from CsA+AZA+P to CsA+MMF+P because of CsA toxicity or deterioration of renal function. The CsA dose was lowered at the same time. The MDA/4-HNE, CG and GSH concentrations were determined 1 month before and after the onset of the MMF treatment. The CG content was evaluated following the 2,4-dinitrophenylhydrazine oxidation period another 6/34 patients died 44.6 months after RT (from 12 to 146.6 months after RT) (from 12 to 140.6 months after RT) (from 12 to 146.6 months after RT) (from 12 to 146.6 months after RT) (from 12 to 146.6 months after RT)

Results:

Before conversion 1 month after conversion p

| Treatment          | MDA/4-HNE [µmol/l] | CG [nmol/g of protein] | GSH [µmol/g of Hb] | CsA dose [mg/kg b.m] |
|--------------------|-------------------|------------------------|-------------------|---------------------|
| MMF (−) (n=16)     | 2.21              | 5.61                   | 2.48              | 4.08 ± 1.43         |
| MMF (+) (n=16)     | 1.52 ± 0.46       | 0.89 ± 0.28            | 3.87 ± 1.10       | 4.50 ± 1.36         |

Conclusion: Methyl prednisolone, Tacrolimus, Everolimus, MMF and FT-720 produced immunosuppressive effects. After 19 days transplant size, weight and growth-success were noted. Immunosuppressives permissive for growth and vascularisation were used in further, group of outbred rats receiving metanephric allografts. Explants were assessed by histology, immunohistochemistry, and PCR analysis.

Results: No immunosuppressives inhibited metanephric vitality in culture. Methyl prednisolone, Tacrolimus, Everolimus, MMF and FT-720 produced growth rates and histology equivalent to controls in syngeneic transplants. Cyclosporine and dexamethasone impaired transplanted growth. FT-720 and a combination of Tacrolimus and FT-720 were permissive for allograft development and minimised histological acute rejection compared with controls. The combined treatment reduced Tcell infiltrates from 10.97%±1.8% to 2.5%±1.2% (P=0.0004) with similar reductions in for B cell and macrophage staining. Methylprednisolone didn't inhibit rejection whilst Everolimus, MMF and Tacrolimus alone produced a reduced inflammatory cell infiltrate but rejection remained severe.

Conclusions: Two currently-used immunosuppressive agents are both permissive for development and effective in inhibiting rejection of allogeneic transplants. Clinical transplantation of foetal organs may not require new, complex immunosuppressive regimens or tolerance-induction approaches. Knowledge of current drugs’ effects on the developing kidneys of children of transplantated mothers may not be applicable since the placental barrier is absent in this model.

PO-389 EFFORTS TO INCREASING DONOR POOL: LONG-TERM RISK FACTORS IN LIVING UNRELATED DONOR RENAL TRANSPLANTATION

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To clarify the role of living unrelated donor renal transplantation, we performed multi-variate risk factors analyses affecting graft and patient survival in 1945 living donor kidney transplantations (967 unrelated vs. 978 related donors) at our institute. The minimum and mean follow-up periods were 12 and 87.8 months, respectively. Of these, living unrelated donors were composed of volunteers (781), exchange donors (86), distant relatives (54), spouses (43), and close friends (3). The mean recipient age was 39.7 ± 7.8 years, exchange donors (86) Ewak, Lysiak-Szydlowska W., Rutkowski B. 1Department of Nephrology, Transplantology and Internal Diseases, 1St Department of Surgery, Medical Academy of Gdańsk, Poland.

PO-390 PERMISSIVE AND EFFECTIVE IMMunosuppression FOR FOETAL KIDNEY TRANSPLANTS

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Purpose: Transplantation of foetal organ rudiments is a promising approach to organ failure. We transplanted rat metanephros to syngeneic recipients, showing growth, vascularisation, normal histology and measurable function. Transplants between allogeneic rats are invariably rejected. An appropriate immunosuppressive regime would require agents which inhibit rejection but not developmental and vascularisation.

Methods: Immunosuppressive toxicity was tested in organ culture with varying concentrations of agents. Syngeneic rats were transplanted with metanephros and treatment-group rats received immunosuppressives. After 19 days transplant size, weight and growth-success were noted. Immunosuppressives permissive for growth and vascularisation were used in further, group of outbred rats receiving metanephric allografts. Explants were assessed by histology, immunohistochemistry, and PCR analysis.

Results: No immunosuppressives inhibited metanephric vitality in culture. Methyl prednisolone, Tacrolimus, Everolimus, MMF and FT-720 produced growth rates and histology equivalent to controls in syngeneic transplants. Cyclosporine and dexamethasone impaired transplanted growth. FT-720 and a combination of Tacrolimus and FT-720 were permissive for allograft development and minimised histological acute rejection compared with controls. The combined treatment reduced Tcell infiltrates from 10.97%±1.8% to 2.5%±1.2% (P=0.0004) with similar reductions in for B cell and macrophage staining. Methylprednisolone didn't inhibit rejection whilst Everolimus, MMF and Tacrolimus alone produced a reduced inflammatory cell infiltrate but rejection remained severe.

Conclusions: Two currently-used immunosuppressive agents are both permissive for development and effective in inhibiting rejection of allogeneic transplants. Clinical transplantation of foetal organs may not require new, complex immunosuppressive regimens or tolerance-induction approaches. Knowledge of current drugs’ effects on the developing kidneys of children of transplantated mothers may not be applicable since the placental barrier is absent in this model.

PO-391 RENAL TRANSPLANTATION (RT) IN OLDER RECIPIENTS – ONE CENTRE EXPERIENCE

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Advanced age per se is not a contra indication to RT. However, cardiovascular and infectious complications occur frequently in a group of patients as compare to younger ones. The objective for this study was to analyze results of RT in older recipients. The group consisted of 36 pts (24m, 12f), aged 65 ± 37 years. The donors (18m/16f) were 45 ± 13 y old, and their mean creatinine clearance was 103.83 ± 44.05 ml/min. Mean total ischemic time was 13.7 ± 6.93h. Most commonly used immunosuppressives protocols consisted of prednisone, azathioprine, cyclosporineA or prednisone, mycophenolate mofetil, cyclosporineA. Early complications included: 2/36 pts died (myocardial infarction, pulmonary embolism), 1/36 lost graft due to graft vessel thrombosis, 42% required dialysis due to delayed graft function, 38.7% pts experienced acute tubular necrosis and 41.9% acute rejection. The other most common early complications were urinary tract infections 12/36, necrosis of the ureter 4/36, wound infections 4/36. The mean creatinine levels at first and sixth month after RT were 1.8±0.7 and 1.65±0.64 mg/dl, respectively. During the observation period another 6/34 patients died 44.6 months after RT (from 12 to 120 months) with functioning grafts and 1/34 experienced chronic allograft nephropathy and returned to dialysis.

Conclusions: Our one centre results confirm that RT is a good option of renal replacement therapy in older patients. Thorough recipient selection and preparation as well as tailored immunosuppression is particularly important in that group of patients.

PO-392 IMPROVING RESULTS OF RENAL TRANSPLANTATION FROM ELDERLY DONORS: THE BUDAPEST EXPERIENCE

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As the demand for kidney transplantation has become greater than the avail-
ability of cadaveric organs, the transplant communities worldwide are expanding the traditional donor criteria used for renal transplantation. This policy, under strict criteria, involves the use of elderly (>60 years) brain dead donors. In this study we reviewed our experience of using elderly cadaveric donors for kidney transplantation, investigating the influence of donor parameters on early graft function and graft survival. Our aim was to compare our new data with the outcomes of a period analysed before (1994-1998). A retrospective comparative analysis of three periods was performed: 1994-1998 (P I.), 1999-September, 2000 (P II.) and 2001-2002, July (P III.). The number of elderly donors was 40 for P I., 28 for P II. and 31 for P III., respectively. The mean donor age was 63.4-64.5-63.8 years, mean diuresis 473-219-276 ml/hour. The need of vasopressors during the donor management was 81-85-70%. The number of kidney recipients was 59-30-37, one year graft survival 71.2-91.2% and one year patient survival 82.2-96.6-97.2%, respectively. There has been a considerable improve in the outcomes regarding one year graft- and patient survival. To summarize, we believe that, with careful donor and recipient evaluation, individualized immunosuppression, shorter ischemic time and age-matching, the results of renal transplantation from elderly donors could achieve the outcomes of “optimal” cadaveric kidney transplantation.

**PO-393 IMPACT OF MULTIPLE KIDNEY GRAFT ARTERIES ON REJECTION, FUNCTION AND PATIENT AND GRAFT SURVIVAL AT 3 YEARS FOLLOWING TRANSPLANTATION**

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The use of grafts with multiple renal arteries (MRA) has been considered a relative contraindication because of the increased incidence of immediate surgical complications. Objectives: We conducted this retrospective study to determine whether the use of kidneys with MRA adversely affects post-transplant graft and patient outcome.

Methods: Data of 262 kidney transplantations performed consecutively at our institute between January 1996 and December 2000 were collected retrospectively. Seventy-two patients (27.5%) received grafts with MRA (66 with 2 arteries and 6 with 3 arteries). We divided the study population into 2 groups: single renal arteries (SRA) recipients (n=72) and MRA recipients (n=190). We compared the incidence of acute tubular necrosis, post-transplant hypertension, surgical complications; mean creatinine and proteinuria levels at 1, and 3 years post-transplant; and patient and graft survival.

Results: We found no significant differences among the two groups for the following variables: delayed graft function, creatinine levels (at 1- and 3-years), and graft and patient survival. Proteinuria level at 1 year was significantly higher in MRA recipients but not at 3 years. Immediate vascular complications were significantly higher in MRA recipients: arterial thrombosis was the most common vascular complication (9.6% vs 2.1%, p=0.05), whereas the rate of arterial stenosis was not significantly higher in MRA recipients compared to SRA recipients (6.9% vs 4.2%, p=0.36). The rate of urololgic complications was not different between the two groups.

Conclusions: Renal transplantation with MRA does not influence patient and graft survival at 3 years.

**PO-394 CAUSES AND EFFECTS OF PROLONGED KIDNEY COLD ISCHAEMIC TIME – A UK SINGLE CENTRE PROSPECTIVE AUDIT**

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Background: Prolonged cold ischaemia (CIIT) of kidneys is a significant risk factor for delayed function, acute rejection and reduced graft survival. Data from UK Transplant [RTSM(04)] showed a median CIT of 19 hours (IQ range 16-23h) for all centres in 2002/03. Median CIT in our centre was also 19 hours but the IQ range was 16-23h. UKT data also showed three-month survival reduced by 8% for kidneys transplanted >23h compared to <23h, meaning that each month one kidney transplant fails due to prolonged CIT (RR 1.9).

Purpose: A prospective audit of adult, heart-beating deceased donor kidney transplantation between Jan 2003 and June 2004 to initiate changes in practice to reduce CIT.

Methods: Data was collected from medical notes and UKT. Time cohorts were set and reason codes recorded caused of delays at each stage. Outcomes were measured by delayed function, serum creatinine and transplant survival at 3/12.

**PO-395 PREDICTIVE PROPERTIES OF URINARY IP-10 EXPRESSION FOR SHORT- AND LONG-TERM GRAFT FUNCTION AFTER KIDNEY-TRANSPLANTATION**

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Purpose: The early identification of transplant patients at enhanced risk for developing acute rejection is crucial for the improvement of individual immunosuppressive treatment. The recently described analysis of protein and mRNA for selected candidate markers in urine opens the opportunity to monitor kidney-transplanted patients non-invasively. Since the interferon-gamma induced chemokine for CXCR3+ Th1 cells IP-10 is associated with acute rejection processes we estimated the predictive properties of urinary IP-10 expression for the short- and long-term graft function after kidney transplantation.

Materials/Methods: Urine samples from kidney-transplanted patients were analyzed for IP-10 mRNA and protein expression in retrospective studies by RT-PCR and ELISA. IP-10 levels were correlated with the incidence of acute rejection episodes proven by histological analysis of graft tissue and the long-term graft function reflected by the Glomerular Filtration Rate 6 months post transplantation.

Results: Our follow-up studies revealed that urinary IP-10 mRNA and protein induction identifies patients with developing acute rejection episodes several days before a needle biopsy is taken due to rising serum creatinine levels. Most importantly we demonstrate the predictive properties of enhanced urinary IP-10 protein expression within the first 4 postoperative weeks for the 6-month graft function.

Conclusion: The data indicate a correlation between increased IP-10 levels in urine at early time-points and ongoing intragraft immune activation leading to acute rejection processes and restricted 6-months graft function. This could allow the adjustment of immunosuppressive therapy at an early stage prior to relevant functional graft injury.

**PO-396 LIVING DONATION RENAL TRANSPLANTATION: OUTCOME OF GRAFTS PRESENTING ANATOMICAL ABNORMALITIES**

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In living donation it is their policy to obtain the kidney presenting functional or anatomical abnormalities to minimize the risk for the donor. Of the 236 LKT 59 grafts (25%) revealed AA including 32 with multiple renal arteries (MRA), 7 with multiple renal veins (MRV), 12 with MRA and MRV, 3 with renal artery stenosis, 2 with renal artery aneurysms and 3 with ureteral abnormalities. Demographic details of donors and recipients were comparable for both groups. The 1- and 5-year graft survival was 98% and 93% for NA and 100% and 100% for AA-grafts (log rank: ns). Mean serum creatinine at 1 and 5 years after LKT was 138 and 147 µmol/L for NA and 142 and 173 µmol/L for AA-grafts (T-test: ns). Primary graft function was 96% for grafts with NA and 98% for grafts with AA (Chi-test: ns). There was no statistical significant difference for both groups regarding the incidence of lymphoecyes (NA: 9%; AA: 8%), urinary leakages (NA: 7%; AA: 5%), bleeding (NA: 5%; AA: 8%) and vascular complications (NA: 3%; AA: 2%).

We present results following 236 cases of LKT. The high incidence of grafts with anatomical abnormalities is a result of our local policy to obtain the kidney presenting the lower functional capacity disregarding the presence of multiple
renal vessels. Outcome of recipients receiving grafts with anatomical abnormalities was comparable to those presenting normal anatomy.

### PO-398 RETROPERITONEOSCOPIC LIVE DONOR NEPHRECTOMY (RPLDN): HISTOPATHOLOGICAL FINDINGS OF 0-HOUR BIOPSY SPECIMENS OF DONOR KIDNEY AND POSTTRANSPLANT ALLOGRAFT FUNCTION

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**Introduction:** Retroperitoneal laparoscopic live donor nephrectomy is becoming a standard technique for donor kidney retrieval. However, many authors have reported that about 5% of recipients required hemodialysis after renal transplantation due to poor renal function. We established the technical retroperitoneoscopic live donor nephrectomy (RPLDN) and report the histopathological findings of 0-hour biopsy specimens of the donor kidneys and short- and long-term allograft function.

**Patients and Methods:** Between July 2001 and July 2004, 155 live donor kidney grafts were procured by RPLDN. All procedures were performed through the retroperitoneal approach without opening the peritoneal cavity. The kidneys were retrieved through a 5-cm flank incision or a 5-cm Pfannenstiel incision.

**Results:** One hundred and forty-five cases were of left and 10 cases of right nephrectomy. Fifty-two patients had more than 2 renal arteries. Donor nephrectomy was carried out successfully in all patients. Two cases were changed to open donor nephrectomy. No serious complications were encountered during surgery. Ureteral complications occurred in three patients and were successfully treated with retrograde ureteral stenting. No patients required hemodialysis after transplantation due to acute tubular necrosis. The average serum creatinine level at 2-years after surgery was 1.3mg/dl. 0-hour biopsy specimens of the donor kidney showed normal findings or very mild cortical damage in 80% of the cases.

**Conclusion:** Excellent short- and long-term graft function without any evidence of severe renal cortical damage of donor kidney was obtained by RPLDN.

### PO-397 PLASMA FREE AMINO ACIDS IN RENAL TRANSPLANT PATIENTS

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The kidney plays a major role in the regulation of many body pools of amino acids (AA) through synthesis, degradation and/or urinary excretion. In this study we assessed the effect of renal transplantation on the nutritional status of adult patients, mainly by studying plasma amino acid profile in 77 patients after renal transplantation. Plasma amino acid levels were measured by chromatography method with amino acid analyser, using a lithium-lithium citrate buffer system. Total amino acids concentration was significantly elevated among patients after renal transplantation when compared to healthy controls (3.9±0.7 µmol/ml vs 2.9±0.3 µmol/ml). The mean levels of taurolin and homocystein were considerably higher among transplanted group as compared to control group (0.13±0.04 µmol/ml vs 0.10±0.03 µmol/ml and 0.002±0.0002 µmol/ml vs 0.002±0.00015 µmol/ml). There was no significant difference in concentration of essential amino acids (EAA) including branched-chain amino acids (BCAA), in concentration of sulfur amino acids and aromatic amino acids between patients after renal transplantation and healthy control. No correlation was observed between plasma amino acid levels and the post-transplant period. Among patients on cyclosporine therapy the concentration of plasma taurolin and branched-chain amino acids (BCAA) was significantly reduced as compared to patients with no cyclosporine immunosuppressive therapy (taurolin 0.12±0.04 µmol/ml vs 0.14±0.03 µmol/ml, BCAA 0.36±0.08 µmol/ml vs 0.40±0.09 µmol/ml). Among patients on tacrolimus therapy mean plasma taurolin level was significantly higher as compared to patients without tacrolimus immunosuppression (0.15±0.03 µmol/ml vs 0.12±0.03 µmol/ml). There was no difference in concentration of plasma amino acids between patients who used MMF therapy and who didn’t use MMF therapy.

### PO-399 THE CYP3A4 3A1 GENOTYPE SHOWS CORRELATION WITH SYSTEMIC CLEARANCE (CL) OF SIROLIMUS (RAPAMUNE®) IN A RENAL TRANSPANT POPULATION

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**Background:** Cytochrome P450 3A4 (CYP3A4) is important for the metabolism of sirolimus (SRL). Polymorphisms in the gene affect the production of the enzyme and hence possibly the pharmacokinetics (PK) of SRL. The individual patient systemic clearance (CL), obtained by population Bayes PK methods, as well as the dose-scaled trough levels (Cmin/Dose) are related to genotype categories.

**Methods:** SRL blood concentrations (Cmin; n = 768) in renal transplant patients (n = 41), receiving combination Rapamune® SRL and cyclosporine, were used. The promoter of the CYP3A4 gene was genotyped for polymorphisms by PCR. The individual CL and the Cmin/Dose were regressed against the genotype and weight and sex as covariates in general additive (GAM) and in mixed effects (NONMEM) models.

**Results:** Subgroups of 34 homozygotes (82.9%) and 7 heterozygotes (17%) existed. NONMEM modeling of Cmin/Dose showed significant difference between genotype subgroups (mean ± SD) (3.63 ± 1.17 [1000 L X 1] and 2.86 ± 0.72 [1000 L X 1], respectively; p < 0.001) and insignificant effects for covariates weight and sex. A GAM between individual CL and genotype resulted in a significant relationship (p < 0.05; F-test).

**Conclusion:** Polymorphisms in CYP3A4 appear to associate with the individual patient SRL clearance and with Cmin/Dose. Controlled prospective testing in much larger populations, including haplotypic analysis with full PK population screens, is needed to verify this result.

### PO-400 CMV INFECTION IN HIGH-RISK KIDNEY TRANSPLANT PATIENTS IN ASSOCIATION WITH HLA-TYPE

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**Background:** Cytomegalovirus infection in transplant patients with certain risk factors remains a major hazard in patient management. CMV seronegative recipients (R-), who receive the graft from CMV seropositive donors (D+), have the highest risk of developing acute CMV disease. HLA typing is the gold standard for risk assessment in this subgroup of patients.

**Objectives:** We suppose that the HLA-type may influence the occurrence and the severity of the primer CMV infection of high-risk patients and can be useful in prediction of the acute infection.

**Patients:** Since 2000 till 2004 736 kidney transplantations were performed in our clinic. The HLA-type (A, B, Cw, DR, DQ) of the recipients was determined before the transplantation. Of 736 recipients 132 (18%) were CMV-seronegative recipients (R-), who receive the graft from CMV seropositive donors (D+), have the highest risk of developing acute CMV disease. CMV seronegative recipients (R-) are at higher risk of CMV infection. CMV seropositive donors (D+) are at lower risk of CMV infection.

**Methods:** The HLA typing was performed by the ISS technique (International Society for Organ Transplantation).

**Results:** Of 132 CMV-seronegative patients 25 developed acute CMV infection (19%) during the first posttransplant year. In Class I HLA-types: HLA-A: of 82 HLA-A2-positive patients 18 (22%) of 50 HLA-A2-negative patients 7 (14%) had acute CMV infection. HLA-B: of 35 HLA-B12-positive patients 8 (23%), of 97 HLA-B12-negative patients 17 (17%) had acute CMV infection. HLA-C: of 37 HLA-Cw7-positive patients 10 (27%), of 95 HLA-Cw7-negative patients 15 (16%) had acute CMV infection. In Class II HLA-types: HLA-DR: of 40 HLA-DR6-positive patients 11 (28%), of 92 HLA-DR6-negative patients 14 (15%) had acute CMV infection. HLA-DQ: of 45 DQ3-positive patients 16 (36%), of 87 DQ3-negative patients 9 (10%) had acute CMV infection.

**Conclusions:** HLA-DQ3 was found to be a significant predictor of CMV infection (P < 0.05). Our data suggest that HLA-DQ3-positive recipients are more susceptible to CMV infection.
THE SUCCESSFUL USE OF TACROLISIN IN A RENAL TRANSPLANT RECIPIENT WITH CYCLOSPORINE INDUCED BONE PAIN SYNDROME

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The prevalence of bone pain syndrome(BPS) induced by cyclosporin(A/CsA) is about 1-27%. It has been improved by using calcium channel blockers or inflammatory drugs. CsA was replaced with tacrolimus 5mg/day (trough level: 5-6 ng/mL) but not the same in the adverse effects. We report the successful use of tacrolimus in early period of renal transplantation with cyclosporine induced BPS.

Case: A 38 year old woman developed a deep aching sensation of both knee in 2002. The episode was episodic lasting several hours and aggravated during walking. On physical examination, there were no signs of infection. The diagnosis of bone pain syndrome without sequential treatment, despite a high rate of DGF.

Conclusion: tacrolimus used successfully in early period of renal transplantation with cyclosporine induced BPS.

renal transplantation with cyclosporine induced BPS.

GOAL

The aim of the study was to assess the incidence of chronic C. pneumoniae (Cp) infection and its association with atherosclerosis in a population of patients with ischemic heart disease (IHD).

Methods: 164 subjects – 99 patients (HD group) and a control group of 65 subjects.Chronic Cp infection affected 46.5% of HD patients and 9% of controls (p<0.05). Among HD patients 26.3% had ischemic heart disease (IHD), vs. 6% in the control group. Among Cp-infected HD patients IHD was more frequent than in non-infected HD patients (15%, p<0.05). Cp DNA was detected in 8.3% of vascular wall specimens from HD group and 20% from control (p<NS). Within the period of 32 months of observation of HD group, cardiac pain was observed in 11 (24%) infected patients vs. 3 (5.2%) patients without Cp infection (p<0.05). Exacerbation of previously diagnosed IHD was observed in 8 (44%) cases in Cp infected group vs. 0 in noninfected patients (p<0.05). Chronic Cp infection affects hemodialysis patients more frequently than healthy subjects. Hemodialysis patients with Cp-infection are at the greater risk of exacerbation of existing IHD.

EXCELLENT OUTCOME OF KIDNEY TRANSPLANTATION FROM NON-HEART-BEATING DONORS UNDER TACROLISIN-BASED IMMUNOSUPPRESSION

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Introduction: In Japan, non-heart-beating donors (NHBDs) were the only available source of kidneys from cadaveric donors until recently, and since 1996 we have been performing kidney transplantation from NHBDs under tacrolimus-based immunosuppression without sequential treatment. However, few investigators have reported the long-term outcome in renal transplantation using tacrolimus-based immunosuppression from NHBDs. In this study, we evaluated the long-term outcome in renal transplantation under tacrolimus-based immunosuppression from NHBDs.

Materials and Methods: Between 1996 and 2003, 53 patients underwent cadaveric renal transplantation from NHBDs at our institution. The outcomes from the NHBDs were compared with those of 53 cases of kidney transplantation from living-related donors(LDs). The recipients were matched according to age, number of transplantations, donor’s age, and the date of transplantation.

Results: There was no significant difference in warm ischemic time (NHBDs; 5.9 min vs LDs; 5.0 min, p=0.48) but a significantly longer total ischemic time was observed in NHBDs (666 min vs 77 min, p<0.001). Primary nonfunction did not occur in either group, but the incidence of delayed graft function was significantly higher for NHBDs (61.5% vs 0%) and the discharge serum creatinine level was higher in NHBDs (2.68mg/dl vs 1.48mg/dl; p<0.001). However, there was no statistical difference in the 1- and 5-year graft survival when NHBDs were compared with LDs (96%, 91% vs.98%, 95%, p=0.06). The occurrence of acute rejection was 31% in NHBDs and 40% in LDs, respectively.

Conclusion: Our study demonstrated that excellent results could be obtained in kidney transplantation from NHBDs under tacrolimus-based immunosuppression without sequential treatment, despite a high rate of DGF.

GRAFT TRANSMITTED CANDIDIASIS IN RENAL TRANSPLANTATION

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Introduction: Contamination of renal grafts with Candida is rare but commonly provokes complications in the recipient. We studied incidence, mechanisms of contamination, presentations of complications, therapeutic and prophylactic strategies.

Methods: 37 French transplant centres replied to a questionnaire collating fungal complications in kidney recipients since 1997. We studied the donors and the recipients of contra-lateral kidneys thanks to French Register of Grafts. Results: We collected 10 Candida arteritides, 1 urinoma, 2 graft site abscesses (total=1362 grafts). These grafts came from 9 cadaveric donors not known to be systemic Candida carriers. 6/9 received antibiotic therapy. 5/9 had a digestive breach at the time of harvest. Clinical manifestations were pain (5/13), fever (6/13), increased CRP (9/13) occurring 56.48 days after grafting. In 10/13, conservation fluid (CF) and/or drains were contaminated by Candida. The diagnosis of arteritis was made by Doppler US (100%). Candida infection was confirmed by aneurysm tissue culture (8/10). The outcome of the collections, 1 patient died after arterial rupture. Transplantectomy was performed for 7 patients with arteritis. 4/7 required immediate arterial by-pass repair (ABR) and the 3 other patients required eventual ABR despite anti-fungal therapy. The graft was preserved for 2 patients with prophylactic ABR. Comparing infected recipients from the same donors, anti-fungal prophylaxis is the discriminant factor in Candida arteritis.

Conclusion: The prognosis of renal grafts contaminated with Candida is poor if arteritis occurs. Contamination seems to be linked to antibiotherapy and digestive breach in the donor. CF and drains should be systematically cultured: in presence of Candida, anti-fungal prophylaxis should be considered. Arteritis treatment should include a pre-emptive by-pass surgery.

CHLAMYDIA PNEUMONIAE INFECTION – AN ASSOCIATION WITH ISCHEMIC HEART DISEASE AND ITS EXACERBATION IN HEMODIALYSIS PATIENTS

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The aim of the study was to assess the incidence of chronic C. pneumoniae (Cp) infection and its association with atherosclerosis in a population of patients with ischemic heart disease (IHD).

Methods: 164 subjects – 99 patients (HD group) and a control group of 65 subjects.Chronic Cp infection affected 46.5% of HD patients and 9% of controls (p<0.05). Among HD patients 26.3% had ischemic heart disease (IHD), vs. 6% in the control group. Among Cp-infected HD patients IHD was more frequent than in non-infected HD patients (15%, p<0.05). Cp DNA was detected in 8.3% of vascular wall specimens from HD group and 20% from control (p<NS). Within the period of 32 months of observation of HD group, cardiac pain was observed in 11 (24%) infected patients vs. 3 (5.2%) patients without Cp infection (p<0.05). Exacerbation of previously diagnosed IHD was observed in 8 (44%) cases in Cp infected group vs. 0 in noninfected patients (p<0.05). Chronic Cp infection affects hemodialysis patients more frequently than healthy subjects. Hemodialysis patients with Cp-infection are at the greater risk of exacerbation of existing IHD.
PO-406  TELEMENTORING REDUCES THE LEARNING CURVE IN HAND-ASSISTED LAPAROSCOPIC DONOR NEPHRECTOMY
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Purpose: Hand-assisted laparoscopic live donor nephrectomy (HALDN) is a challenging procedure to learn but it results in excellent allograft function, and may significantly increase organ donation. Telementoring has been shown to reduce the learning curve in other fields. Following an initial period of trans-Atlantic telementoring for HALDN, we looked at outcome parameters for our subsequent independent practice series.

Methods: We prospectively recorded the outcome parameters (operative time, estimated blood loss, warm ischaemic time and length of hospital stay) for HALDN at our institution commencing with the first independent case (group A). These were compared with the same parameters from the initial telemed-tored group of four cases (group B). We were able to compare these groups against the other recognised world series.

Results: The mean operative time was 215 group A vs. 240 minutes group B. Warm ischaemic time was 2.96 minutes group A vs. 3.1 minutes group B. Estimated blood loss was 182mls group A vs. 150mls group B. Length of hospital stay was 3 days (mean) for both groups. There were no conversions to open surgery or blood transfusions in either group. There are statistically significant differences between any of the parameters. Two urinary tract infections and one incisional hernia occurred post-operatively.

Conclusions: We have maintained over 37 subsequent cases the high standards achieved during the period of telementoring for HALDN. These parameters are equivalent to other published series. Telementoring for laparoscopic donor nephrectomy is feasible and effective and seems to maintain a rapid initial advance in the learning curve.

PO-407  THE SECRET STUDY – STUDY ON EVALUATION OF CANDESARTAN CILEXETIL AFTER RENAL TRANSPLANTATION
Christophe Legendre 1, Thomas Philipp 2, Roland Schmieder 3, Georges Mourad 4, Helmut Geiger 5, Bruno Moulin 6, Sophie Nisse-Durgeat 7, Bartlomiej Matlosz 1, Aleksandra Wesolowska 1, Andrzej Mróz 1, Carola Grönhagen-Riska 2, Irmeli Lautenschlager 1. 1Department of Virology, Helsinki University Hospital; 2Department of Medicine, Division of Nephrology; 3Department of Clinical Chemistry, Helsinki University Hospital, Helsinki, Finland.

Purpose: Chronic allograft nephropathy and cardiovascular (CV) complications limit the long-term success of renal transplantation. AT1 might lower CV morbidity and mortality.

Methods: 700 patients following renal transplantation were to be included and followed up for three years in order to evaluate whether the ARB Candesartan Cilexetil (CC) versus placebo (PL) could reduce the incidence of graft failure and CV morbidity.

Results: Following an interim analysis after 18 months, the study was discontinued since the observed event rate was only 25% of what had been expected. At the premature end of the study, data of 502 patients were available. CV morbidity and mortality, graft failure and creatinine doubling did not differ significantly between both groups. Median proteinuria was significantly higher in the CC group. At the premature end of the study, data of 502 patients were available. CV morbidity and mortality, graft failure and creatinine doubling did not differ significantly between both groups. Median proteinuria was significantly higher in the CC group.

Conclusions: The prevalence of HCV infection defined as the presence of viral RNA in renal transplant recipients is high. A significant group of them consists of patients with HCV-limited HCV replication who are negative for anti-HCV. They may represent a low-level “lymphotropic” HCV strain replication. Routine diagnostics based on serum anti-HCV and HCV-RNA measurement fail in this group of patients.

PO-409  PERIPHERAL BLOOD MONONUCLEAR CELLS (PBMC) INFECTION WITH HEPATITIS C VIRUS IN KIDNEY ALLOGRAFT RECIPIENTS
Barthomej Matlosz 1, Dominika Deborska-Materkowska 1, Marcin Chmielewski 2, Joanna Pazik 1, Magdalena Durlik 1. 1Department of Transplantation Medicine and Nephrology, Medical University of Warsaw, Warsaw, Poland; 2Department of Immunopathology of Infectious and Parasitic Diseases, Medical University of Warsaw, Warsaw, Poland.

Purpose: The long-term effects of cytomegalovirus (CMV) infections on kidney allografts are unknown. We examined the impact of persistent intragraft CMV infection on long-term kidney allograft function and survival.

Methods/materials: CMV was diagnosed in 82/72 renal transplant recipients by antigenemia test and viral cultures. Biopsies from 48/82 patients taken after CMV infection and from 15 control patients with no previous CMV infection were available for the immunohistochemical demonstration of CMV antigens and CMV-DNA hybridisation in situ. Five-year follow-up data were available from these 63 patients.

Results: In 17 patients, CMV antigens and/or DNA persisted in the biopsy >2 months after the last positive finding in blood or urine. Patients with persistent intragraft CMV had reduced graft survival (P=0.041) compared with patients with no intragraft CMV. Cox regression analysis showed persistent CMV as a risk factor for reduced graft survival (RR 3.5, P=0.03). Recipients with persistent intragraft CMV had lower clearance at one and two years (OR 7.7, P=0.004; OR 4.3, P=0.026). In multivariate analyses including several potential pre- and posttransplant risk factors, persistent CMV was an independent risk factor for lower clearance at one and two years (OR 5.0, P=0.024; OR 5.0, P=0.027).

Conclusion: Persistent intragraft CMV infection was associated with reduced kidney allograft function and survival.

PO-410  POLYOMA BK VIREMIA AND OTHER VIRAL INFECTIONS COEXISTENCE IN KIDNEY AND PANCREAS/KIDNEY TRANSPLANT RECIPIENTS
Barthomej Matlosz 1, Aleksandra Wesołowska 1, Andrzej Mróz 1, Jolanta Zegarska 1, Magdalena Durlik 1, WojciechRowski 1, Jacek Szmidt 1, 1Department of Transplantation Medicine and Nephrology, Medical University of Warsaw, Warsaw, Poland; 2Department of Immunology, Transplantology and Internal Medicine, Medical University of Warsaw, Warsaw, Poland; 3Department of General and Transplantation Surgery, Medical University of Warsaw, Warsaw, Poland.

PO-408  PERSISTENT CYTOMEGALOVIRUS INFECTION IN KIDNEY ALLOGRAFTS IS ASSOCIATED WITH INFERIOR EARLY GRAFT FUNCTION AND SURVIVAL
Ilkka Helanterä 1, Petri Koskinen 1, Pärlrik Finne 1, Raija Logino 2, Czesia Grünhagen-Riska 1, Irmieli Lautenschlager 1. 1Department of Virology, Helsinki University Hospital; 2Department of Medicine, Division of Nephrology; 3Department of Clinical Chemistry, Helsinki University Hospital, Helsinki, Finland.

Purpose: The long-term effects of cytomegalovirus (CMV) infections on kidney allografts are unknown. We examined the impact of persistent intragraft CMV infection on long-term kidney allograft function and survival.

Methods/materials: CMV was diagnosed in 82/72 renal transplant recipients by antigenemia test and viral cultures. Biopsies from 48/82 patients taken after CMV infection and from 15 control patients with no previous CMV infection were available for the immunohistochemical demonstration of CMV antigens and CMV-DNA hybridisation in situ. Five-year follow-up data were available from these 63 patients.

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Conclusion: Persistent intragraft CMV infection was associated with reduced kidney allograft function and survival.

PO-407  THE SECRET STUDY – STUDY ON EVALUATION OF CANDESARTAN CILEXETIL AFTER RENAL TRANSPLANTATION
Christophe Legendre 1, Thomas Philipp 2, Roland Schmieder 3, Georges Mourad 4, Helmut Geiger 5, Bruno Moulin 6, Sophie Nisse-Durgeat 7.

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PO-409  PERIPHERAL BLOOD MONONUCLEAR CELLS (PBMC) INFECTION WITH HEPATITIS C VIRUS IN KIDNEY ALLOGRAFT RECIPIENTS
Barthomej Matlosz 1, Dominika Deborska-Materkowska 1, Marcin Chmielewski 2, Joanna Pazik 1, Magdalena Durlik 1.
leukopenia) and anti-CMV IgM rise or positive ppp65 test. Herpes simplex and varicella-zoster infections were diagnosed by characteristic skin lesions.

Results: Viral infection was diagnosed in 47 out of 112 patients and was connected with higher risk of BK replication (RR=2.33, p<0.038). The highest risk was observed in the case of persistent HBs antigenemia (RR=9.3; p=0.003), herpes simplex infection (RR=3.08; p=0.024) and varicella-zoster virus (RR=2.76; ns).

Conclusions: BK virus replication is linked to other viral infections commonly seen in transplant patients. Whether the relationship is causative has to be determined by further investigations.

PO-411 RENAL TRANSPLANTATION AT RECEPTORS WITH HCV CHRONIC INFECTIONS – SEVEN YEARS EXPERIENCE

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Purpose: The number of the anti-positive HVC pts. who had dialysed is permanently growing, many of them being on waiting lists for transplantation from cadaver donors or from living donors, knowing that survival is superior in the case of renal transplantation than dialysis.

Materials: From 05.1997 to 05.2004 in our dept. were transplanted 68 anti- (+)HVC pts., aged 25 to 69 yrs., from which 31 F and 37 M. All the pts. were HBV, HVC, HIV, CMV & herpes tested. The CMV serology was (+) for all the pts. The pts. were accepted for transplant if they had: normal transaminase during the last year or lack of ARN-HVC in serum and they didn’t have clinical, ultrasound, endoscopic signs of liver cirrhosis. At the beginning, the immuno-suppressive treatment associated Neoral, Imuran/Cept and Prednison all pts. 12 of them changed Neoral for Rapamune because of the chronic allograft nephropathy occurred. 12 pts. received induction: 12 Simulect, 7 Zenapax. None of them was treated with antilymphocytic serum. The mean follow-up interval was about 27 months.

Results: The survival at 1 year was of 96% and 92% for the graft. At 3 years, the survival was 90% and 82% for the graft. There were 19 (32,7%) acute rejections treated with metil-prednisolone. Transitory increase of transaminase was noticed in 20 pts. (29,4%).

Conclusions: The anti-HVC (+) pts. have a graft and a general survival comparable to those from the general lot. The hepatic dysfunction under immunosuppressive treatment is minimum and it doesn’t damage the general results of the renal transplantation.

PO-412 UROLOGICAL COMPLICATIONS FOLLOWING 3638 CONSECUTIVE KIDNEY TRANSPLANTATIONS

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Urological complications are regarded as devastating after kidney transplantation. We evaluated the incidence and contributing factors of urological complications following kidney transplantation during the last two decades. Urological complications, after 3638 (2223 males) consecutive kidney transplants performed at our institution between 1981 and 2004 were retrospectively analysed. The mean age of patients was 51 years (range 1-71). In 5% a living related allograft was used, 10% were retransplantations. A modified Leadbetter-Politano technique was used for the ureteric implantation. The overall incidence of urological complications was 3.5%. In 2% of the patients nephrostomy and antegrade pyelography were performed as uretral stenosis or urine leak were suspected. Urinary leaks and ureteral strictures were found in 1% each. A combined leakage and stricture was found in 0.2% of the cases. Open surgical reconstruction was required in 33% of the cases of strictures or leaks, the rest could be treated with an internal/external stent. A lymphocele necessitating a drainage procedure was found in 1% of all patients, a blood clot in the bladder requiring intervention was encountered 0.5% of the patients. A higher incidence of diabetes, 30% vs. 23% was found in the patients with complications. Episodes of acute rejection were, not over-represented in the complication group. Urological complications did not alter the 5-year patient or graft survival.

Urological complications are unavoidable, but with prompt detection and careful management graft loss can be kept almost negligible. The majority of cases with leaks or renal leaks can be managed by percutaneous stenting techniques, thus reducing the need for surgery.

PO-413 ANGIO-INVASIVE FUNGAL INFECTIONS FOLLOWING RENAL TRANSPLANTATION: A NORTH-INDIAN STUDY

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Fungal infections constitute an increasing challenge in renal transplant recipients who use potent immunosuppressive agents. Reports of 880 renal transplant recipients admitted to this tertiary care hospital in north India, during the period 1977-2002 were studied, for evidence of systemic fungal infections. Eighty-five patients (9.6%), including 76 males and 9 females, with a mean age of 24.2 ± 18.5 yrs. were identified to have systemic fungal infections. The angio-invasive fungi accounted for 39 of 85 infections (46%), aspergillosis-20 and mucormycosis-19. None angio-invasive fungal infections included candidiasis-25, cryptocoecosis-16, phaeohypho-mycosis-3 and histoplasmosis-2. Time of onset of angio-invasive fungal infections was 13.9 ± 13.9 months post transplant. Ante-mortem diagnosis was made only in 36% cases with 73% in case of candida and cryptococcal infections. Assess in these medical conditions identified were cytomegalovirus disease in 35%, chronic allograft dysfunction in 19%, viral hepatitis and neutropenia in 16% each and post-transplant diabetes mellitus in 13% of patients. A comparative analysis of fungal infections seen in patients before 1991, when majorly received azathioprine and prednisolone and those transplanted after 1991, when cyclosporine became an essential part of immuno-suppressive protocol, showed a much higher incidence of angioinvasive infections in the later period. Overall mortality was also higher in these patients, mucormycosis (89%) and aspergillosis (70%) as compared with non-invasive fungi like candidiasis (40%) and cryptococcosis (50%). To conclude angio-invasive fungi constituted 46% of the fungal infections in renal transplant recipients. Their incidence has shown marked increase after 1991 following introduction of cyclosporine with a consequent higher mortality.

PO-414 LYMPHOPROLIFERATIVE DISORDERS AFTER RENAL TRANSPLANTATION: AN ANALYSIS OF 17 PATIENTS

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The risk of lymphoma after renal transplantation is about 20 times greater than in the general population. At our center, where 1500 renal transplants have been performed, 17 patients were diagnosed to have a post transplant lymphoproliferative disorder (PTLD). They constituted 69.7% of all malignancies seen in these patients. The median time interval between transplantation and PTLD was 36 months (range 3m-144m). Of these, 4 had early PTLD (interval <1 year). Fifteen received cyclosporine, azathioprine and prednisolone while two patients received azathioprine and prednisolone only. Four patients presented with fever of unknown origin, 5 had abdominal pain or mass, 2 had headache. Weight loss, pathological fracture, gastrointestinal bleed, hematuria and neck swelling were the initial complaints in one patient each. Multicentric PTLD was observed in 9 patients. Eight patients had PTLD at a single site - lymph nodes (4), brain (1) and abdominal mass (3). Three patients presented only at autopsy. EBV by PCR was negative in 3 patients tested for it, while one had evidence for EBV on autopsy. Polyomypic PTLD was observed in one patient while 13 had monomorphic PTLD and one had multiple myeloma. Two patients had Tcell PTLD.

Eight patients died before treatment. Four patients received chemotherapy, 2 received rituximab, 2 received radiotherapy and one patient underwent surgery. One patient responded to reduction of immunosuppression and is alive 2 years after diagnosis. Among the 8 treated patients, only 2 are alive 2 years after diagnosis.

PO-415 GALLSTONE DISEASE IN KIDNEY TRANSPLANTATION PATIENTS

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Immunosuppressive medication predisposes transplantation (b) patients to the formation of gallstones often causing severe complications.

Purpose: Our purpose was to find out the risk of developing gallstones after kidney transplantation and to chart the complications of gallstone disease.

Materials and Methods: 304 patients, who a functioning kidneys, transplanted between 1990-2000, practically all on cyclosporine-azathioprine-steroids, and
followed (median 7 years) by the Helsinki Nephrological Unit were screened with US for gallstones. Clinical data were gathered from the Finnish Kidney Transplantation Registry.

**Results:** 245 (81%) patients had no gallstones in the US, 31 (10%) had gallstones (in 12 already seen before tx) and 28 (9%) had had cholecystectomy (19 before tx). Patients with a pretx history of gallstones were significantly older than patients without (52.3 vs. 44.2 years, p<0.01). Males had an increased risk of developing posttx anostomes. After tx, non-fatal biliary complications had occurred in 4/12 patients with pretx gallstones and to 1/28 patients with posttx gallstones. No significant difference was found in use of statins, lipid values nor weight gain between the patients without gallstones, patients with pretx and patients with posttx gallstones.

**Conclusion:** The high risk of biliary complications after tx supports the requirement of gallstone screening and cholecystectomy pretx. Males have a higher risk of developing posttx gallstones.

**HIGH EXTRACELLULAR CALCIUM AND LOW MAGNESIUM LEVELS CONTRIBUTE TO TACROLIMUS INDUCED ALLOGRAFT NEPHROTOXICITY: A PILOT STUDY**

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**Purpose:** Animal studies have demonstrated that high concentrations of calcineurin inhibitors (CNI) may cause direct renal tubular toxicity, and this effect was shown in transplant and extracelluar calcium and magnesium levels. Isometric tubular vacuolization and dilatation in renal allograft biopsy frequently may be attributed to CNI toxicity. We hypothesized that high level of serum calcium and hypomagnesaemia play an important role in promoting tacrolimus induced direct tubular toxicity.

**Methods:** We conducted an observational, case control study of patients with elevated creatinine and recent kidney transplant. All patients underwent ultrason sound guided biopsy. We identified 15 consecutive patients who had isometric tubular vacuolization, and 13 patients with elevated creatinine, but without this histological finding. Calcium and magnesium blood levels in the “peribipi” period were compared using nonparametric statistical tests (Mann-Whitney U test).

**Results:** In regards with age, sex and time between the transplant and biopsy, the differences between 2 groups were statistically insignificant. The serum calcium levels (median: 9.7) were significantly higher, and the serum magnesium levels (median:1.6) were significantly lower in patients who had biopsy suspected CNI toxicity, when compared to control patients, who had lower calcium levels (median:8.8) and higher magnesium levels (median:1.9). Exact one sided p for calcium level was p=0.0001, and for magnesium level p=0.0036.

**Conclusion:** Renal transplant patients with histological features of CNI nephrotoxicity tend to have higher calcium and lower magnesium levels, than transplanted patients without tacrolimus induced nephrotoxicity. A reasonable question is whether maintaining lower calcium levels and higher magnesium levels may prevent or ameliorate CNI induced tubular injury and nephrotoxicity.

**KAPOSI’S SARCOMA IN RENAL TRANSPLANT RECIPIENTS**

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Kaposi’s sarcoma (KS) is a relatively common posttransplant malignancy in the Mediterranean countries. In the present study we investigated the frequency, clinical manifestations and outcome of renal transplant patients who developed KS in Croatia.

**Methods:** We have retrospectively evaluated the database and reviewed charts and pathology reports of 584 renal transplant recipients treated at our institution. Clinical presentation, immunosuppressive protocol, treatment and outcome of patients with KS were recorded. We had no possibility to investigate the expression of HHV-8.

**Results:** KS occurred in four male patients (0.68% of all renal transplant recipients) age ranging from 16 to 60 years with the onset of clinical presentation ranging from 6 to 18 months after transplantation (median 6 months). Two patients were of Albanian origin. All patients received triple immunosuppressive treatment with corticosteroids. The disease presented with the purple or bluish papules on the skin and palates without involvement of the visceral organs or lymph nodes. Immunosuppression was ceased in our first patient who rejected graft and underwent transplantation and died after 10 years and the heart failure. Three other patients responded well to reduction of the immunosuppressive therapy and local irradiation therapy. Their grafts function well.

**Conclusion:** KS is not common in Croatian renal transplant recipients. It seems that the combination of ethnic (Albanian origin) and iatrogenic factors played role in development of KS in two of our patients. KS occurred early after transplantation. Our results demonstrated that reduction of immunosuppression should be method of the first choice for patients with the skin-limit disease. Importance of the careful and regular physical examination could not be overemphasized.

**DAILY SODIUM INTAKE REFLECTED BY URINARY SODIUM EXCRETION AND POST-TRANSPLANT HYPERTENSION IN KIDNEY ALLOGRAFT RECIPIENTS**

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**Purpose:** Post-transplant hypertension (post-Tx-HT) is a well known risk factor for long-term allograft failure and mortality in kidney allograft recipients. Although dietary sodium intake seems important for post-Tx-HT, no detailed investigation has been conducted on it. Therefore, we investigated the effect of dietary sodium intake reflected by 24 hours urinary sodium output on post-Tx-HT.

**Methods:** Thirty-two patients with post-Tx-HT were enrolled to the study. They were divided into two groups including standard group (group 1) in which they have previous knowledge of dietary advice and second strict sodium diet group (group 2) in which they were on diet of daily 80-100 mEq sodium. The patients were randomized and 24-hours urine were collected for sodium measurement. Blood pressures and allograft functions were recorded before and after three months.

**Results:** In baseline, there was no significant difference in age, sex, creatinine clearance, systolic and diastolic blood pressures, transplantation duration, antithyphfetic drugs and urines sodium levels between the groups. Between the groups, urines sodium, systolic and diastolic blood pressures were significantly lower after three months in group 2 (p=0.001, p=0.001 and p=0.034, respectively). While 7 of 18 patients needed lower doses of anti-hypertensive treatment in group 2, 3 patients needed higher doses and one lower dose in group 1 (p<0.05).

**Table 1. Parameters after three months in both groups**

| Group 1 (2F/12M) | Group 2 (3F/15M) |
|-----------------|-----------------|
| Before | After | p | Before | After | p |
| Urine Na (mEq/d) | 191±117 | 237±113 | NS | 190±75 | 106±48 | 0.0001 |
| SBP (mmHg) | 140±16 | 132±13 | NS | 146±21 | 116±11 | 0.0001 |
| DBP (mmHg) | 86±7 | 80±9 | NS | 89±9 | 72±10 | 0.0001 |
| C/Cl(m/m) | 62±13 | 58±15 | 0.04 | 56±15 | 63±14 | NS |

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, Cl/Cl: Creatinine Clearance, NS: Not significant, F: Female, M: Male.

**Conclusion:** Twenty-four-hour urine sodium excretion should be checked regularly in post-Tx-HT patients and it seems useful marker whether the patient complies to low sodium intake or not.

**APOTOTIC CELLS IN ACUTE AND CHRONIC REJECTION OF KIDNEY TRANSPLANTS SHOW NUCLEIC ACIDS DAMAGED BY REACTIVE OXYGEN SPECIES (ROS)**

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During acute rejection in kidney transplants the tubulointerstitial is invaded by mononuclear cells and tubular epithelial cells become damaged. Chronic rejection shows transplant vasculopathy and glomerulopathy. In both cases cell death by apoptosis is an important feature. The aim of this study was to examine whether there are nucleic acids, which are damaged by ROS, in apoptotic cells during rejection of kidney transplants and which role they play during the process of apoptosis.

Biopsies of kidney transplants from 6 patients with acute and 7 with chronic rejection were embedded in plastic resin. On semi-thin sections (1μm) of renal cortex DNA-fragmentation was detected by in-situ-end-labelling. Tissue transglutaminase and 8-Hydroxyguanosine which is a marker for damage by ROS on nucleic acids, were determined by immunohistochemistry. Cells showing strong DNA-fragmentation and tissue transglutaminase expression were considered to be apoptotic. Particularly in distal tubules apoptotic cells were seen. In acute rejection also proximal tubular epithelial cells were apoptotic in regions of mononuclear infiltrates. More cells, which were apoptotic and showed damage by ROS, were found in acute interstitial rejection than in chronic rejection, which exhibited more fibrosis and sclerosis. The apoptotic cells showed nuclear (genomic DNA) and cytoplasmatic (RNA) damage by ROS.

In conclusion during acute as well as chronic rejection apoptotic cells are damaged by ROS which may be produced during apoptosis itself as well as be a consequence of cell damaging impacts. A possible cause for the oxidative damage might be the infiltration of mononuclear cells and ischemia by tubulo-lentenial oedema.
**PO-420**

**RELATIONSHIP BETWEEN SERUM CYSTATIN C, DECREASED HYPERHOMOCYSTEINAEMIA AND CYSTATIN C LEVELS (p pts and connection negative correlation the cystatin C and homocysteine levels.**

In kidney transplanted and uraemic patients there is an increased risk of atherosclerosis, increased lipoprotein oxidation. The serum paraoxonase (PON) is a HDL associated hydroxylase, which inhibits LDL oxidation.Aims our study determined serum paraoxonase activity, phenotype and dyslipidaemia with relationship cystatin C, homocysteine levels are renal transplanted, dialysed pts compare the values with healthy controls. 110 healthy controls, 115 renal transplanted (43.5±6.9 years) and 112 haemodialysed pts (61.3±8.1 years) also in study. The PON activity determined spectrophotometry (412nm). In kidney transplanted pts the concentrations of PON activity were higher than in dialysed pts. (121,10±7.86 vs. 87.35±5.72 U/L, p < 0.01). In transplanted pts have high total and LDL cholesterol, and ApoB levels. The hyperhomocysteinaemia were the highest in dialysed pts (25.52±6.71 umol/l - p <0.01) and the values of transplantated (15,46±5.02 umol/l). The paraoxonase activity, homocysteine and cystatin C concentrations have negative correlation in transplanted and homocysteine levels.

After kidney transplantation significantly increased paraoxonase activity and decreased hyperhomocysteinaemia and cystatin C levels (p < 0.01). In dyslipidaemic transplanted pts the ratio low of PON/HDL and PON/ApoAl may lead decreased antioxidant capacity of HDL than in healthy controls.

**Method:** We measured: ROS, TAOC, free and total MDA (f-MDA) in 22 siroimol treated pts (cystatin C 1.2±0.2 mg/dl, age 49±9.9 years) compared to 19 CRF pts (cystatin C 3.5±1.2 mg/dl, age 67±16 years) and 30 controls (C) (age 59±9 years).

Results: ROS were significantly higher in Tx than in CRF and in both groups when compared to C. TAOC was higher in Tx than in CRF and CRF pts had lower TAOC than C; all these differences being statistically significant. 1-MDA was significantly higher in Tx and CRF when compared to controls. 1-MDA concentrations of CRF were significantly higher than Tx. 1-MDA was within the normal range in all the groups. Age and sex did not correlated with 1-MDA/TAOC ratio between groups (1).

Table 1. Mean and SD of the measured variables

|            | ROS     | TAOC    | 1-MDA (umol/L) | 2-MDA (umol/L) |
|------------|---------|---------|----------------|----------------|
| Tx (22)    | 388.4±75.3* | 431.6±81.1* | 0.5±0.2        | 5.5±1.3        |
| CRF (19)   | 336.7±61.4* | 362.7±45.7*  | 0.5±0.3        | 6.9±1.5*       |
| C (30)     | 287.5±58.9* | 383.2±24.1*  | 0.4±0.1        | 1.7±0.4*       |

* p<0.01, ** p<0.001, *** p<0.0001, § p=0.005, # p=0.003, # p=0.003, † p<0.004

**Conclusion:** Different degrees of impaired kidney function seem to sustain lipid peroxidation. CRF pts show higher ROS without proportional TAOC increase. Normal renal function after Tx seems to improve the OS reducing 1-MDA but determining a less dramatic effect on ROS production counterebalanced by an increased TAOC.

**PO-421**

**COMPARATIVE MEASUREMENTS BETWEEN THE HVC-VARRIER AND VIRUS-FREE SEROPOSITIVE PATIENTS**

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Renal transplant have a higher prevalence of HCV infection.

**Aim:** To compare the free radical-antioxidant balance and the biochemical parameters in the cases of HCV carrier and non-infected seropositive renal recipients.

**Method:** HCV-PCR (Polymerase Chain Reaction;Roche), total antioxidant status (TAS,Randox), Glutathion-S-transferase alpha (GST-a;Biotrin), Myeloperoxidase (MPO,Randox) and the traditional liver enzymes measurements were done in 756 anti-HCV positive patients.

Results: 74% of the seropositive patients had active C viruses proved by PCR technique. In the case of virusaemia decreased MPO level (179±110 mg/ml) was measured compared to the virus-free patients' MPO concentration (289±131 mg/ml). The patients had significantly decreased TAS level compared to healthy controls (1,22±0,1 mmol/l - p<0,05), but it did not differ between the virus carriers (0,9±0,16) and non infected group (0,8±0,27). The GST-a concentration was significantly higher (6,9±6,1 mg/l) in the HCV-PCR+ patients compared to PCR(-) group (2,4±1,9 mg/l). However, the traditional liver enzymes did not differ between the two groups.

Conclusion: We suppose that increased autoantibody creation could be present in the virus carriers, because of the decreases MPO level. The virus caused small liver damage that if any- can only be predicted by the sensitive GST, due to the fact that the traditional liver-function parameters are normal in both groups. The total antioxidant capacity does not weaken in the infected group compared to the non-infected recipients. We did not find differences in generally measured laboratory parameters at all seropositive patients, because these PCR+ recipients are only virus carriers, however they are infectious. This can be only proved by PCR technique.

**PO-422**

**OXIDATIVE STRESS IN UREMIC AND SIROIMOL TREATED KIDNEY TRANSPLANTED PATIENTS**

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**Purpose:** Malondialdehyde (MDA), Reactive Oxygen Species (ROS) and Total Antioxidant Capacity (TAOC) indicate the oxidative status (OS): involved in accelerated atherosclerosis of chronic renal failure (CRF) or kidney transplantation patients (Tx, pts). Data on free-MDA (f-DA) chemically active, are controversial.

Methods: We measured: ROS, TAOC, free and total MDA (t-MDA) in 22 siroimol treated Tx pts (cystatin C 1.2±0.2 mg/dl, age 49±9.9 years) compared with 19 CRF pts (cystatin C 3.5±1.2 mg/dl, age 67±16 years) and 30 controls (C) (age 59±9 years).

Results: ROS were significantly higher in Tx than in CRF and in both groups when compared to C. TAOC was higher in Tx than in CRF and CRF pts had lower TAOC than C; all these differences being statistically significant. MDA was significantly higher in Tx and CRF when compared to controls. MDA concentrations of CRF were significantly higher than Tx. MDA was within the normal range in all the groups. Age and sex did not correlated with MDA/TAOC ratio between groups (1).

Table 1. Mean and SD of the measured variables

|            | ROS     | TAOC    | 1-MDA (umol/L) | 2-MDA (umol/L) |
|------------|---------|---------|----------------|----------------|
| Tx (22)    | 388.4±75.3* | 431.6±81.1* | 0.5±0.2        | 5.5±1.3        |
| CRF (19)   | 336.7±61.4* | 362.7±45.7*  | 0.5±0.3        | 6.9±1.5*       |
| C (30)     | 287.5±58.9* | 383.2±24.1*  | 0.4±0.1        | 1.7±0.4*       |

* p<0.01, ** p<0.001, *** p<0.0001, § p=0.005, # p=0.003, † p<0.004

**Conclusion:** Different degrees of impaired kidney function seem to sustain lipid peroxidation. CRF pts show higher ROS without proportional TAOC increase. Normal renal function after Tx seems to improve the OS reducing 1-MDA but determining a less dramatic effect on ROS production counterebalanced by an increased TAOC.

**PO-424**

**COST-EFFECTIVENESS OF A COMBINED IMMUNOSUPPRESSIVE/ANTI-VIRAL REGIMEN IN KIDNEY TRANSPLANTATION**

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**Background:** Medical prescription after kidney transplantation must prevent both rejection and infectious complications. We assessed the cost-effectiveness of a new combined drug regimen.

**Patients and methods:** Patients transplanted from 1/2000 to 3/2003 (period 1), receiving basiliximab, tacrolimus and steroids +/- mycophenolate, were compared to patients transplanted between 4/2003 and 7/2004 (period 2), receiving basiliximab, tacrolimus, mycophenolate and steroids. Anti-viral strategy was preemptive in period 1, and prophylactic with valganciclovir in period 2. Complications over the first 6 months were retrieved from medical charts. Costs were computed using 2003 data for the hospital stay (CHF 400/day).
TREATMENT OF CMV INFECTION OR DISEASE IN SOLID ORGANS TRANSPLANT PATIENTS WITH VALGANCICLOVIR

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Background: Valganciclovir (VGC) has proved successful for the prophylaxis against Cytomegalovirus (CMV) in high risk transplant recipients. We have recently used VGC for the treatment of CMV in transplant recipients.

Methods: 15 transplant recipients (11 kidney, 2 heart, 3 lung) were treated between 6 to 26 weeks after transplantation. CMV serostatus was D+/R+ (n=11), D+/R- (n=3), and D-/R+ (n=1). Three patients had received valaciclovir and 8 patients VGC prophylaxis during 3 months after transplantation. Six patients were treated for CMV infection and 9 for CMV disease (retnitis n=1, gastrointestinal n=3, pneumonia n=1, CMV syndrome n=4). VGC was administered for 2 to 3 weeks (900 - 1800 mg per day, adjusted to the renal function) followed by 2 to 4 weeks of secondary prophylaxis (450 - 900 mg per day). Viral load monitoring was performed initially using a quantitative rapid culture, and more recently a quantitative real time PCR assay.

Results: Clinically, all 9 symptomatic patients responded to treatment. Virologically, VGC turned blood culture negative for CMV within 2 weeks in all patients, and was associated with a ≥2 log decrease in blood CMV DNA within 3 weeks in 9/9 tested patients. With a follow-up of 6 months, asymptomatic recurrent CMV was noted in 6 cases, and CMV syndrome in one case. VGC was clinically well tolerated in all patients. Laboratory abnormalities were observed in 3 patients: increase in transaminases, thrombocytopenia and pancytopenia (1 each), all 3 reversible after VGC dose reduction.

Conclusion: Our experiences suggest that VGC is safe and effective to treat CMV in organ transplant recipients.

IMPACT OF EARLY-LOW GRADE PROTEINURIA ON LONG-TERM GRAFT SURVIVAL

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Purpose: Persistent massive proteinuria 1 year after transplantation is recognized as a risk factor for graft loss. However, whether earlier low-grade (<1 g/day) proteinuria and its change within the first year after transplantation also constitute risk factors is unknown.

Methods: 484 consecutive renal allograft recipients treated with the same immunosuppressive regimen. The patients had a thorough evaluation at 3 and 12 months after transplantation, and were followed up in our institution; the median follow-up period was 7.2 years (range: 0.4 to 15.4 years).

Results: Mean recipient age was 44±1.3±6.6 (24% male, 98.3% Caucasians). Creatinine combined with azathoprine (56.6%) or with MMF (23.4%) was preferentially used. At 3 months, creatinine was 136±65 µmol/l, and proteinuria was present in 35.2% (87.4% of these patients had low-grade proteinuria. Early low-grade proteinuria constituted a strong independent predictor of long-term graft survival. Early low-grade proteinuria was present in 35.2% (87.4%, of these patients had low-grade proteinuria.

Conclusion: Early low-grade proteinuria was an independent risk factor for long-term graft loss. Better short-term arterial pressure control lead to reduction in proteinuria and is associated improved long-term graft survival.
Results: Mean recipient age was 44.4 ± 2.6 years, Mean recipient creatinine was 1.88 ± 1.28 mg/dl. All patients received cyclosporin (CsA) or tacrolimus (Tac) based immunosuppression underwent a 40% dose reduction of their calcineurin inhibitor and were then randomised to receive either AZA (1 mg/kg/day) or MMF (1g bd). Renal allograft function was assessed by isotope GFR measurements. Allograft fibrosis was measured by computerised histomorphometry of protocol needle core biopsies performed at trial entry and 6 months later. Results: 21 patients receiving cyclosporin (AZA 11, MMF 10) and 22 patients receiving tacrolimus (AZA 10, MMF 12) were recruited into the study. All groups were well matched for potentially confounding variables. The pre-trial decline in GFR was reversed in both tac and MMF groups.Effect of the short-term change in systolic arterial pressure on long-term graft loss:

Univariate analysis: CGFR slope:
- Adjustment on initial arterial pressure (AP): 0.78 ± 0.66 NS
- Adjustment on initial AP and proteinuria: 0.79 ± 0.67 NS
- Adjustment on initial AP, proteinuria and creatinine: 0.81 ± 0.69 NS

HR 95% CI P value

| Glomerulosclerosis | 0.85 | 0.74-0.99 | 0.03 |
|--------------------|------|-----------|------|
| Interstitial fibrosis | 0.81 | 0.72-0.92 | 0.007 |
| Hydropplasia | 0.81 | 0.68-0.95 | 0.01 |

Conclusions: Early elevated systolic and pulse arterial pressures are risk factors for long-term graft loss. Better arterial pressure control within the first year after transplantation improves long-term graft survival.

PO-430 EFFICACY OF ERYTHROPOIETIN THERAPY IN THE TREATMENT OF ANAEMIA OF THE KIDNEY TRANSPLANT PATIENTS

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Anaemia has negative impact on the cardiovascular morbidity and mortality of kidney transplanted patients. The therapy with recombinant human erythropoietin (RhuEPO) can correct anaemia and improve renal function after transplantation. We evaluated the effectiveness and safety of RhuEPO treatment in kidney transplanted patients.

Out of 1230 adult, kidney transplanted patients followed up at our department 150 were treated with EPO. In a retrospective study we analysed the results of those patients who received Epoetin beta for the minimum of 4 weeks. We evaluated serum haemoglobin (Hb)(g/L), serum creatinine (µmol/L) and the dose of EPO (IU/kg/week) after 12 weeks loading dose and 12 weeks maintenance treatment. The data of iron supplementation were also evaluated.

34 patients received subcutaneous EPO treatment. Average age: 46.6 ± 2.5 years, time elapsed since transplantation was 71.4 months. 82% of patients received calcineurin inhibitor based immunosuppressive therapy, in 68% combined with Mycophenolate mofetil (MMF).

Baseline data: Hb: 106.67 ± 1.56, se creatinine: 190 ± 12.8
24 weeks: Hb: 118.27 ± 1.81, se creatinine: 186 ± 12.8

The EPO dose was 75,47 ± 15.2 at 0-12 weeks, 70.57 ± 1.15 at 12-24 weeks, the difference is not significant. The Hb levels were significantly higher at 12 weeks and 24 weeks, than at the beginning of the therapy (p < 0.00001). The Hb values at 12 and 24 weeks did not show significant difference (p = 0.206). 82.35% of the patients received oral iron supplementation. No side effects were observed, the graft function remained stable.

Conclusion: The RhuEPO is effective and safe in the treatment of the anaemia of kidney transplanted patients.

PO-431 THE EFFECT OF EXTENDED RELEASE FLUVASTATIN TREATMENT ON HYPERLIPIDAEMIA IN KIDNEY TRANSPLANT PATIENTS

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The posttransplantation dyslipidaemia is a well known risk factor in the development of cardiovascular disease (CV). The CV incidence is 6-8 times higher in organ transplanted patients.

Case 1: a 35-year-old OLT man presented on post-op day 19 with fever(39°C), palmo-plantar as well as mucous vesicle lesions that contained HSV2. This was associated with an increase in alanine aminotransferase (ALT)x10 and g-glutamyl transpeptidase(x5) levels. Liver histology found HSV2-related lesions. The pre-op HSV serology was positive. He was treated with IV ACV for 1 month, and recovered without sequelae.

Case 2: a 58-year-old OLT man presented on post-op day 12 with fever(39°C), disseminated skin and mucous vesicles containing HSV2. In addition, ALT had increased 50-fold. Liver histology found HSV2-related hepatitis. This was a primary HSV2 infection. He completely recovered within 20 days with IV ACV (2 weeks), and hyperimmune IV globulins.

Summary: 12 weeks Fluvastatin ER treatment significantly lowered the TC and LDL levels, lowered the TG levels and improved the TC/HDL ratio. No side effects or drug interactions were observed. Fluvastatin ER can be used safely in kidney transplanted patients.

PO-432 A PROSPECTIVE RANDOMISED TRIAL OF MYCOPHENOLATE MOFETIL AND AZATHIOPRINE AFTER CALCINEURIN REDUCTION IN RENAL ALLOGRAFTS WITH ESTABLISHED CHRONIC ALLOGRAFT NEPHROPATHY

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Purpose: This trial investigated the effects of calcineurin dose reduction plus the introduction of a non-nephrotoxic immunosuppressive agent, azathioprine (AZA) or mycophenolate mofetil (MMF), in renal allograft recipients with established chronic allograft nephropathy (CAN).

Methods: Patients with biopsy proven CAN and receiving cyclosporin (CsA) or tacrolimus (Tac) based immunosuppression underwent a 40% dose reduction of their calcineurin inhibitor and were then randomised to receive either AZA (1 mg/kg/day) or MMF (1g bd). Renal allograft function was assessed by isotope GFR measurements. Allograft fibrosis was measured by computerised histomorphometry of protocol needle core biopsies performed at trial entry and 6 months later.

Results: 21 patients receiving cyclosporin (AZA 11, MMF 10) and 22 patients receiving tacrolimus (AZA 10, MMF 12) were recruited into the study. All groups were well matched for potentially confounding variables. The pre-trial decline in GFR was reversed in both Tac and MMF groups. Compared to CsA + MMF group but not with CsA + AZA. Renal allograft fibrosis increased during the 6 months in the patients treated with CsA + MMF but remained stable in the other groups.

Conclusions: Tac reduction plus either MMF or AZA improved renal function without changing established allograft fibrosis. For patients receiving CsA, dose reduction plus MMF improved renal function despite significant worsening of allograft fibrosis, whilst AZA did not have this effect.

PO-433 DISSEMINATED AND SEVERE HERPES SIMPLEX TYPE-2 (HSV2) INFECTION IN ORGAN-TRANSPLANT PATIENTS

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We report on three cases of severe disseminated HSV2 infection associated with DNAemia that occurred in two orthotopic liver-transplant (OLT) and one renal-transplant patients. In OLT patients, this was associated with HSV2-related acute hepatitis. The rapid onset of IV acyclovir (ACV) therapy led to a rapid recovery.

Case 1: a 35-year-old OLT man presented on post-op day 19 with fever(39°C), palmoplantar as well as mucous vesicle lesions that contained HSV2. Treatment with IV ACV for 1 month, and recovered without sequelae.

Case 2: a 58-year-old OLT man presented on post-op day 12 with fever(39°C), disseminated skin and mucous vesicles containing HSV2. Liver histology found HSV2-related lesions. This was a primary HSV2 infection. He completely recovered within 20 days with IV ACV (2 weeks), and hyperimmune IV globulins.

Case 3: a 55-year-old woman presented, at 9 years after renal transplantation, and 5 months after Rituximab therapy (which was given for cryoglobulin-associated nephropathy) with fever(39.5°C), diffuse skin and mucous vesicles containing HSV2. In addition, ALT had increased 50-fold. Liver histology found HSV2-related hepatitis. This was a primary HSV2 infection. He completely recovered within 20 days with IV ACV (2 weeks), and hyperimmune IV globulins.

Conclusions: High fever (39.5°C), diffuse skin and mucous vesicles containing HSV2. In addition, ALT had increased 50-fold. Liver histology found HSV2-related hepatitis. This was a primary HSV2 infection. He completely recovered within 20 days with IV ACV (2 weeks), and hyperimmune IV globulins.

Diffuse skin and mucous vesicles containing HSV2. In addition, ALT had increased 50-fold. Liver histology found HSV2-related hepatitis. This was a primary HSV2 infection. He completely recovered within 20 days with IV ACV (2 weeks), and hyperimmune IV globulins.
containing HSV2. This was associated with an interstitial pneumonitis, a dramatic increase in serum creatinine, and pancytopenia. HSV2 was found in lungs and bone marrow. The pre-op HSV serology was positive. She was successfully treated with 3 weeks of IV ACV. Although rare, HSV2-disease in Africa after organ transplantation might be life-threatening, but can be cured if ACV therapy is initiated early in the course of the disease.

**PO-434 RECURRENT GLOMERULAR DISEASES AFTER RENAL TRANSPLANTATION**

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**Purpose:** Recurrent glomerular diseases are important causes of graft dysfunction after renal transplantation.

**Methods:** From October 1985 to March 2004, 1152 renal transplants were performed at the Baskent University School of Medicine. Forty-nine patients with glomerular diseases including membranoproliferative glomerulonephritis (MPGN) (n: 26); focal segmental glomerulosclerosis (FSGS) (n: 18), and systemic lupus erythematosus (SLE) (n: 5) are retrospectively analyzed.

**Results:** The mean follow-up period was 9.5 years. Recurrence of the disease occurred in all of the 6 patients with HLA haplotype B8, and mean graft survival was 79.4 (range between 15 and 158) months in this group (p<0.05). One patient with FSGS, had disease recurrence in her third transplant after having experienced recurrences in the former grafts. Patient characteristics, donor source and cold ischemia times in cadaveric grafts were similar in both groups. In all of the 6 patients with HLA haplotype B8, recurrence was observed at a mean of 19.5±1.9 months.

**Conclusion:** The only risk factor that was identified was this HLA haplotype. Recurrent disease is a significant problem after renal transplantation and is associated with decreased graft survival.

**PO-435 CHALLENGES IN RENAL TRANSPLANTATION – A SINGLE CENTER EXPERIENCE**

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**Purpose:** Study evaluate the living donor nephrectomy, complications, evolution and long-term results after surgery and assess if abnormal renal vascular anatomy represented a problem in performing transplantation.

**Material and Methods:** From 06.1997-12.2004, 522 renal transplantsations (446 living and 76 cadaver donor) have been performed in our center, with an average of 70/year, rising to 107 in 2004. From 446 living donors were 216 left (446 living and 76 cadaver donor) have been performed in our center, with an average of 70/year, rising to 107 in 2004. From 446 living donors were 216 left.

**Results:** No major complications in 446 nephrectomies. Minor complic.: minor bleeding 4.7%, renal art. spasm 7.8%, only 1 case - blood transfusion and average blood loss was 165 ml. Other complic.: minor resp. complic. 2.2%, pneumothorax 1.7%, postop. ileus 1.3%, bladder voiding probl. 2.6%, UTI 1.5%. All complic. solved before discharging. Long-term complic.: persistent wound pain 1.3%, parasthesia 1.1%, wound hernia 0.6%. GOL was assessed on 92 cases using the SF 36 Health Survey Test and it was normal. For arterial anastomosis special techniques were used.

**Conclusions:** The preop. general evaluation, immunological and renal pedi- cule evaluation is a must. In order to increase transplants number we accept the borderline vasc. living donor. The living donor nephrectomy respected in our center the international accepted mortility. No major complic. appeared. Mortality was 0. Different vasc. anatomy of renal pedicle found in 33% did not stumble the renal transplantation.

**PO-436 INFLUENCE OF COLD ISCHEMIA TIME AND HLA MATCHING ON EARLY AND DISTANT FUNCTION OF THE TRANSPANTED KIDNEY**

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**Results:** From October 1985 to March 2004, 1152 renal transplants were performed at the Baskent University School of Medicine. Forty-nine patients with glomerular diseases including membranoproliferative glomerulonephritis (MPGN) (n: 26); focal segmental glomerulosclerosis (FSGS) (n: 18), and systemic lupus erythematosus (SLE) (n: 5) are retrospectively analyzed.

**Methods:** The mean follow-up period was 9.5 years. Recurrence of the disease was detected in 30 of the 49 patients after a mean post transplant follow-up pe- riod of 28.1 months (range between 1 and 157) and the average graft survival in this group was 41.3 months. The diagnosis of the recurrent disease was made by renal biopsies in all patients. Nineteen patients were recurrence free and mean graft survival was 79.4 (range between 15 and 158) months in this group (p<0.05). One patient with FSGS, had disease recurrence in her third transplant after having experienced recurrences in the former grafts. Patient characteristics, donor source and cold ischemia times in cadaveric grafts were similar in both groups. In all of the 6 patients with HLA haplotype B8, recurrence was observed at a mean of 19.5±1.9 months.

**Conclusion:** The only risk factor that was identified was this HLA haplotype. Recurrent disease is a significant problem after renal transplantation and is associated with decreased graft survival.

**PO-437 EXCELLENT GRAFT FUNCTION IN KIDNEY TRANSPLANT RECIPIENTS TREATED WITH EVEROLIMUS, LOW-CSA AND BASILIXIMAB AT 24 MONTHS**

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**Body:** Endpoints for an extension of a trial of the proliferation signal inhibitor everolimus (Ceritan®, E) in conjunction with low-dose CsA (Neoral®) corti- costeroids and basiliximab (Simulect®) were assessed at 24M.

**Methods:** 256 patients randomized to either E 1.5mg/day (N=117) or 3 mg/day (N=139) completed an open label 1 year trial. 203 pts. were enrolled into a 2nd yr extension. CsA C2-targets (ng/mL) were 500-700 (week 0-8) and 350-450 (after week 8). E target blood trough levels were ≥3 ng/mL.

**Results:** Overall 68.8% patients completed 24 M. Occurrence of efficacy fail- ure (combined BPAR, graft loss, death or loss to follow-up) at 24M was 20% and 25% (p=NS) in the ITT population for the 1.5 and 3 mg dose, respectively. Efficacy failure was lower for the extension patient population and was compa- rable between E 1.5 mg and 3 mg groups (12% and 17%, p=NS), as was the incidence of BPAR (12% and 14%, p=NS). Renal function and CMV infection were comparable between both arms. Lipids were stable through 24M in both arms.

**Conclusions:** E in conjunction with low-dose CsA and basiliximab maintained good efficacy and renal function at 24M. Better patient and graft survival were achieved with 1.5mg Everolimus.

**PO-438 IS RENAL TRANSPLANTATION LONG TERM OUTCOME RELATED TO THE DISTANCE BETWEEN HOME AND THE TRANSPLANTATION CENTER?**

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Since the number of cadaveric organs in some Italian regions is still not suf- ficient to supply the large request for renal transplantations, many kidney re- cipients need to move to distant transplant centers. Aim of our study was to describe the possible effects of long distances on outcomes.

**Methods:** In the period May 2000 – Jun 2004, 155 adult renal transplanted patients were examined for four parameters: patient and graft survival, re- nal function and number of BPAR. Grafts and patients lost within the first 30 days post-transplant were excluded. Distance from the transplantation center was analyzed in two groups: 0 to 300 Km (50 patients) and > 300 Km (105 patients).
patients). There were no statistically significant differences in the baseline characteristics of the two groups.

**Results:** We didn’t find any significant difference in 1-year and 3-year patient survival (group A: 98.0% vs 93.3%; group B: 95.0% vs 89.3%; p=0.01) and 1-year and 3-year graft survival (group A: 96.0% vs 91.4%; group B 86.3 vs 78.9%; p=0.07). The number of patients who experienced one or more episodes of BPAR was comparable (group A: 17/50 - 34%; group B 44/105 - 41.4%; p=0.5).

**Conclusion:** In our experience the management of the large number of patients coming from long distances is successful, with neither statistically significant differences in patient and graft survival, nor in renal function or number of BPAR.

**PO-439 PERIOPERATIVE ACUTE LUNG INJURY IN RENAL TRANSPLANT RECIPIENTS IS NOT A HYDROSTATIC PULMONARY EDEMA**

Zoran Vukcevic, Jonathan Hakim, Amit Basu, Henkie Tan, Akhtar Khan, Ron Shapiro, Amadeo Marcos, Thomas E. Starzl Transplantation Institute, University of Pittsburgh Medical Center, Pittsburgh, PA, USA.

**Purpose:** Volume status of the recipient during renal transplantation is a predictor of initial graft function. Although these patients are frequently volume contracted, intraoperative dialysis, NPO, haemodilution and reoxygenation are necessary. We hypothesized that haemodynamic parameters were more important factors currently under investigation.

**Materials:** Intraoperative i.v. fluids in renal transplant recipients are not re-identifiable.

**Results:** Med: paO2/FiO2 at the onset of transplant was 375, and at the end 253. Wilcoxon signed-rank test confirmed that studied patients did experience a significant deterioration in pulmonary oxygen transfer during the transplant procedure (mean paO2/FiO2 drop was 131.5, with z=4.74 and 1-tail p<0.001). Computation of Spearman rank-order correlation coefficient did not show that this intraoperative pulmonary injury was caused neither with total volume (mL/kg) of i.v. fluids infused: rs=0.03, 1-tail p=0.43, nor rapidly of fluid infusion (mL/kg/hour), for each patient. Rank order correlation statistics were used to test the relationship between intraoperative i.v. fluids and pulmonary oxygen transfer.

**Conclusion:** Intraoperative i.v. fluids in renal transplant recipients are not responsible for pulmonary dysfunction. More liberal intraoperative fluid therapy is safe for respiratory system and may be good for initial allograft function.

**PO-440 TOTAL PARATHYROIDECTOMY IN RENAL TRANSPLANT RECIPIENTS AND DIALYSIS PATIENTS FOR THE TREATMENT OF RESISTANT SECONDARY HYPERPARATHYROIDISM**

Spiros Drakopoulos, Maria Koukoula1, Vasilios Vougas, Dimitrios Pistolas, Katerina Balaska1, Theofanis Apostolou1, Valsamakis Hadjiconstantinou1, Olga Paniani2, Spiros Drakopoulos1.

**Introduction:** In this retrospective study, 277 ESRD patients evaluated treated received kidney transplant between 05/01/2004 and 08/31/2004. Pulmonary oxygen transfer indices (paO2/FIO2) were recorded for each patient at the beginning and at the end of the transplant procedure. Intraoperative fluids (cristaloids and colloids) administered during the operation were recorded as mL/kg and mL/kg/hour, for each patient. Rank order correlation statistics were used to test the relationship between intraoperative i.v. fluids and pulmonary oxygen transfer.

**Methods:** We identified 5 with viral load above 10^4 copies/ml, while viral load of 17 samples was low, median 295/ml. Quantification of positive urine samples identified 5 with viral load > 10^4/ml (median 9.9 x 10^4/ml, 5.5 x 10^4 – 9.2 x 10^4/ml). 23 urine samples had viral load < 10^4/ml, median 310/ml. Patients with high viral load in urine were also positive for BK in plasma. The distribution of positive samples has shown peak of viraemia three months postoperatively and decrease of positivity six months as shown in table 1.

**Conclusion:** Tendency to progressive disappearance of BK positivity was observed both in plasma and urine which may be attributable to reduction of immunosuppression and especially the decrease of corticosteroids, or other factors currently under investigation.

**PO-441 MONITORING OF BK POLYOMA VIRUS IN RENAL TRANSPLANT RECIPIENTS. PRELIMINARY RESULTS OF A PROSPECTIVE STUDY**

Maria Koukoula1, Ugrum Grispsi2, Dimitrios Pistolas1, Katerina Balaska1, Theofanis Apostolou1, Maria Anagnostopoulou2, Valsamakis Hadjiconstantinou1, Olga Paniani2, Spiros Drakopoulos1.

**Materials:** 24 de novo renal transplant recipients, median age 50 years, were studied for median period 25 weeks. Plasma and urine samples were collected at three monthly intervals and examined for BKV with real-time PCR. 182 samples were examined (91 plasma, 91 urine).

**Results:** BKV was detected in 18 (19.8%) plasma and 28 (30.8%) urine samples in 13 and 16 patients respectively. Quantification of positive plasma samples showed 1 patient with viral load above 10^4 copies/ml, while viral load of 17 samples was low, median 295/ml. Quantification of positive urine samples identified 5 with viral load > 10^4/ml (median 9.9 x 10^4/ml, 5.5 x 10^4 – 9.2 x 10^4/ml). 23 urine samples had viral load < 10^4/ml, median 310/ml. Patients with high viral load in urine were also positive for BK in plasma. The number of patients who experienced one or more episodes of BPAR was comparable (group A: 17/50 - 34%; group B 44/105 - 41.4%; p=0.5).

**Conclusion:** To evaluate prospectively the presence of BK polyoma virus (BKV) in renal transplant recipients.

**PO-442 ANAESTHESIA MANAGEMENT FOR RENAL TRANSPLANTATION-A REVIEW OF 277 PATIENTS**

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**Introduction:** In this retrospective study, 277 ESRD patients evaluated treated underwent renal transplantation performed at the Akdeniz University Faculty of Medicine, from January 2000 to May 2003 was carried out.

**Results:** Average age and weight were 34.2 years (range: 7-66 years) and 61.9 kg (range:17-98 kg), respectively. Sixty five patients were recipients of cadaveric transplants, 112 patients received kidneys from living related donors. Few patients presented with severe anaemia (five patients) and gross electrolyte abnormalities (seven patients). Hypertension was the most common primary cause of ESRD in our patients (25%). Diabetic nephropathy was the second most common primary cause (17%). Thirty patients had over hydration and 9 patients had dysrhythmia preoperatively. Twenty-four patients received...
blood transfusions intraoperatively. Two hundred fifty one patients received furosemide and 122 patients received mannitol before reperfusion. No per operative mortality or major morbidity was recorded.

**Conclusion:** Anaesthesia for renal transplantation is safe and effective using a selected range of drugs and techniques. Pretransplant medical optimization, careful preoperative assessment, adequate monitoring and precise fluid management together with appropriate postoperative analgesia typify the per operative care of renal transplant recipients.

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**PO-443**

**RECOMBINANT HUMAN GRANULOCYTE COLONY-STIMULATING FACTOR EFFECTIVELY INCREASES THE WHITE BLOOD CELL COUNT IN LEUKOPENIC RENAL TRANSPLANT RECIPIENT WITHOUT INCREASING THE INCIDENCE OF REJECTION**

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**Background:** Leukopenia is a common adverse effect of immunosuppressive drugs and increases the risk of infection in organ-transplant patients. Recombinant-human-granulocyte-colony-stimulating-factor(rh-G-CSF) is widely used in leukopenic patients. However some data suggested that it increases the incidence of acute rejection.

**Objective:** To evaluate the safety and efficacy of rh-G-CSF in leukopenic renal-transplant patients.

**Material and methods:** From January 1, 2002-December 31, 2004, 264 kidney transplantations were performed. The induction was either with Anti-Thymocyte-Globulin(ATG) or with basiliximab. Maintenance immunosuppression utilized Rapamycin(Rapa), Cyclosporine(CSA) and early withdrawal of corticosteroids. Mild rejection was treated with corticosteroids, moderate and severe rejection with ATG. 37 episodes of severe leukopenia (WBC<2000/mm³) developed in 26 patients, who were treated by rhG-CSF. The cause and duration of leukopenia, white blood cell counts(WBC) before and after treatment, occurrence of infection and incidence of rejection was determined.

**Results:** ATG(group1) induced leukopenia occurred 20 and Rapamycin with Cyclosporine(group2) in 17 patients. The WBC counts after rhG-CSF-treatment was significantly higher, the duration of leukopenia shorter and the cumulative dose of rh-G-CSF less in group1 than in group2 (p<0.05). One infection occurred in group1 and six in group2. No rejection episode was observed during rhG-CSF treatment or within 1 month post therapy.

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**PO-444**

**LIVER CELL APOTOSIS AND PROLIFERATION IN HCV INFECTED RENAL TRANSPLANT PATIENTS**

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**Purpose:** Hepatocellular apoptosis and proliferation activity (PA) were assessed in liver biopsies of RT patients with HCV infection and were correlated with necroinflammatory activity (grade and stage), disease outcome, viremia and genotype.

**Methods:** Ninety liver biopsies including 31 follow up biopsies were examined. DNA fragmentation was detected by TUNEL assay and PA by immunohistochemical ki67 expression. Apoptotic index (AI) and PA were defined by the chemical ki67 expression. Apoptotic index (AI) and PA were defined by the chemical ki67 expression. Apoptotic index (AI) and PA were defined by the chemical ki67 expression. Apoptotic index (AI) and PA were defined by the chemical ki67 expression. Apoptotic index (AI) and PA were defined by the chemical ki67 expression.

**Results:** Histological evaluation revealed no significant changes in 8 (13,6%), acute hepatitis in 2 (3,4%) and chronic hepatitis in 49 (83%) cases. A low apoptotic index (AI) (0-2,5) was observed in 31 (52, 5%) and a high (>5) in 12 (20,3%) cases. There was no PA in 22 (37,9%) cases whereas it was >1,35 in 17 (29,3%). AI showed a significant correlation with viral load, resulting in 1 log10 higher HCV RNA levels in those patients with high number of apoptotic cells (p=0,003). This finding was verified by multivariate analysis (OR=6,67, 95% CI 1,14-39,9, p<0,03). Both a significant correlation with hepatitis grade and stage, disease progression and genotype, whereas a significant positive correlation was observed between AI and PA (p=0,03).

**Conclusion:** Apoptotic cell death seems to be pathogenetically associated with high viral load probably through a direct cytopathic pathway. The low PA points towards a suppressed liver cell proliferation which may be linked to viral effects and/or the immunosuppressive therapy.

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**PO-445**

**EFFECT OF LOW DOSE ALENDRONATE IN OSTEOGENIC/OSTEOPOROTIC ASIAN RENAL TRANSPLANTS – A SINGLE CENTRE EXPERIENCE**

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**Introduction:** Osteopenia and osteoporosis are frequent complications in kidney transplant patients(KTP). Modest benefit in BMD (bone mass densitometry) scoring has been achieved with Alendronate (ALEN) treatment in the Caucasian population. This single-centre prospective case- control cohort study investigates the effectiveness of ALEN on BMD in 67 unselected Asian KTP.

**Methods:** 44 osteopenic and 23 osteoporotic KTP determined by WHO criteria were prospectively evaluated for BMD T score at the lumbar spine(TL) and hip(TH) and serum biochemical markers over a period of two years - 36 patients were started on low dose ALEN (70mg) daily (Group A) and 31 received no treatment (Group B) whilst maintained on standard immunosuppression. Previous transplants were excluded. The two groups (Group A v/s B) had no significant difference in age (45.4 ± 7.8 v/s 49.2 ± 7.2 years); transplant age (49.7 ± 41.0 v/s 48.2 ± 42.6 months); gender (females: 44.4% v/s 51.6%); race (Chinese: 80.6% v/s 96.8%); menopausal women (4 v/s 8); baseline MDRD GFR (46.1 ± 14.1 v/s 48.5 ± 42.6 ml/min); biochemical markers; steroid dose (6.4 ± 2.6 v/s 7.2 ± 3.2 mg/daily); T score (-1.3 ± 1.3 v/s 0.9 ± 1.2 g/cm²) and TH score (-2.4 ± 0.9 v/s -1.7 ± 0.9 g/cm²).

**Results:** Group A had a mean increase in TL and TH score of 0.34 v/s 0.03 g/cm² (p<0.001) and 0.23 v/s -0.06 (p=0.001) respectively. The percentage change in TL(TS) was 125.3% v/s -51.3% (not significant). ALEN was well tolerated (only one drop out) and was not associated with graft dysfunction (MDRD GFR: 50.4±18.5 v/s 49.8±22.5 ml/min) or calcium metabolism abnormalities. There were 3 fractures in group A and 5 in group B.

**Conclusion:** Treatment of osteopenia/osteoporosis in Asian KTP with low dose ALEN significantly improves bone mass densitometry at the lumbar spine and hip without any adverse effect on renal function.

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**PO-446**

**IMPROVED OUTCOMES OF RENAL TRANSPLANTATION FROM NON-HEART BEATING DECEASED DONORS**

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To alleviate chronic shortage of renal graft, non-heart beating donors (NHBD) have been accepted as the organ resources in Japan. In this study, the outcomes of renal transplantation (RTx) from NHBD were retrospectively analyzed.

**Patients:** Between 1975 and 2004, 265 RTx from NHBD were performed at our institute. Mean age of the recipients and donors were 39±13 years and 43±17 years, respectively. The recipients were divided into four groups according to a period as follows: 1975-1979 (Group 1: n=18), 1980-1989 (Group 2: n=87), 1990-1999 (Group 3: n=91), and 2000-2004 (Group 4: n=69).

**Results:** Overall graft survival rates at 1, 5 and 10 years were 79%, 65% and 30%, respectively. The figure shows Kaplan-Meier curves of graft survival in each group.

**Conclusion:** The outcomes of RTx from NHBD have continually improved. NHBD could contribute to an increase in the number of other solid organs for transplantation including liver and pancreas.
Background: The high incidence of skin tumours in transplant patients is well recognised, especially in populations with heavy sunlight exposure, such as in Australia. It has recently been recognised that patients in Northern Europe also have an increased incidence of skin tumours, despite the lower levels of sun exposure, implicating other risk factors such as immunosuppressive regimes.

Methods: We reviewed skin tumours that developed in the renal transplant population of our Northern European city over a 25 year period, including case notes and histology reports for transplant patients attending dermatology clinics with suspected skin tumours.

Results: Between January 1980 to January 2005, 701 renal transplants were performed on patients within the local area. 84 patients (12%) developed at least one skin tumour, corresponding to a 16-fold increased risk in transplant patients compared to the general population. 42% had multiple lesions (range 2-15). The SCC-BCC ratio was 2.5:1. The head and neck region was the commonest site of presentation at 68%. The mean length of time from transplant to excision of first skin tumour was 81 months (range 6-289). The mean age of patients who later developed skin tumours was 53 at the time of transplant.

Conclusion: Skin tumours are a significant complication affecting transplant patients in our region, despite the area having a relatively low level of sun exposure. Whilst further research is needed into the exact mechanism and hence prevention of skin tumours in transplant patients, we believe that transplant patients would benefit from surveillance at a specialised dermatology clinic.

Factors Predicting GLOMERULAR FILTRATION RATE IN NHBD KIDNEY TRANSPLANTATION

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Introduction: Kidneys from non-heart-beating donors (NHBD) are increasingly being used. They have comparable survival and long-term function to kidneys from heart-beating donors, but intermediate-term function varies, and registry data has shown such function to be predictive of graft survival. We aimed to evaluate the possible factors predicting glomerular filtration rate (GFR) at 1 and 2 years post-transplant.

Methods: We reviewed a series of 103 consecutive NHBD kidney transplants, and analysed the impact of various possible predictors on GFR with a multiple regression analysis model.

Results: The only factor individually associated with significant differences in GFR at both 1 and 2 years was donor age (p=0.003 and p=0.033); although recipient age >60 was associated with impaired function at 1 year (p=0.011) and high recipient cardiovascular risk score (CVRS) associated with decreased function at 2 years (p=0.020).

The multiple regression model demonstrated the difficulty in predicting the function, as the best model could only achieve \( r^2 = 0.230 \) (r=0.479, p=0.016) and \( r^2 = 0.324 \) (r=0.569, p=0.014) for first and second year respectively. The factors included, in order of importance, were: donor age, duration of delayed graft function, recipient CVRS, cold ischaemic time, total warm ischaemic time and recipient age.

Conclusion: Intermediate-term function in NHBD kidney transplants is difficult to predict, but there are certain factors which help with this. However, our best model could only account for 52% of the variability in the GFR at 2 years, the greatest impact may be due to the unknown factors which characterise NHBD transplants, especially from uncontrolled donors.
and 24 months after Ktx (groups A and C) or 24, 30, 36, 42 and 48 months after Ktx (group B).

Renal function after 24 month of observation was significantly better in group C (SCr µmol/L: C, 94.6±16.8 vs. A: 110.5±22.1; B: 121.1±30.9; p<0.05). In tacrolimus-treated recipients TRP and TmPO4/GFR remained within normal values during the whole observation period. In groups A and B TRP improved during the first year of observation and after 2 years reached values observed in group C (TRP: A: 0.67±0.1, B: 0.72±0.13, C: 0.76±0.07, p<0.05) whereas TmPO4/GFR remained aggravated in groups A and B after 2 years (A: 0.78±0.19; B: 0.91±0.25; C: 0.94±0.15; p<0.05).

Conclusion: Tacrolimus-treated patients exhibit significantly faster recovery from tubular phosphate reabsorption impairment comparing to cyclosporine.

Tacrolimus-based immunosuppression leads to better kidney allograft function during 2 years of observation.

PO-452 DETERIORATION OF RENAL FUNCTION IN RENAL TRANSPLANT RECIPIENTS DESPITE CONVERSION TO PROTOCOL WITHOUT CALCINEURIN INHIBITORS

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Established antiproliferative and non-nephrotoxic activity of sirolimus is exploited in the treatment of patients with chronic graft dysfunction. In this paper we call attention to the possible incidence of nephrotic syndrome with progressive renal impairment in patients with chronic nephropathy after rapid conversion from cyclosporine to sirolimus. Four male recipients, aged 35-45 years, with chronic renal failure in the course of glomerulonephritis were transplanted in 1997-1999. For the first 49-65 months the immunosuppressive regimen consisted of cyclosporine, azathioprine and prednisone. After that time, due to chronic nephropathy evidenced by biopsy, conversion to sirolimus was performed and cyclosporine was withdrawn. Concomitant immunosuppression included mycophenolate mofetil and prednisone. Serum creatinine level prior to conversion was 1.7-2.5 mg/dL (average 2.0 mg/dL) and improved by 0.1-0.5 mg/dL monthly in two patients, while in the other two serum creatinine level was stable at 2 mg/dL for last six months. Trace proteinuria was found in 3 patients, while one had 200 mg/dL. After 2-4 months of sirolimus treatment proteinuria progressed (240-850 mg/dL), oedema, hypoproteinemia, hypoalbuminemia and hyperlipidemia developed, and serum creatinine rose to 2.5-3.2 mg/dL. Biopsy was performed in two patients. One revealed membranous glomerulonephritis, and the other posttransplant glomerulopathy. After four to five months reversion to calcineurin inhibitor was performed. Proteinuria diminished to 0-150 mg/dL, nevertheless serum creatinine was continuously rising. One year after the conversion three patients returned to dialysis. The fourth patient, who was earlier reconverted, has a serum creatinine level of 2.9 mg/dL.

Conclusions: 1) Conversion to protocol without calcineurin inhibitors can be associated with the experience of nephrotic syndrome which was previously controlled by calcineurin inhibitors.
2) The converted patients require careful monitoring of proteinuria and renal function.
3) Early reversion to calcineurin inhibitor may prevent irreversible deterioration of graft function.

PO-453 HISTOLOGICAL FINDINGS IN PROTOCOL BIOPSY AT 1 AND 6 MONTHS AFTER LIVING KIDNEY TRANSPLANTATION AND ALLOGRAFT FUNCTION AT 1-YEAR

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The aim of our study was to identify borderline (BR) and subclinical rejections (SR) as well as histological markers of chronic allograft nephropathy (CANG) among protocols biopsies performed at 1 and 6 months after living kidney transplantation assessing their possible implications for graft function at 1 year. A paired allograft biopsies (n=20) were reviewed according to Banff scoring schema. BR was scored in 35% and 40% and SR in 10% and 30% of patients at 1 and 6 month biopsy, respectively. The mean CAN score (sum of histological markers for chronicity) increased significantly on the 6 month biopsy, 2.15±1.5 vs 4.31±2.47 (p<0.01).

Mean creatinine clearance deteriorated from 1 to the 6 month value (71.9±17.2 vs 63.2±22.6; p<0.05), but significantly improved at 12 months (63.2±22.6 vs 69.4±23.6; p<0.01). The group with risied 1 year serum creatinine above 200mcmol/L (n=5) had significantly increased body mass index (BMI) at 12 months and a greater percentage of experienced delayed graft function (DGF). In conclusion, 1 and 6 month biopsy may be valuable to determine BR and SR and to prognosticate the outcome of renal allograft function. The presence of DGF and a rise in BMI in association with an untreated finding of BR and SR in protocol biopsies from older donors, might lead to a rapid impairment of the graft function.

PO-454 THYMoglobulin induction decreases acute rejection rate in living unrelated kidney transplantation

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Introduction: Thymoglobulin (Thymo) is an effective immunosuppressive-agent for induction and rescue-therapy in transplantation. Efficacy of Thymo-induction in living unrelated kidney transplant recipients (LUKTR) is examined. Methods: LUKTR (n=26) received Thymo-induction (1.5 mg/kg/d for 3 days with maintenance immunosuppression. Renal function and T-lymphocyte-subsets were monitored. These results were compared to a Control-Group (n=29) who received no induction. Results: At 12-months, 7 patients in Control-Group experienced acute rejection, with one graft lost; while another had delayed graft function (DGF). No rejection episodes (p=0.011 vs. Control) or DGF noted in Thymo-group. No clinically important infections or malignancies occurred in either group, although the number of circulating CD4-T-cells remained <40% of the starting value at 6-months.

Conclusions: Thymo-induction in LUKTR is associated with decreased acute rejection episodes, which may translate into improved long-term kidney allograft survival.

PO-455 INFLUENCE OF INTRA-OPERATIVE HEMODYNAMIC FACTORS ON IMMEDIATE AND DELAYED RENAL GRAFT FUNCTION

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Purpose: To assess the influence of the intra-operative management of hemodynamic factors of the patient on immediate and delayed renal graft function.

Materials and methods: Between June 1980 and December 2004, 1336 renal transplants were done in our Department. We analysed several per-operative hemodynamic factors: central venous pressure (CVP), volumes of fluid, fresh frozen plasma (FFP) and whole blood transfused and its influence on renal graft function parameters.

Results: Median age of the patients was 41.0 ± 13.8 years. Overall, kidney transplant survival rates at 1, 5 and 10 years were 91.2%, 78.1% and 60.2%. Mean CVP at the time of renal graft reperfusion was 13 cm of H2O with no difference in patients with immediate and delayed graft function. There were however some differences when considering groups of patients with CVP >10 and CVP ≤10 cm of H2O. On average more than 2200 ml of saline solutions were infused during the surgery. Patients receiving FFP (67.8%) had a lower incidence of acute rejection (39 vs. 46%) and a higher 10 year graft-survival.
A RANDOMIZED, OPEN-LABEL, COMPARATIVE POSITIVE EFFECT OF BISPHOSPHONATES IN THE INFLUENCE OF CARDIOVASCULAR DONOR RISK

Influence of CVP on renal graft

| Cystatin C | n (%) | P |
|-----------|-------|---|
| <10 mg/L  | 431 (63.8) | 433 (64.4) |
| 10-20 mg/L| 228 (32.9) | 221 (32.9) |
| >20 mg/L  | 41 (5.9)   | 31 (4.6)   |

Immediate graft function

| Cystatin C | n (%) | P |
|-----------|-------|---|
| <10 mg/L  | 76%   | 80%   |
| 10-20 mg/L| 93.9% | 95.5% |
| >20 mg/L  | 51.4% | 63.9% |

Conclusions: The last patient completed the 52-week primary endpoint visit in March 2005, which will allow us to report aggregate safety and efficacy data in the full presentation.

PO-457 DOES A POSITIVE FLOW CYTOMETRY CORSS MATCH INFLUENCE THE OUTCOME OF A CADAVERIC RENAL TRANSPLANT?

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Purpose: To evaluate the significance of positive T-cell & B-cell flow cytometry (FCXM) on cadaveric renal transplantation.

Methods: FCXM were performed in our centre over 7 years. Kidneys were allocated according to donor age, donor history of hypertension or diabetes, and cardiovascular cause of death. A progressive decline in graft function was noticed in 10 patients who experienced acute rejection. Multiple linear regression analysis revealed that donor age greater than 50 years (B=19.6, 95% CI 7.3–31.9, P=0.002), donor history of hypertension or diabetes (B=15.3, 95% CI 8.2–28.4, P=0.002), and post-transplant DGF (B=13.9, 95% CI 3.2–23, P=0.014) were independently associated with higher serum creatinine values at 12 months, whereas cardiovascular cause of donor death was not found as independent predictor of serum creatinine.

Conclusion: There were no statistically significant differences in patient demographics between cohorts (see Table). To date, this is the largest prospective, randomized clinical trial of conversion from CsA or TAC early after transplantation, with corticosteroids and either azathioprine or mycophenolate mofetil for immunosuppression.
**PO-460** CONVERSION FROM MMF TO EC-MPS ON AN EQUIMOLAR OR HIGHER THAN EQUIMOLAR BASIS: COMPARATIVE ANALYSIS OF SAFETY AND TOLERABILITY VARIABLES.

LATIN AMERICAN MYRPMOS STUDY GROUP

Mario Abdul Filho, Nephrology, Nephrology and Urology Institute and Medical School of Rio Preto, Sao Paulo, Brazil

Mycophenolate immunosuppressive efficacy decreases with dose reduction. This retrospective analysis has been performed to compare the tolerability of patients exposed to equimolar or higher than equimolar MPA doses after conversion from MMF using enteric-coated mycophenolate sodium (EC-MPS; myfortic®). A multicenter, open-label, 6-month trial assessed the safety and tolerability of the conversion of stable renal transplant recipients from MMF to EC-MPS. Patients were converted to EC-MPS 720 mg b.i.d. (equimolar to MMF 1000 mg b.i.d.) even if previous MMF dose was lower than equimolar (Mean: 760 mg bid). Two groups were retrospectively analyzed, Group A: 171 patients converted to equimolar doses and Group B: 47 patients converted to higher than equimolar doses. Analysis was done for: 1-adverse events incidence using χ^2-safety laboratory variables at different time points and their interaction (groups vs time) using ANOVA for repetitive measures.

| Table 1  |
|----------|
| Adverse Event | Group A (%) | Group B (%) | p   |
| Adverse Events | 58.48 | 57.45 | 1.00 |
| Upper GI | 11.69 | 13.00 | 0.80 |
| Lower GI | 11.11 | 14.89 | 0.44 |
| Diarrhea | 8.00 | 10.60 | 0.57 |
| Leukopenia | 1.75 | 4.25 | 0.29 |
| Anemia | 2.33 | 2.12 | 1.00 |
| Infections | 42.11 | 30.00 | 0.40 |
| Dose Adjustments | 9.94 | 14.80 | 0.43 |

No statistical significant differences for groups at different time points were found in the two analysis (χ^2 or ANOVA) no interaction of groups with time was identified (ANOVA).

No no discontinuations of study medication were reported, 85% of the patients tolerated higher doses with EC-MPS without dose adjustments.

**Conclusion:** Conversion from MMF to EC-MPS at equimolar or higher doses was identified (ANOVA). Our data indicate that IG induction therapy prevented from severe IgG deficiency in the early posttransplant so that a significant IgG deficiency (>20% of non-IG patients (day 10, p=0.005). However, only 1-year serum IgG levels were associated with occurrence of multiple and severe infections (p<0.05). As the Ig preparation contained all of the regulatory antibodies tested, intra-venous administration of these antibodies may explain the elevated anti-F(ab)2 antibody levels (IgG, p=0.005; IgA, p=0.04) and the decreased frequency of low IgA anti-hinge (p<0.05) and anti-Fab antibody levels (IgG, p=0.004; IgA, p=0.01) of Ig patients on day 10.

**PO-461** IMMUNOGLOBULIN INDUCTION THERAPY IN RENAL TRANSPLANT RECIPIENTS – EFFECTS ON IMMUNOGLOBULIN AND REGULATORY ANTIBODY LEVELS

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We showed previously that high pretransplant regulatory antibodies (anti-Fab, anti-F(ab)2, anti-hinge) were associated with better kidney graft outcome. To analyze the effect of immunoglobulin induction therapy on these antibodies, we performed a prospective randomized study in 50 renal transplant recipients who were randomly assigned to receive 7x10g IG and 7x10g albumin infusions, respectively. IG and non-IG patients showed no significant differences in 1-year graft outcome and acute rejection incidence (12%/16%). IG induction resulted in up-regulation of serum IgG (p<0.001) and IgA (p=0.04) within the first 20 days posttransplant so that a significant IgG deficiency (<9g/l) occurred only in 28% of non-IG patients (day 10, p=0.005). However, only 1-year serum IgG levels were associated with occurrence of multiple and severe infections (p<0.05). As the IG preparation contained all of the regulatory antibodies tested, intra-venous administration of these antibodies may explain the elevated anti-F(ab)2 antibody levels (IgG, p=0.005; IgA, p=0.04) and the decreased frequency of low IgA anti-hinge (p<0.05) and anti-Fab antibody levels (IgG, p=0.004; IgA, p=0.01) of IG patients on day 10.

We data indicate that IG induction therapy prevented from severe IgG deficiency in the early posttransplant period but had no significant effects on severe infectious complications in the first year posttransplant. IG induction enhanced anti-Fab, anti-F(ab), and anti-hinge immunoregulatory antibody levels early posttransplant which may provide graft protective effects.

**PO-462** OUTCOME OF RENAL TRANSPLANTATION FROM NON-HEART-BEATING DONORS

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Purpose: Our centre established a non-heart beating donor (NHBDD) organ retrieval programme in 2002. The majority of NHBDD retrieved organs yield in both kidneys being transplanted in our centre (uncommon with heart-beating donors due to nationwide organ sharing). We aimed to identify any difference in outcome between the first (R1) and second (R2) recipient from a NHBDD, as these transplants are usually performed consecutively rather than simultaneously.

**Methods:** Consecutive NHBDD renal transplants from the start of the programme were reviewed. All donors were Maasstrict category III controlled NHBDD. The “delay” between the R1 and R2 transplants was taken as the difference in cold ischaemic time.

**Results:** 40 transplants were performed over a period of 32 months. On 17 occasions both kidneys from a NHBDD were transplanted. Median (range) donor age was 47 (20-67) and recipient age was 48 (22-78) years. Primary graft function was seen in 15.8% of patients, delayed graft function in 73.7%, and primary non-function in 10.5%. Median disialysis duration was 12 (2-35) days; median hospital stay was 15 (8-31) days. There was no difference in outcome between R1 and R2 patients, despite a mean delay of 3 hours 3 minutes. Overall, mean (SD) creatinine at one year was 139 (± 60). One-year graft survival was 84%.

**Conclusions:** Despite a high incidence of delayed graft function, renal transplantation from NHBDD results in acceptable rates of graft survival at one year. Transplantation of both kidneys from a NHBDD in our centre does not affect early outcome.

**PO-463** DISSEMINATED VARICELLA INFECTION IN ADULT RENAL ALLOGRAFT RECIPIENTS

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Varicella Zoster Virus (VZV) infection may cause primary infection or Varicella Zoster reactivation. This infection is rare after renal transplantation in adults. We report three cases diagnosed in our transplant patients. One of them was VZV seropositive before transplantation and has suffered from disseminated Zoster. The two others were a primary infection without multivisceral involvement.

According to the literature, no immunosuppressive drug was significantly associated with an increased susceptibility to VZV infection. Early treatment with Acyclovir is fundamental in infection control. Detecting VZV seronegative patients before kidney transplantation is relevant because vaccination may minimize the risks of future infection.

**PO-464** ADULT DUAL IPSILATERAL TRANSPLANTATION USING NON-HEART-BEATING DONORS

Colin H. Wilson, John F. Asher, D. Vjayanand, Hugh L. Wyrley-Birch, Ajay Gupta, Juan Del Rio Martin, Derek M. Manas, David Talbot. The Liver/Renal Unit, The Freeman Hospital, High Heaton, Tyne and Wear, United Kingdom.

**Introduction and Methods:** Renal transplantation using non-heart-beating donors (NHBDD) is an established treatment for end stage renal failure in an era of organ shortage. We reviewed our experience of dual transplantation from NHBDD’s with respect to indications for the procedure and outcomes.

**Results:** In 2004 5 patients had two kidneys from the same donor implanted in an isplilateral fashion. Two of the recipients received dual transplants when the glutathione-s-transferase (GST) enzyme assay of the preservation solution during machine perfusion was considered too high for single transplantation (recipient serum creatinine at 6 months: 95 and 159 µmol/l). One recipient received both kidneys after a second potential recipient failed a pre-transplant cross-match and there was insufficient time to call a second recipient (155 µmol/l). A further controlled NHBDD, the cannula was misplaced and the recipient received both kidneys (9 months: 269 µmol/l). The last patient had a dual transplant from a diabetic donor with renal impairment (3 months: 242 µmol/l).

**NHBDD Algorithm**

| Clinical situation | 2003 | 2005 |
|--------------------|------|------|
| GST assay > 200 µmol/l | Discard | Dual Tx |
| Poor donor/miscplaced cannula | Discard | Dual Tx |
| Perfusion Flow Index < 0.4 (ml/min/100g/mMg) | Discard | Discard |
| PFI < 0.4 and GST < 200 | Single Tx | Single Tx |
| Cold ischaemia > 24 hrs | Discard | Dual Tx |

# Poster Presentations Kidney

| Poster Presentations | Kidney |
|---------------------|-------|
| Colin H. Wilson      |       |
| John F. Asher        |       |
| D. Vjayanand         |       |
| Hugh L. Wyrley-Birch |       |
| Ajay Gupta           |       |
| Juan Del Rio Martin  |       |
| Derek M. Manas       |       |
| David Talbot         |       |
| The Liver/Renal Unit |       |
| The Freeman Hospital |       |
| High Heaton, Tyne    |       |
| Wear, United Kingdom |       |
**Discussion:** This experience has led us to change our NHBD algorithm (see table). By implanting both grafts in one iliac fossa, the second remains available should re-transplantation be required. However, we are still wary of transplanting kidneys with poor machine perfusion flows- those at the greatest risk of early vascular thrombosis.

**PO-465** PROPHYLACTIC URETERIC STENTS TO REDUCE MAJOR UROLOGICAL COMPLICATIONS IN RENAL TRANSPLANT RECIPIENTS

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**Introduction:** Urine leak and ureteric stenosis remain relatively common complications following renal transplantation, with a reported incidence ranging between 0.5 and 20%. Some centres advocate routine insertion of ureteric stents, in all renal transplant recipients, to reduce the incidence of these major urological complications (MUC’s).

**Methods:** In conjunction with the Cochrane Renal Group, all randomised controlled trials examining the use of double J stents to prevent urological complications in renal transplant recipients were identified by a combination of computer literature searches, handsearching and personal communication.

**Results:** Seven studies randomised a total of 1154 patients. The overall MUC rate was 5.3%. Universal prophylactic stenting group reduced the complication rate from 9.3% to 1.5% (Relative Risk 0.25; 95% confidence intervals 0.08 - 0.80; p<0.002). Stents were associated with an excess risk of urinary tract infection (RR 1.49; 1.04 - 2.15; p=0.03). Subgroup analysis suggested that this risk was dependent on the antibiotic regime used. Stented transplant recipients receiving the equivalent of co-trimoxazole 480mg per day, whilst the stent was in situ, had an infection rate equivalent to non-stented patients and significantly lower when compared with other stented patients (RR 0.58; 0.43 - 0.77; p<0.001).

**Conclusions:** Routine placement of ureteric stents in recipients of renal transplants reduces the incidence of major urological complications. Stents are associated with an increased risk of urinary tract infection but concurrent administration of co-trimoxazole significantly reduces this risk. The optimum type, length, caliber and duration of stenting remain to be established.

**PO-466** STEROID FREE IMMUNOSUPPRESSION REGIMEN IN LIVE DONOR RENAL ALLOGRAFT RECIPIENTS – A PROSPECTIVE RANDOMISED STUDY (SINGLE CENTER EXPERIENCE)

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**Objective:** The purpose of this work was to prove the safety of steroid free immunosuppression regimen in live donor renal transplantation.

**Background:** Steroids have played a main role in renal transplantation since more than four decades. However, chronic use of steroids is associated with a lot of comorbidities in the form of cardiovascular diseases, bone loss, diabetes mellitus, obesity, as well as body configuration. Recent studies have proved the safety of using steroid free regimen in renal transplantation, although there are limited data regarding steroid avoidance in live donor renal transplantation using new immunosuppression (FK506-MMF-SIMULECT) in a prospective randomized controlled study.

**Methods:** 72 patients were randomized to receive either FK-MMF-SIMULECT induction and steroids only for 3 days (36 patients) (Study group) or FK - MMF-SIMULECT induction and steroids maintenance (36 patients) (Control group). Median follow up was six months.

**Results:** Patient survival was 100% in both groups. Graft survival was 97.2% in both groups. Biopsy proven acute rejection episodes were 25% in both group. Mean serum creatinine was 1.2 mg/dl in steroid free group and 1.1 mg/dl in control group. Posttransplant hypertension were 11% and 33% respectivley. Posttransplant D.M.were 8.3% and 19.4% respectivley. Posttransplant wait gain were 6% and 15% respectively.

**Conclusion:** Steroid free regimen using newer immunosuppression has comparable rejection incidence as steroid based one but with significant reduction in steroid comorbidities. Long term follow up and protocol biopsies are required for further evaluation.

**PO-467** LIMITING BLOOD TRANSFUSION AFTER RENAL TRANSPLANTATION

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**Aim:** To examine blood transfusion practice following renal transplantation.

**Patients and Methods:**
- 50 consecutive renal transplant recipients in one centre.
- Two patient groups: those who received blood transfusion (n=28) and those who did not (n=22).
- Indications for transfusion were surgical bleeding (n=14) and dilutional anaemia (n=14).
- Serum haemoglobin (Hb), albumin and patient weight were examined immediately pre-operatively then at day 1, 7, 14, 28, and 90. Pre-operative ferritin levels were recorded.
- The presence of biopsy proven acute rejection (AR) and delayed graft function (DGF – defined as a need for dialysis in the first week) were assessed.
- Non-parametric analyses of variance were performed as appropriate (GraphPad InStat).

**Results:**
- Blood transfusion rate was 56%.
- Day 28 and 90 Hb was significantly lower in the transfused group vs. non-transfused (9.5g/dl vs. 11.3g/dl, p=0.003 and 10.5 vs. 12.3, p=0.05 respectively).
- A highly significant association was demonstrated between DGF and the need for blood transfusion (p=0.0001). This was not seen with acute rejection.
- Day 1 and 14 albumin levels were significantly lower in the transfused group (26 vs. 29, p=0.01 and 33 vs. 38, p=0.002 respectively).
- There was no significant difference in pre-operative ferritin levels between groups.

**Conclusion:**
- Incidence of transfusion is high and strategies are to be developed to reduce this figure.
- Blood transfusion may suppress bone marrow activity leading to the delayed recovery of Hb demonstrated here.
- In delayed graft function benefit may be obtained from additional therapies to promote erythropoesis post-operatively.

**Ongoing work:**
- A pilot study of erythropoietin therapy in DGF.
- Assessment of functional iron deficiency to identify patients to treat with IV iron therapy.

**PO-468** PERSISTENT LEFT VENTRICULAR HYPERTROPHY AFTER RENAL TRANSPLANTATION: PREDICTORS AND OUTCOME, A SINGLE CENTER EXPERIENCE

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Persistent or de novo left ventricular hypertrophy (LVH), is a risk factor for death and congestive heart failure following Renal transplantation. Our aim was to determine the risk factors for persistent LVH after transplantation and to study its impact on renal transplantation outcome. We included 72 live donor renal allograft recipients with mean age (years) of 39±12 of transplantation who had functioning grafts after one year of transplantation. Cardiac status of all of them were assessed before transplantation and serially up to one year post-transplantation by echocardiography. The patients were divided into 2 demographically well-matched groups. The first group included 33 patients who had persistent LVH. The second group (39 patients) served as a control. Both groups were meticulously followed up for 10 years.

Univariate analysis showed that the significant predictors for persistent LVH after renal transplantation were high serum creatinine at one year post-transplantation, the occurrence of medical infection, acute rejection and chronic rejection. The occurrence of chronic rejection and medical infection were the only valid predictors on multivariate logistic regression analysis. Moreover, patient and graft survival were significantly lower in persistent LVH group (p=0.012). Persistent LVH is common in renal transplantation who suffered from medical infection or chronic rejection and it carries a worse outcome for renal transplant recipients.
CONTINUOUS GLUCOSE MONITORING EARLY AFTER KIDNEY GRAFT IN NON-DIABETIC PATIENTS MAY PREDICT POST-TRANSPLANTATION DIABETES

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Background and Aims: Tight blood glucose (BG) control improves clinical outcome in critically ill patients presenting hyperglycemia. Hyperglycemia early after kidney transplantation has not yet been studied prospectively although diabetes is a recognized complication of transplant recipients.

Materials and Methods: From November 2003 to July 2004, we included 43 consecutive non diabetic patients who received a kidney transplant (28M:15F; age: 45±13 years, BMI: 23.9±1.6 kg/m²). During the first four days after transplantation, we measured fasting BG, and daily BG profile was assessed by the continuous monitoring device CGMS®. Capillary BG readings were recorded just after transplantation procedure and at least four times per day for CGMS® calibration thereafter.

Results: Immediately after surgical procedure, capillary BG was 12.2±3.8 mmol/l. At day 1, fasting BG was 9.6±1.3 mmol/l and progressively decreased to 6.0±1.5 mmol/l at D3. CGMS® reported daily BG at 10.2±2.4 mmol/l on D1; 7.7±1.3 on D2; 7.5±1 on D3. Time spent over 7.8 mmol/l was 20.7±1hrs on D1, 11.8±4hrs on D2, 10.3±7.5hrs on D3 and 9.7±5.5hrs on D4. From D1 to D4, only 22.9% of patients spent less than 6hrs/day with BG>7.8 mmol/l, whereas 42.9% spent more than 12hrs/day with BG>7.8 mmol/l. No risk factor could be identified for early post-transplant hyperglycemia, but fasting BG level on D1 was higher in patients who later developed diabetes 3 months after transplantation (p<0.05).

Conclusion: Our data demonstrate almost constant hyperglycemia in the immediate followings of kidney transplantation in non-diabetic subjects. CGMS® recordings underscore intensity and duration of BG excess that could point out patients at risk for later post-transplant diabetes.

PROSPECTIVE STUDY COMPARING GASTROINTESTINAL DISORDERS IN DE NOVO RENAL-TRANSPLANT PATIENTS RECEIVING MYCOPHENOLENATE MOFETIL OR ENTERIC-COATED MYCOPHENOLENATE SODIUM

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The aim of this study was to assess gastrointestinal (GI) side-effects in de novo renal-transplant (RT) patients receiving mycophenolic acid (MPA). 93 RT patients received mycophenolate mofetil (MMF) (group I), and 37 patients received enteric-coated mycophenolate sodium (EC-MPS) (group II). Each month, every patients completed a questionnaire on GI disorders. In case of diarrhea, the frequency and severity were similar in both groups. Weight loss was observed in only 3 patients receiving MMF. Diarrhea occurred, its frequency and its severity were similar in both groups. Weight loss was observed in only 3 patients receiving MMF. None of the patients developed a malabsorption syndrome. 4 patients in the MMF group underwent esophago-gastro-duodenoscopy. 2 patients in group I underwent also a colonoscopy which was found to be normal. In only one patient of group I, standard stool culture was positive. Diarrhea disappeared spontaneously in 10 patients of the MMF group and in all patients of the MPS group. In the 8 remaining patients of group I, it required MMF discontinuation in 3 patients and MMF dose reduction in 5 patients. In conclusion, gastrointestinal tolerance of both MMF and EC-MPS is similar in de novo renal-transplant patients during the first year post-transplantation.

ADIPONECTIN, LEPTIN AND THYROID HORMONES IN PATIENTS ON RENAL REPLACEMENT THERAPY: ARE THEY RELATED?

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Background: Renal function affects thyroid function and adipokynes in many ways. We aimed to assess the adiponectin and leptin in relation to thyroid functional status in patients with chronic renal failure treated conservatively, hemodialyzed patients and kidney allograft recipients.

Methods: The study was performed on 33 patients with chronic renal failure, 64 hemodialyzed patients, 54 kidney allograft recipients and 38 healthy volunteers. Thyroid volume was estimated sonographically, thyroid hormones by MEIA, serum adiponectin and leptin were assessed by RIA.

Results: Serum TSH, free T4 and free T3 were within the normal range. Adiponectin correlated significantly with T3, hematocrit, hemoglobin platelet count, BMI and urea in kidney allograft recipients patients. In hemodialyzed patients adiponectin correlated with free T4 and TSH, whereas leptin correlated with T3. Multiple regression analysis showed that adiponectin was independent of depression only related to serum concentration of T3 and urea in kidney transplant recipients and to T4 and adequacy of dialysis in hemodialyzed patients. In univariate analysis in patients with chronic renal failure, adiponectin correlated with T3 and platelet count, in healthy volunteers adiponectin correlated only with T3 and was not correlated with T4.

Conclusions: We described novel relations between adiponectin and thyroid hormones, in patients with kidney diseases However, possible preexisting thyroid dysfunction prior to transplantation (during dialysis therapy) and immunosuppression after transplantation make all these findings relatively complex. Therefore, the relations between adiponectin and thyroid axis in patients with chronic renal failure, hemodialyzed subjects or in kidney transplant recipients merit additional studies.

HEPATICIN: IS THERE A LINK BETWEEN ANEMIA, INFLAMMATION AND LIVER FUNCTION IN KIDNEY TRANSPLANT RECIPIENTS AND HEMODIALYZED PATIENTS?

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Hepcidin is a small defensin-like peptide whose production by hepatocytes is modulated in response to anemia, hypoxia or inflammation. Uptregulation of acute-phase proteins is present in the majority of dialyzed patients and after kidney transplantation, thus an inappropriate hepcidin expression appears conceivable in these populations. Hepcidin could also act as an indicator of functional iron deficiency in these patients. Hepcidin correlations with markers of iron status, erythropoietin therapy and markers of inflammation were assessed in 97 hemodialyzed patients-HD, 80 kidney allograft recipients-Tx (maintained on CSA, Az/MMP and prednisone) and in the healthy volunteers-CG. Hepcidin and high sensitivity CRP were estimated using commercially available kits. Iron, TIBC, TSAT, erythrocyte count, Hb, Ht platelet count, albumin, cholesterol were lower in HD than Tx and CG. Ferritin and hepcidin were significantly higher in HD and Tx relative to CG. Hepcidin correlated positively with triglycerides, aspirate amionotransferases, lymphocyte count, ferritin, albumin and erythrocyte count and negatively with erythrocyte count, Hb and Ht in HD. Hepcidin did not correlate with CRP, a marker of inflammation. In multiple regression analysis triglycerides and albumin were predictor of hepcidin in HD. In Tx hepcidin correlated only in ferritin. In CG hepcidin was not related to any studied parameters. Elevatated hepcidin in HD may be due to functional iron deficiency and anemia, but not to inflammation. Liver plays an important role in the synthesis of hepcidin. Lack of correlation between GFR, residual renal function might suggest that kidneys do not play a major role in hepcidin metabolism. Grant 2P05B07798 from KBN.

ST2 INVOLVEMENT IN THE RECURRENTNESS OF FOCAL SEGMENTAL GLOMERULOSCLEROSIS AFTER KIDNEY TRANSPLANTATION

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Idiopathic Nephrotic Syndrome (INS) is a glomerular disease of unknown origin, which includes Minimal Change Nephrotic Syndrome (MCNS) and Focal Segmental Glomerulosclerosis (FSGS). INS relapse has been shown to be associated with a pathogenic circulating factor, early T cell activation and Th2 commitment. These observations led us to study the expression of ST2 gene products (soluble ST2 and membranous ST2L proteins) in INS. ST2L mRNA levels in PBMC and soluble ST2 concentrations were measured by semi-quantitative RTPCR and ELISA, respectively, in patients with MCNS relapse and remission, as well as in FSGS patients with or without recurrence following transplantation. Sera activity of patients with or without recurrence was tested on an immortalized mouse podocyte cell line. MCNS patients displayed high ST2L mRNA levels compared to controls and healthy individuals. In FSGS patients, pregrag ST2L mRNA and soluble ST2 levels were similar in relapsing and non-relapsing patients. On the other hand, after transplantation, patients with FSGS relapse exhibited low ST2L mRNA levels but the soluble ST2 concentrations were significantly increased (p<0.001). Coculture of podocyte cells with sera from patients with FSGS recurrence induced podocyte detachment associated with a cytokeratin disorganization, but not with desmocollin 2 expression in comparison with the constitution of ST2. By contrast, desmocollin 2 expression and morphological changes were detected.
when podocytes were incubated with sera from patients without recurrence. Soluble ST2 seems to be a permeability factor candidate since its concentration is associated with relapse or recurrence. These data also suggest a direct involvement of soluble ST2 in podocyte injury.

**PO-474** TRAIL, DR4, DR5 EXPRESSION IN EARLY BIOPSY SPECIMENS PREDICTS LONG-TERM GRAFT FUNCTION FOLLOWING RENAL TRANSPLANTATION

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Purpose: Many cytokines participate in rejection by inducing inflammation or apoptosis. Tumor necrosis factor related apoptosis-inducing ligand (TRAIL) is a cytokine which can induce apoptotic cell death. Recent studies showed expressions of TRAIL, death receptor 4(DR4), and DR5 in specimens of acute rejection were markedly upregulated. We investigated immunohistochemically whether expressions of TRAIL, DR4, DR5 in stable biopsy specimens 100 days after transplantation could predict subsequent graft dysfunction.

**Methods/Materials:** Specimens from 21 patients were adequate for this study. We examined expression of TRAIL, DR4, DR5 immunohistochemically staining biopsy specimens obtained 100days and the sections were used for image analysis with a computer system. As an index of renal function, the change of Ccr between 100days and 5years after transplantation (ΔCcr) was used.

**Results:** The patients were divided into two groups by optical density of TRAIL, DR4, and DR5 in the sections (group A and B, group C and D, group E and F, respectively). The ΔCcr of group B (high density of TRAIL) (20.50±17.86) was significantly higher than that of group A (low density of TRAIL) (6.09±7.81) (p<0.05). The ΔCcr of group D (high density of DR4) (23.42±12.34) was significantly higher than that of group C (low density of DR4) (8.97±6.45) (p<0.05). The ΔCcr of group F(high density of DR5) (19.34±10.32) was significantly higher than that of group E (low density of DR5) (8.76±6.43) (p<0.05).

**Conclusion:** Increase in expression of TRAIL, DR4, and DR5 in early biopsy specimens were related to decline of long-term graft function.

**PO-475** ADULT LIVE DONOR RENAL TRANSPLANTS WITH MULTIPLE RENAL ARTERIES: DOES IT INCREASE MORBIDITY?

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**Background:** Live donor kidney grafts with more than one renal artery have been considered a relative contraindication because of presumed increase risk of complications. The aim of this study is to determine the outcome of live donor kidney grafts with multiple renal arteries.

**Patients and Methods:** Between January 1984 to September 2004, 269 adult live donor kidney transplants were performed. 37 (13.7%) grafts had more than one renal artery (26 cases two, 8 three and 3 had four renal arteries). Within this study we analysed the incidence of post-transplant surgical and medical morbidity and discussed vascular reconstructions. The outcome is compared with other published studies. The mean follow up period of 43 months (range: 3-132 months).

**Results:** There were no graft losses due to vascular/surgical complications. One patient developed renal artery stenosis in a small branch. Urological complication occurred in two cases. The mean systolic (<140mmHg), diastolic (<90mmHg) blood pressures and antihypertensive medications (2 agents) were within the acceptable ranges at follow up periods. The mean serum Cr levels at 1 month, 6 months, 1, 5 and 10 years post transplant were 151umo/l, 127umo/l, 159umo/l and 270umol/l respectively. The actuarial graft survival rates after 1, 6 months, 1, 5 and 10 years were 97.1%, 89.7%, 85.6% and 57.8% respectively. The 10 year patient survival rates for multiple and single renal artery graft groups were 92.3% and 92.9% respectively.

**Conclusion:** In this study the number of renal arteries did not adversely effect the outcome of live donor transplanted kidneys. Live donor allografts with multiple renal arteries can be safely and successfully transplanted.

**PO-476** RENAL TRANSPLANTATION IN PATIENTS WITH CORONARY HEART DISEASE

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**Purpose:** To retrospectively analyze patient/graft survival and cardiac complications in 45 patients with significant coronary heart disease.

Patients and methods: Out of 533 renal transplants performed 1993-1997 45 underwent coronary angiography for specific symptoms and abnormal non invasive tests. 24 patients had diffuse coronary heart disease (group A), 21 a circumscribed stenosis (group B). 19 patients of group B underwent revascularization prior to transplantation. All of them were considered high risk patients at the time of evaluation. 40 patients without documented coronary heart disease formed group C.

**Results:** In group A 4 patients died from heart failure (month 6 and 20) and 3 patients for other reasons. 2 patients had myocardial infarction (month 1 and 48) but survived. 3 grafts were lost. In group B 6/21 patients died, all of them from heart failure (month 6-84) 1 patient suffered myocardial infarction at month 103. 4 grafts were lost. One year patient and graft survival was 83.3% and 75% in group A, 95.2/90.4% in group B, 96.5/89.1% in group C and the 8-year patient/graft survival was 37.5/25% in group A, 52.3%/54.1% in group B, 71.3/56.5% in group C.

**Conclusion:** Despite revascularization a high cardiac complication rate is seen in patients with limited coronary heart disease. Graft survival, however, is similar to that seen in patients without proven coronary heart disease. Therefore, patients with a revascularized coronary heart disease can be accepted for transplantation as long as their cardiac function allows the surgical procedure and careful posttransplant monitoring is guaranteed.

**PO-477** HIGH INCIDENCE OF GLUCOSE METABOLISM DYSFUNCTION AFTER DE NOVO KIDNEY TRANSPLANTATION

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**Introduction:** Despite decreasing rates of biopsy proven acute rejections (BPAR), New Onset Diabetes Mellitus (NODM) after transplantation increases the risk of graft loss, cardiovascular complications and mortality. In study the criteria recommended by the American Diabetes Association to diagnose NODM, impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) were used after performing an oral glucose tolerance test (OGTT) at 3 month post-transplant.

**Methods:** This is a 3 month interim analysis on the first 115 patients enrolled in a 6-month prospective randomized trial conducted in 700 patients. At transplant, patients were stratified according to diabetes and randomized 1:1 to receive either cyclosporine microemulsion or tacrolimus in combination with basiliximab, mycophenolic acid and steroids.

**Results:** The analysis was performed for all patients together to maintain the integrity of the trial. At 3 month the overall incidence of BPAR and graft loss was 7.3% and 3.5%. Out of 115 patients enrolled, 16 were diabetic and 99 were non-diabetic at entry. By month 3, 16 patients had discontinued the study. Amongst the remaining 85 non-diabetic patients at baseline, 7 (8%) were identified as developing clinical diabetes and were started on hypoglycemic treatment. Glucose metabolism abnormalities were identified in additional 32 patients (38%) by OGTT: NODM: (N=12), IFG (N=12), or IGT (N=8).

**Conclusion:** Glucose metabolism abnormalities are more frequent after renal transplantation than previously reported suggesting underdiagnosis. Routine OGTT could help identify NODM and allow minimization of resulting risks by early appropriate management.

**PO-478** MINIMAL INVASIVE DONOR NEPHRECTOMY COMPARED TO TRADITIONAL OPEN AND LAPAROSCOPIC APPROACHES

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**Background:** Best therapy for chronic renal insufficiency is transplantation especially living organ donation. From 1996-2004 we performed 75 living kidney donations with different techniques: traditional open (ODN), laparoscopic (LDN) and minimal invasive open donor nephrectomies (MIDN).

**Methods:** 75 donors were evaluated retrospectively. ODN (n=27) was performed via flank incision and extraperitoneal removal of the kidney, MIDN (n=34) retroperitoneally via a 10 cm long pararectal incision. In LDN (n=14) the kidney was mobilised laparoscopically and removed by a 10 cm long pararectal incision. Data on hospital stay, surgery time, warm-ischemia time (WIT) and daily applied analgetics were evaluated statistically with pair-wise multiple comparison procedures.

**Results:** Total operation time was significantly shorter for LDN (153 ± 26 minutes) and MIDN (153 ± 26 minutes) than for ODN (248 ± 59 minutes) (p<0.01). Intraoperative WIT for ODN was 2.2 ± 1.1 minutes, 3.6 ± 1.4 minutes in LDN and 1.1 ± 0.5 minutes in MIDN with significant better values in both (p<0.05). Daily drug-application after surgery until discharge was significantly lower in LDN and MIDN. Opiates were also stopped earlier (LDN: day 4, MIDN: day 4) than in ODN (day 9) (p<0.05). Postoperative stay in MIDN (4,45
days) was significantly shorter than in ODN (8.8 days) and LDN (8.3 days) (p < 0.05). Neither perioperative complications concerning wound infection, urinary retention, bleeding, nor nosocomial infections prolonged the hospital stay.

**Discussion:** MDN is a versatile less traumatic, safe and fast method with advantages in WIT, postoperative stay and cosmetic results compared to laparoscopic and conventional donor nephrectomy procedures and reveals equivalency in procedure time compared to ODN and size of surgical access compared to LDN.

**Conclusions:** MDN is a versatile less traumatic, safe and fast method with advantages in WIT, postoperative stay and cosmetic results compared to laparoscopic and conventional donor nephrectomy procedures and reveals equivalency in procedure time compared to ODN and size of surgical access compared to LDN.

**References:**

1. Ospedaliera Universitaria Senese, Siena, Italy.
2. Department of Pathology, Instituto de Clinical and Experimental Medicine, Prague, Czech Republic.
3. Department of Clinical and Experimental Medicine, Prague, Czech Republic.

**Background:** Renal ischemia/reperfusion injury (IR) and hypertension represent major alloantigen-independent risk factors contributing to the development of chronic allograft nephropathy. We developed a model of accelerated MHC independent renal injury, where high-renin hypertension aggravates functional and morphological changes induced by I/R. We evaluated the effect of mycophenolate mofetil (MMF) on the progression of accelerated nephropathy.

**Methods:** 38 anesthetized uninephrectomized hypertensive transgenic (MREN-2) rats (TGR) received clip on renal pedicle for 45 minutes. Animals were treated with MMF 10 mg/kg/d (n=10), 20 mg/kg/d (n=10) or placebo (n=10) via gavage for 12 weeks. Four animals were sham operated and not treated. Proteinuria and blood pressure were evaluated throughout the experiment. At the end of the experiment, kidney function was evaluated and kidneys harvested for morphological and immunohistochemical analysis.

**Results:** At week 12, both MMF-treated groups had lower proteinuria as compared to placebo group (MMF 10: 22.4±9.8, MMF 20: 20.9±5.6 vs. 126.7±35.6, p<0.01; Sham 28.1±4.1 mg/day) and reduced glomerulosclerosis (MMF 10: 11.4±7.8, MMF 20: 5.2±2.7 vs. 20.9±10.9, p<0.05; Sham 15.7±9.2%). There were no differences in systolic blood pressure among groups. MMF-treated rats had lower CD4+ (MMF 10: 61.2±46.4, MMF 20: 29.3±18.2 vs. 125.3±42.8, p<0.01; Sham 84.9±6.1 cells/field of view) and CD28+ (MMF 10: 13.7±10.2, MMF 20: 10.0±8.1 vs. 37.8±14.3, p<0.01; Sham: 31.8±7.6 cells/field of view) T-cells infiltration and CD14 macrophages infiltration (MMF 10: 5.5±6.4, MMF 20: 2.5±2.8 vs. 16.7±4.1, p<0.01; Sham 12.2±4.6 cells/field of view) than placebo-treated rats.

**Conclusion:** Our results thus support the hypothesis about the key role of immune mechanisms in progression of chronic nephropathies.

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**Conclusion:** Our results thus support the hypothesis about the key role of immune mechanisms in progression of chronic nephropathies.
splitting donor nephrectomy (MS-DN) using a smaller incision located anterior to the 11th rib. Aim of the present study was to evaluate the effect of muscle splitting donor nephrectomy and donors less frequently had multiple renal arteries (9% vs. 27% CL). Kidney extraction time and skin-to-skin time were significantly longer for MS-DN as compared to CL (123 vs. 95 minutes, p<0.001 and 171 vs. 145 minutes, p<0.003, respectively). Blood loss was significantly less after MS-DN (227 vs. 300 ml, p=0.02). Peroperatively, one small venous bleeding occurred in each group conservatively treated in our interventional radiology department with excellent results.

At 12 months, BPAR, Graft Loss and Deaths were reported in 19%, 2% and 51% respectively. 28 participants gave identical answers for each scenario and of those whose answers changed, 19 would accept increased risk as recipient's need increased. Questions regarding different recipients were identically phrased and found significant differences between the groups.

Conclusion: In order to donate patients are willing to accept a much higher risk to their own lives than doctors would allow, some up to 50%. Those presented with risk in terms of death, suggesting risk communication methods do bear impact on response.

**PO-487 EXPERIMENTAL STUDY ON THE RENAL MACHINE PERFUSION VARIABLES IN ORGANS FROM NON-HEART-BEATING DONORS (NHBD)**

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Aim: To study the variables during pulsatile perfusion of kidneys (Waters-RM3) after prolonged warm ischemia (WI).

Methods: Pig experimental model of NHBD with 70 minutes of WI. Two groups: GI (without WI) and GII (with WI). One kidney was perfused in RM3 and the other was preserved static in UW at 4°C. We studied renal resistance (RR) and flows (F).

Results: Initial and final F were higher in GI than in GII (61.5 ± 30.5 mL/min; 161 vs 60.2 mL/min). RR diminished during perfusion in GI (from 0.9 to 0.3) and GII (from 1.9 to 0.9). In GI urine production started in the first perfusion hour whereas in GII started in the fourth hour, being the mean production at 6h 12.3 and 3.3 mL respectively. In GI and GII, the weight gain was 30g. Urine N-acetyl-glucosaminidase (NAG) levels in GI indicated high tubular lesion. In GII NAG decreased achieving similar levels to the GI group at the sixth perfusion hour.

Conclusion: RR values are indicative of the organ quality, suggesting the usefulness of the pulsatile perfusion to assess organ viability together with biopsy findings and renal function.

**PO-488 RISK PERCEPTION AND COMMUNICATION IN LIVING ORGAN DONATION**

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This study considers the concept of risk within the context of living organ donation for renal transplantation. Its aim is to understand what risk potential donors are willing to undergo and whether risk communication methods bear impact upon this response.

Method: A questionnaire was sent to donors at Guy’s Hospital, London between May 2003 and January 2005. Participants were asked to consider how much risk they may be prepared to undergo in order to donate when presented with different clinical scenarios. Two questionnaires were designed and were identical except in the risk communication. Questionnaire A was phrased in terms of risk of death (i.e. 1 in 3000) and B in terms of survival (i.e. 99.97%).

Results: 51 questionnaires were returned, 26 A and 25 B (66% return rate). Mean follow up was 298 days. 49 would have still donated had the risk of death been higher. 22 would accept a 5% risk of death to donate to their closest relative. Over 70% of these were from group B. The modal risk of death accepted by group A was 1% and by group B was 50%.

28 participants gave identical answers for each scenario and of those whose answers changed, 19 would accept increased risk as recipient's need increased.

Questions regarding different recipients were identically phrased and found significant differences between the groups.

Conclusion: In order to donate patients are willing to accept a much higher risk to their own lives than doctors would allow; some up to 50%. Those presented with risk in terms of survival are prepared to accept higher risks than those presented with risk in terms of death, suggesting risk communication methods do bear impact on response.

**PO-485 ENTERIC-COATED MYCOPHENOLATE SODIUM (EC-MPS) IN DE NOVO RENAL TRANSPLANT RECIPIENTS: SAFETY AND EFFICACY RESULTS OF A 1-YEAR PROSPECTIVE STUDY**

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Dose changes or interruptions during MMF treatment are common and may reduce the need for re-operation for these complications. Dose reductions or interruptions during MMF treatment are common and may reduce the need for re-operation for these complications. Only 37 patients (26%) required an EC-MPS dose reduction for 5 days (DR), 22 were due to adverse events, of which 6 were due to GI disorders, 8 of them were due to infections. Mean time to first DR was 60±67 days with a mean duration of 159±143 days. Dose interruptions (DI) were reported in 14 patients (10%), 13 of which were due to adverse events, with GI disorders accounting for 3, infections for 7. Mean time to first interruption was 88±87 days with a mean duration of 10±12 days.

Conclusion: myfortic® in combination with Neoral, demonstrated good efficacy and tolerability in de novo renal transplant recipients. Low rates of myfortic® Dose reductions and interruptions were observed, few of them due to GI events. Thus, myfortic® may be beneficial for long-term graft and patient outcomes.
PO-488 RISK FACTORS AND OUTCOME OF TRANSPLANT RENAL ARTERY STENOSIS (TRAS) IN ADULT RECIPIENTS
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Purpose: To determine the predisposing factors for transplant renal artery stenosis (TRAS) and to assess the impact of TRAS on graft survival after angioplasty.

Methods: We retrospectively reviewed the records of 29 renal allograft recipients with transplant renal artery stenosis (TRAS) and compared the control group with the TRAS group.

Results: Clinical presentation included refractory hypertension in 22 cases (75.8%) and rapid deterioration of renal function in 11 cases (37.9%). Predisposing factors for TRAS included CMV infection (41.4% vs. 12.1%; p = 0.018) and initial delayed graft function (48.3% vs. 15.5%; p = 0.02) respectively in the TRAS and the control group. Acute rejection occurred more frequently in patients from the TRAS group (48.3%) compared with the control group (27.6%), although the difference was not significant (p = 0.06). Overall graft survival was significantly higher in the control group, compared with the TRAS group (p = 0.03).

Conclusion: Despite angioplasty, patients who develop TRAS have a worse graft survival than patients who do not. CMV infection is a reliable risk factor for TRAS and acute rejection is likely to play an active role in TRAS pathogenesis.

PO-489 HAND ASSISTED LAPAROSCOPIC BILATERAL NATIVE NEPHRECTOMY
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Introduction: Bilateral native nephrectomy (BNN) is an uncommon procedure and has previously been performed by open transperitoneal or staged retroperitoneal surgery. Hand Assisted Laparoscopic (HAL) surgery was attempted in 5 renal transplant patients referred for BNN with the aim of decreasing somatic morbidity and providing earlier recovery from surgery.

Methods: Indications for surgery were: recurrent urinary tract infection (n=2), resistant hypertension (n=1) and acquired renal cystic disease (n=2) with loin pain and a complex mass in one and erythropoietin resistant anaemia in the other. All HAL BNN were performed with the patient in a supine position via the transperitoneal approach using a periumbilical incision for the GelPort(TM) (Applied Medical, USA) and 2x 12mm and 1x 5mm ports on each side. The operating table was tilted upward toward the side of nephrectomy and tilt was reversed for the second nephrectomy.

Results: Mean patient age was 44 years (range 35 to 57 years). Mean length of surgery was 317 minutes (range 235 to 404 minutes) and postoperative length of stay was 5 days (range 3 to 7 days). No patient required blood transfusion and mean intraoperative blood loss was 400ml (range 50 to 830mls). 2 patients had temporary postoperative ileus that resolved with conservative management. 1 patient had a post operative chest infection. 1 patient developed a port-site hernia that required elective surgical repair 6 weeks later.

Conclusions: HAL BNN is a complex minimally invasive surgical procedure in high-risk patients but was technically feasible with minimal intraoperative blood loss and no conversions in this series. Postoperative stay was short providing early return to normal activities.

PO-490 QUALITY OF LIFE OF DIABETIC PATIENTS PRIOR TO AND AFTER KIDNEY ONLY OR SIMULTANEOUS PANCREAS KIDNEY TRANSPLANTATION
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Purpose: Pancrase and kidney transplantation are now proven therapies for diabetic patients with renal failure. The objective of this study was to compare perceptions of diabetic kidney ± pancreas transplant recipients before and after transplantation, and diabetic patients currently on the transplantation waiting list.

Methods: A modified questionnaire incorporating the Ferrans Quality of Life Index (QLI) and Health-Related Quality Of Life (HROQL) was distributed to kidney only (n=101) or simultaneous pancreas kidney (n=32) recipients and renal failure patients awaiting transplantation (n=212). Satisfaction in various aspects of life (overall quality of life, health/functioning, psychological/spiritual, social, economic, and family relationships) was scored and analysed using SPSS to determine if there were any statistically, or any patients’ perception of their quality of life as well as details of comorbidities, graft function, rejection episodes, hospitalization, employment status and adverse effects of medications were also incorporated into the questionnaire.

Results: Results have shown that dialysis patients were generally dissatisfied with energy levels, diet, lifestyle restrictions, employment, sleeping patterns, and time required for treatment. Patients were more satisfied with their general well-being post transplantation, especially with sexual relationships, peace of mind (financial/family), and personal appearance. Most patients thought that their transplanted kidney(s) would function for at least 10 years after transplantation. Most dialysis patients also indicated that they would prefer xenotransplantation to dialysis if it were available, practical, and safe in the clinical setting.

Conclusions: Understanding the impact of transplantation on all aspects of quality of life may lead to improved management of patient compliance and adverse effects of therapy.

PO-491 THE DONORS’ PERSPECTIVE: A COMPARATIVE ANALYSIS OF SATISFACTION AFTER OPEN VS. LAPAROSCOPIC LIVING DONOR NEPHRECTOMY
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Laparoscopic donor nephrectomy offers low morbidity and excellent outcomes. Yet donor satisfaction has not been studied in detail.

All living donors were included (1977-2003). Open donor procedures were performed before 05/2000 and by hand-assisted laparoscopic technique thereafter. To evaluate donor satisfaction, a previously validated questionnaire was sent to all donors living in Switzerland.

162 donors were included (71 open and 94 laparoscopic). Baseline characteristics of both cohorts were comparable. Postoperative complications were mostly mild without differences between techniques.

111 of 130 questionnaires were returned (85%). Almost no donor felt pressured to donate or had been concerned about living with one kidney. The type of the surgical procedure and worries about the scar were not important in their decision to donate. The cohort of laparoscopic donors reported less postoperative pain, less pain after one week and a quicker return to normal activities.

They were also more satisfied with medical care and emotional support. After the procedure 92% of all donors had no concerns about living with one kidney and 97% agreed with the statement “I would do it again”.

Conclusion: In the long run almost all donors were very satisfied and would do it again, regardless of the technique. Due to significant somatic and psychological short term benefits, laparoscopy should be the technique of choice for living kidney donation.

PO-492 IDENTIFICATION OF PARAMETERS THAT CONTRIBUTE TO A SUCCESSFUL KIDNEY RETRANSPANTATION
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About 25% of the patients on the waiting list are retransplant candidates. Compared to primary grafts these patients have a higher incidence of graft loss, due to the sensitization by the primary graft. Discussion is emerging whether it is ethical to offer organs to these patients. We analyzed all retransplants performed from 1985 - 1996 (N = 9571) within Eurotransplant, and performed a multivariate analysis asking for the factors independently influencing graft outcome. Donor age, transplantation period, sensitization and HLA matching were found to be independent parameters influencing graft survival. The hazards ratio (HR) of these factors varied between 1.42 - 1.92. In a consecutive study (1996 - 2004, N = 3806 retransplants) we questioned the value of the dogma of repeated mismatches, earlier reported to be deleterious for the consecutive grafts. Repeated HLA-A, B and HLA-DQ mismatches had no influence on graft outcome. Repeated HLA-DR mismatches in sensitized patients were found to influence graft outcome in a multivariate analysis (HR = 2.35). Finally, we questioned the influence of specific HLA-DR antigens expressed by the recipient on the outcome of the retransplant. In a multivariate analysis we observed that patients expressing HLA-DR1 and/or HLA-DR5 had a significantly higher graft survival than patients not expressing these antigens (HR = 0.77 and HR = 0.79 respectively). We conclude that histocompatibility related parameters significantly contribute to the success of a retransplantation.
PO-493 PREVALENCE OF ANAEMIA ON MYCOPHENOLATE MOFETIL (MMF) IN RENAL TRANSPLANT PATIENTS
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2 Biostatistics Department, Pitié Salpêtrière, Paris, France.
This study was carried out to evaluate the prevalence of anaemia in the early post renal transplant period.
Methods: Our cohort of patients who received a renal allograft from 1993 to 2003 was entered into the study. The immuno-suppressive protocol consisted of antithymocyte globulin and steroids for all the patients. At induction, patients received azathioprine (AZA) from 1993 to 1996 and MMF from 1996 to 2003. Data of the month after transplantation were collected. Statistical analysis re-
correction was done for each patients taking into account the transfusion threshold and Hb at admission.
Results: 188 patients receiving AZA and 223 receiving MMF were included. Hemodialysis was necessary in 14% of the AZA group and 23% of the MMF group (p=0.03). CMV disease was more frequent in the MMF group (9.4% vs 3.7%, p<0.003). Before transplantation, Hb was higher in the MMF group (11.4 ± 1.9 vs 10.2 ± 2 g/dL, p<0.001). Transfusions during the first month post transplantation were more frequent in the MMF group (90.1% vs 47.3%, p<0.001). After standardisation, transfusions remained more frequent in the MMF group, even after adjustment for the occurrence of a tubulopathy, of a CMV disease and of tacrolimus treatment (adjusted RR 3.7 (2.0-6.7)).
Conclusion: It is associated with an increased risk of anaemia and trans-
fusion in the immediate post transplantation period. The risk is reduced there-
after, probably because of an increase of the inosine monophosphate dehy-
drogenase evidenced in the red blood cells.
PO-494 CORNER SAVING URETERAL REIMPLANTATION TECHNIQUE WITHOUT USING STENT
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Purpose: Complication rates differ from center to center according to the sur-
gical technique used by these centers. In this study we present our new tech-
nique which will simplify reconstruction even in a small caliber ureter. Our surgical technique used by these centers. In this study we present our new tech-
ique which will simplify reconstruction even in a small caliber ureter.
Methods: During 1975 to 1983, we performed 300 ureteroneocystostomies using the modified Polliano-Leadbetter technique. Later, extravesical Lich-Gregor technique was used in combination with temporary ureteral stenting. After September 2003, we began corner saving technique. Eighty two renal transplantations were performed since September 2003. Sixty one recipients were men, 21 were women. Sixty two out of 82 were living related, 20 were cadaver. Mean recipient age was 32±10.9 (7-63). Mean donor age was 38±13.1. Ureteral reimplantation was performed by running 60 monofila-
ment polydioxanone suture. A running suture which is started from three mil-
limeters ahead from the middle of the posterior wall finished three millimeters afterward. After the last stitch, both ends of suture material are pulled to lessen the tension. The anterior and posterior wall of the ureter and bladder are approximated tightly. Anterior wall is sewn either with the same suture or another running suture. After this technique, we have not used double J stent or any other stent for preventing ureteral stenosis at the anastomosis side.
Results: There are 2 (2.4%) ureter complications. One leak was from renal pelvis of the transplanted kidney and other the one was from the anastomo-
sis side. Both successfully treated by placing percutaneous ureterocystostomy catheter. None of the complications were required surgery.
Conclusion: With low complications rate, we believe that, our new technique is a safest way to perform ureteroneocystostomy.
PO-495 USEFULNESS OF PULSATILE MACHINE PERFUSION IN KIDNEYS FOR TRANSPLANT
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Aim: To study the usefulness of pulsatile perfusion of kidneys with risk factors of compromised viability (RFCV).
Methods: 1.Pulsatil machine (RFMV) of kidneys having RCFV: Donor age > 60, brain death (BD), hypertension, Diabetes Mellitus (DM), Non-heart-beating donors (NHBD). 2. Study of renal resistance (RR). 3. Study of renal post-transplant function of the RCFM-perfused kidneys (GI) and the non-perfused contra-lateral kidneys (GII) in static preservation.
Results: Between July and December 2004, 22 kidneys were perfused. Kind of donor: 17 BD and 5 NHBD, mean age of 57.9 years (30-79 years), 16 GI kidneys were transplanted (5 BD and 11 NHBD). The GI non-transplanted kidneys were from BD; 3 of them discarded because of biopsy findings, and 3 because of too high RR. 11 cases were compatible (8 BD and 3 NHBD). Mean perfusion time was 768 minutes (465-1110 min.). Post-transplant creatinine evolution was similar between GI and GII (2.0 ng/dL (GI) and 1.6 mg/dL (GII) at 30 days, and 1.7 mg/dL (GI and GII) at 90 days). Conclusion: RR is useful to assess the suitability of kidneys for transplant. It is necessary to increase the number of cases to test our technique in following periods of time in order to assess the usefulness of pulsatile perfusion and its effect on graft survival.
PO-496 TACROLIMUS RELATED NEUROLOGIC AND RENAL COMPLICATIONS. A SINGLE CENTER EXPERIENCE
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Purpose: After September 2001, we started tacrolimus (TAC) instead of ciclosporine A (CyA) in liver transplant patients. Tacrolimus is also potent imm-
unosuppressive drug and enables safer steroid withdrawal compared to CyA.
Methods: We performed 73 liver transplantations. Thirty four (46.5%) were children.
Results: During this period we encountered 16 (22%) tacrolimus related com-
lications. 12 were neurologic(NC), 4 were nephrotic, 4 cadaveric donors and 12 living donors. Nine of the patients were in pediatric age. There were 4 female and 12 male. Mean age 26±20 (6-99) years. Cholestatic and metabolic diseases in pediatric patients were the most common indications for liver trans-
plantation. Tacrolimus blood levels were normal in ranges. In 4 cases with nephroticly we switched to rapamycin(RAPA). Cases with NC, we switched to RAPA in 3 and CyA in 5. All trozenemia and in 6 (55%) Wilson disease patients had NC. Wilson disease was statistically significant risk factor for NC(p<0.02). NC patients received antiepileptic therapy. Death unrelated to NC occurred in one and refractory epilepsy developed in another patient who had previous epilepsy. NC reversed in all except one case. Renal functions also im-
poved in all cases. Creatinine clearance increased from 33.8±12.8 to 52±19.
We switched to rapamycin within first week after liver transplantation in 3, but we did not encounter any vascular complications.
Conclusion: Most transplant centers TAC has been first choice after liver transplantation. But NC and nephroticly are important morbidity in liver transplantation. Wilson disease and Trozenemia are more susceptible to neu-
rologic side effects of TAC. In these cases we recommend drugs which have less neurologic side effects. Nephrotic side effects of TAC can be reversed by RAPA.
PO-497 A PROSPECTIVE STUDY OF HUMAN HERPESVIRUS 6 (HHV-6) INFECTION IN RENAL TRANSPLANTATION
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Purpose: The aim of the study was to find out the relationship between kidney transplantation and HHV-6 infection.
Methods: Pretransplantation sera from 120 renal transplant recipients and their donors were analyzed for IgG to HHV-6 using enzyme – linked immunoas-
say. In the group of recipients serum samples obtained before and after 2, 4, 12, 48 weeks from the day of transplantation were tested for anti-HHV-6 IgM antibodies using indirect immunofluorescence assay. A real-time quantitative PCR assay was performed to determine the load of HHV-6A and -B DNA in samples positive for serum anti HHV-6 IgM.
Results: HHV-6 infection occurred in 43% of the patients. HHV-6 IgM serocon-
version was noted in 25 patients (12 recipients and 13 donors). 5 patients had two seroconversions (3 recipients and 2 donors). HHV-6 IgM antibodies were detected in 68% of the recipients and 52% of the donors.
Conclusions: HHV-6 infection was detected in persons with positive HHV-6 IgM. HHV-6 IgM seroconversion was more likely observed in the first 4 weeks after transplantation and was associated with WBC (p<0.002) and PLT (p<0.001) decrease as compared with those without seroconversion. The risk of HHV-6 IgM seroconversion in the HHV-6 IgG seronegative group (51 BD and 5 NHBD) was 5 times higher than that of HHV-6 IgG positive donors. Approximately 25% of patients with HHV-6 IgM seropositive patients (RR =2.24). IgM antibodies to HHV6 appeared in four from five patients who received allograft from HHV-6 seropositive donor and who were seronegative at the time of transplantation. In the group of HHV-6 sero-
positive recipients, the presence of IgG antibody in the sera of the donor has no association with the occurrence of IgM seroconversion.
Conclusions: HHV-6 is activated in many cases in the early posttransplant period. HHV-6 seronegative recipients were HHV-6 seropositive with IgM antibodies. HHV-6 IgM seroconversion can be triggered by HHV-6 infection. HHV-6 IgM seroconversion may be triggered by HHV-6 infection.
OUTCOME OF A THIRD KIDNEY TRANSPLANT: IS IT WORTH IT?

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In this retrospective study we assessed the outcome of recipients who received a third KT in our institution between 1989 to 2004 (n=35). There were 28 men and 7 women (median age = 43 years). In all the cases but two immunosuppression was triple and was sequential with induction therapy (thymocyte globulins: n = 26, OKT3: n = 6, anti-CD25 Moab: n = 1), steroids, azathioprine or mycophenolate mofetil and either ciclosporine A (n = 16) or tacrolimus (n = 19). The median follow-up is 5 years (0.5-7). Current patient and graft survival and the survival rate of graft and patient. All of the patient had a daclizumab in continuation, and/or interruption, and/or reduction was observed in 51 patients, Delayed graft function was present in 14 patients (40%), 10 patients presented with acute rejection (28.5%); of these five were steroid-resistant. Renal function was excellent with a mean creatinine clearance (± SD) of 58 (16.7) ml/min at day 90, 62 (20) ml/min at day 180, and 60 (21), 57 (24.5) and 57 (23) ml/min at 1.3 and 5 years, respectively. 15 patients presented with technical complications, including lymphocele (4), perirenal hematoma (2), ureteral stenosis (2), renal artery stenosis (2), and others reasons (5). 17 patients experienced infection episodes leading to re-hospitalization: 7 pyonephrosis, 4CMV infections, 3 peritransplant infections.

Conclusion: A third KT is associated, overall, with good results as far as patient and graft survivals are concerned. Complications, such as AR, technical problems, or infection are within the average range. Therefore, contemplating a third KT is worth it!

PO-499 PREDICTIVE FACTORS FOR MYCOPHENOLIC ACID DOSE MODIFICATION DURING THE FIRST YEAR AFTER RENAL TRANSPLANTATION

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The aim of this study was to determine factors associated with mycophenolic acid (MPA) dose modification during the first year after renal transplantation (RT). 130 patients were included in this study. MPA dose modification, i.e. discontinuation, and/or interruption, and/or reduction was observed in 51 patients, i.e. 39% in group I whereas MPA dose remained unchanged in 79 patients i.e. 60% in group II. The median time between the renal transplantation and the first dose reduction was 60 (15-290) days. Donors’ and recipients’ ages, the percentage of highest panel reactive antibodies and at the time of RT the, the number of previous RT, and serum creatinine level at 1 month were significantly higher in group I. Donor creatinine clearance, one month creatinine clearance, and pretransplant lymphocyte counts were significantly lower in group I. Dose modification occurred also significantly more frequently; (i) in patients receiving mycophenolate mofetil vs. enteric-coated mycophenolate sodium, (ii) in those who received polyclonal antibodies vs. anti-CD25, (iii) in those who received sirolimus, and finally (iv) in those who had a positive cytomegalovirus (CMV) viremia. The number of positive CMV viremia was also significantly higher in group I. Patients who were treated by cyclosporine A had significantly less MPA dose modification than those who were treated by tacrolimus or sirolimus or serum creatinine > 4.5 mg/dl were the exclusion criteria.

Results: After 3 years of follow-up two patients had further impairment of renal graft function, in 3 recipients graft function stabilized and in remaining 12 cases an improvement of serum creatinine was observed (mean value 2.4 vs. 1.74, p <0.003). Total blood cholesterol decreased significantly after third year of treatment with MPM (mean value 228.5 vs. 207.1 mg/dl, p <0.05). Blood pressure values were comparable before and after treatment conversion.

Conclusion: Our preliminary data confirm other reports that MPM for AZA conversion is beneficial for long term renal allograft function and lipid profile in recipients diagnosed with CAN.

PO-502 BONE MINERAL DENSITY CHANGES IN RENAL TRANSPLANT PATIENTS ON LOW-DOSE STEROIDS. A FOUR YEAR PROSPECTIVE STUDY

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Objectives: To investigate the long-term evolution of bone mineral density (BMD) in renal transplant patients on low-dose steroids.

Methods: 94 patients with functioning grafts, 72 on tacrolimus and 22 on cyclosporine-based immunosuppression were included in the study. BMD was measured in lumbar spine (L2-L4) and femoral neck (FN) by DEXA, in the first month after transplantation and yearly thereafter.

Results: There were no variations in lumbar spine BMD in the overall group but BMD increased in FN (p < 0.001) during the follow-up. However, three different patterns were identified at 12 months: BMD increased in L2-L4 by 8.7% in 29 patients (30.8%), remained stable in 31 (33%) and decreased by 5.8% in 33 (35.1%). The improvement was maintained through out the follow-up (0.830 ± 0.162 g/cm2 at baseline and 0.909 ± 0.169 at 4 years; p < 0.001) and there was a parallel increase of BMD in FN (p < 0.01). While lumbar bone loss mostly occurred in the first 12 months. Patients with BMD gain had lower BMD in L2-L4 at baseline (p < 0.01) and higher levels of calcitriol at 12 months (p < 0.01). There were no differences among the groups in graft function, IPTH levels, postmenopausal women or steroids’ doses. After 12 months, 30 patients were treated with calcium supplements and vitamin D3, no changes in L2-L4 and FN were observed.

Conclusions: About one third of patients had bone loss during the first year after transplantation. Oral calcium and calcidiol did not improve lumbar mineral bone. 
PO-503  S-CYSTATIN C AS PREDICTIVE PARAMETER FOR ACUTE ALLOGRAFT REJECTION IN PATIENTS AFTER RENAL TRANSPLANTATION

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Purpose: Rejection after renal transplantation is a common and dangerous complication. Nowadays kidney biopsy and histological examination is considered to be gold standard to differentiate between rejection and other reasons for transplant function loss. Nevertheless kidney biopsy might be followed by dangerous complication. Right now there is no parameter to be considered the most eligible for early clinical diagnoses of rejection without biopsy. Aim of the study was to evaluate whether S-cystatin C is a more reliable parameter indicating acute allograft rejection (AAR) following kidney transplantation compared to creatinine, urea or creatinine clearance (Crea-Ci).

Methods: We analyzed postoperative courses of 70 consecutive renal transplant patients of one center. Only biopsy proven rejection episodes were considered.

Results: 1. 19 of the investigated patients developed biopsy proven AAR or borderline rejection (BR). In 68% of the patients experiencing AAR or BR a simultaneous increase of S-cystatin C and S-crea was observed. Meanwhile GFR decreased while urea showed indifferent courses. 2. In certain cases S-cystatin C was the only parameter indicating AAR. 4. Crea-Ci showed to be the most unreliable parameter.

Conclusion: 1. S-Cystatin C should be considered as a more reliable parameter than Crea-Ci. 2. S-cystatin C and the related GFR seems to be a save and more effective indicators for kidney function and AAR especially under outpatient clinical use. 3. In certain cases S-cystatin C might be useful to detect AAR at an earlier time point. 4. This might result in superior long term graft function.

PO-504  ACCIDENTAL TRANSPLANTATION OF A KIDNEY WITH A RENAL CELL CARCINOMA FOLLOWING LIVING DONATION: MANAGEMENT AND 1 YEAR FOLLOW UP

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Cases of transmission of cancer from organ donors are limited. To our knowledge transmission of a renal cell carcinoma from a living donor (LKD) was not reported so far.

Courses of a LKD accidentally presenting a renal cell carcinoma within the kidney graft and the corresponding recipient were studied. Follow up to 1 year is now completed.

A 56 years old father was evaluated as a LKD for his 27 years old daughter. Evaluation revealed 2 cysts at the upper pole of the right kidney. Since it is our policy to remove the kidney presenting anatomical or functional abnormalities right sided donor nephrectomy was performed. Prior kidney transplantation the wall of the prominent cyst was partially removed and examined by routine histology. Two weeks after successful kidney transplantation (KT) results of histology revealed a highly differentiated renal cell carcinoma within the cyst wall. Following careful evaluation the recipient was re-operated and the upper pole of the kidney graft was resected 5 weeks after KT. The primary immunosuppression was switched to a rapamune based regimen. Graft function remained stable with a serum creatinine of 163 µmol/L. One year after LKD and KT the donor and the recipient are without any evidence of tumor recurrence. Our policy in LKD to obtain the kidney presenting anatomical variations proved to be beneficial for the donor. In case of transmission of cancer from kidney grafts partial resection of the kidney preserving graft function might be justified. However, a much longer follow up is required.

PO-505  KIDNEY TRANSPLANTATION WITH CONCOMITANT UNILATERAL NephrectomY: A MATCHED-PAIR ANALYSIS ON COMPLICATIONS AND OUTCOME

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Background: This study was conducted to examine the impact of kidney transplantation with simultaneous unilateral nephrectomy on perioperative morbidity and patient and graft survival. Patients: From January 1990 to May 2004, 75 kidney transplants with simultaneous unilateral nephrectomy were performed (group NE+). Of those, 49 had polycystic kidney disease (PKD). Patients of group NE+ were matched with 75 kidney transplants without nephrectomy (group NE-) for recipient age, cold ischemia time, donor age, time of dialysis and pre-transplant morbidity score. Immunosuppressive therapy in both groups consisted of cyclosporine A, prednisone, mycophenolate mofetil or azathioprine and, in certain cases basiliximab or antithymocyte globulin.

Results: Mean follow up was 4.1 yrs (range 0.3 - 11.7 yrs). Patient survival rate at 1 and 5 yrs in group NE+ was 95% and 84% versus 95% and 93% in group NE- (p=0.56) with a kidney function rate between 85% and 74% in group NE+ versus 89% and 79%, resp. in group NE- (p=0.89). Perioperative (90 days) mortality rate in group NE+ was 1.3% and 2.7% in group NE- (p=0.56). Major perioperative complications occurred in 8% (n=6) of patients in group NE+ and in 4% of patients in group NE- (n=3; p=0.30).

Conclusions: Kidney transplantation with concomitant unilateral nephrectomy has no negative impact on patient or graft survival and can be performed with an acceptable morbidity rate.

PO-506  ALLEmtuzUMAB IN A NOVEL IMMUNOSUPPRESSION PROTOCOL FOR KIDNEY TRANSPLANT

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Introduction: Side effects from long term immunosuppression and chronic allograft nephropathy have become a matter of paramount importance. New strategies to prolong the lifespan of renal allografts and decrease the side effects of chronic immunosuppression are needed. The introduction of new agents and stratified immunosuppression protocols led to a reduction in rejection rates from over 50% to less than 40% in our unit, as others. In an attempt to minimize the morbidity of conventional immunosuppression without increasing rejection rates we have conducted a study based on the use of an anti-CD52 monoclonal antibody: alemtuzumab.

Material and Methods: Twenty consecutive patients were included in this study and received Alemtuzumab, on days 0+1, followed by maintenance immunosuppression with mycophenolate daily and low-dose tacrolimus for the first six months. Subsequently, tacrolimus was switched to sirolimus. Routine follow-up of patients and renal function were monitored. Lymphocyte populations were monitored before and after transplantation.

Results: Follow-up of the patients ranged from 3 weeks to 6 months. Tacrolimus levels were maintained between 5-8 nmol/L. The rejection rate was 0% at 3 months. No steroids were required except for perioperative administration to cover reperfusion and the first dose of Alemtuzumab. A mild neutropenia in three patients resolved spontaneously. Complications included CMV infection, myocardial infarction, cellulitis and deep vein thrombosis (one patient each). No patient has developed malignancy.

The mean creatinine level at four weeks was 157 mmol/L.

Conclusion: Alemtuzumab based immunotherapy is an effective and safe alternative to conventional regimens. The avoidance of steroids and limited use of calcineurin inhibitors might reduce long term graft damage as well as steroid-related morbidity.

PO-507  POSTOPERATIVE COMPLICATION RATE AND DONOR RECOVERY RATES IN A CONSECUTIVE SERIES OF 90 LAPAROSCOPIC LIVE DONOR NEPHRECTOMIES

Monika Kaushik, Nicholas R. Brook, Simon S.J.F. Harper, Mark D. Kay, Atul Bagul, Rosemary Elwell, Michael L. Nicholson. Cardiovascular Sciences - Transplant Group, University of Leicester, Leicester General Hospital, Leicester, United Kingdom.

Purpose: Laparoscopic live donor nephrectomy (LDN) has the potential to overcome some of the disincentives to kidney donation but has yet to be widely adopted in the UK. This study presents results of postoperative complication rates and donor recovery times of a consecutive series of 90 LDN from a single centre.

Methods: 90 live donors (mean age 45yrs) underwent transplantation. There was no selection on the basis of BMI (18-45 kg/m²) or difficult vascular anatomy. In general the left kidney was preferred to right in view of renal vein length. All patients received postoperative analgesia using PCAS. Subcutaneous heparin and TED stockings were used for thromboembolic prophylaxis. Donors were allowed to resume normal activities at their own discretion.

Results: There was no mortality and episodes of thromboembolism. 2 operations were converted to open, both because of bleeding (1 from renal artery and 1 port site bleed).

Table 1. Donor recovery rates (mean±SD)

| Inpatient stay | 4±1 days |
|---------------|----------|
| Duration of PCAS | 42±12 hours |
| Driving | 2±2 weeks |
| Shopping | 2±2 weeks |
| Exercising | 4±3 weeks |
| Return to work | 6±2 weeks |
The postoperative complications were: chest infection 6(6.7%); L1 dermatome paraesthesia 3(3.3%); wound infection 4(4.4%); pulmonary oedema 2(2.2%); ileus 2(2.2%); testicular pain 2 (2.2%); persistant wound pain 1(1.1%). Recepti-
transplantation was complicated by 1 graft loss due to thrombosis and 2 ureteric stenoses. 
Donor recovery rates (mean ± SD) are presented in Table 1.

Conclusions: There is an appreciable mortality in fit and healthy individuals undergoing LDN. This new operation was associated with some unexpected complications. Nonetheless, donors returned to the normal activities of life quickly following LDN.

**PO-509 COMPARISON OF RIGHT AND LEFT LAPAROSCOPIC LIVE DONOR NEPHRECTOMY**

Mark D. Kay, Nicholas R. Brook, Monika Kaushik, Simon J.F. Harper, Atul Bagul, Michael L. Nicholson. Cardiovascular Sciences - Transplant Group, University of Leicester, Leicester, United Kingdom.

**Purpose:** Laparoscopic live donor nephrectomy (LDN) may reduce some of the disincentives to kidney donation. Many surgeons are reluctant to procure the right kidney laparoscopically because of its short vein. The aim of this study was to compare the anatomy and function of right and left kidneys retrieved by LDN.

**Methods:** 84 transperitoneal LDN were performed, 66 left and 18 right. Two different right sided LDN techniques were used: initially after laparoscopic dissection of the kidney and renal vessels, the inferior vena cava (IVC) was controlled with a Satinsky clamp introduced through a mid right upper quadrant incision, through which the kidney was removed (n=8). Subsequently, the IVC was completely mobilised by laparoscopic retro caval dissection (n=12). This allowed use of a linear stapler-cutter, including the caival oristum with the renal vein. The right kidney was then removed through a short Pfannenstiel incision. All left kidneys were removed through a Pfannenstiel incision.

**Results:** Left kidneys had longer renal veins (38 vs 27 mm; P<0.05), but there were no differences in arterial length (32 vs 31 mm). Three right kidneys required renal vein lengthening using recipient saphenous vein grafting. Two left LDN were converted to open operation for bleeding. Operating time was shorter for right sided LDN (132 vs 182 min; P<0.05). Operating time was not different right or left renal veins. The functional results of right and left kidneys are equivalent.

**PO-508 THE INCIDENCE AND OUTCOME OF TRANSPLANT RENAL ARTERY STENOSIS (TRAS) – SINGLE CENTER EXPERIENCE**

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**Introduction:** The incidence TRAS varies from 1% to 23% depending on the definition and diagnostic techniques.

**Purpose:** The aim of this study was to determine the incidence of TRAS in our institution and to analyze the treatment options, and the outcome.

**Material and methods:** Retrospective analysis of all medical records of 896 kidney allograft recipients transplanted between 1998 and 2004 was performed to find patients with TRAS.

**Results:** The incidence of TRAS in our institution over the last 17 years was 1.0% (9 patients). Time from KTx to first symptoms of TRAS ranged from 5 weeks to 4 years (median 4 months). In three patients refractory hypertension occurred and six patients developed allograft dysfunction. Screening color-Doppler ultrasonography showed hemodynamic changes associated with TRAS in six patients and the definitive diagnosis of TRAS was confirmed by angiography in all patients. Two patients with anastomotic stenosis underwent surgery and seven patients had percutaneous transluminal angioplasty (PTA) with stenting in 3 cases. Both surgical as well as PTA treatment was successful in all but one patients. One patient treated with PTA alone developed chronic insufficiency of the renal allograft and finally he lost his graft. In the remained patients all symptoms resolved after treatment.

**Conclusions:** In our material TRAS was an uncommon complication after KTx. If recognized properly, it can be treated by surgery or PTA with a high success rate.

**PO-510 NORMOTROPIC VERSUS HYPOTROPIC EX VIVO PRESERVATION SOLUTION AND A STANDARD HYPOTROPIC METHOD IN RENAL ALLOGRAFTS**

Mark D. Kay 1, Sarah A. Hosgood 1, Simon J.F. Harper 2, Douglas Rees 2, Michael L. Nicholson 1. 1Cardiovascular Sciences - Transplant Group, University of Leicester; 2Res-Del International Ltd. London.

**Purpose:** The aim of this study was to assess renal function after an ex vivo warm flush with a novel non-phosphate buffered preservation solution (RS-I). 

**Method:** Porcine kidneys were flushed with either AQIX® RS-I at 30°C or a hyperosmolar citrate preservation solution at 4°C at a pressure of 1000mmHg after 5-10 minutes warm ischaemic time, followed by cold storage for 2 hours (N = 6 per group). An assessment of renal function was made by perfusing the organs with autologous blood at 37°C, with an initial circulating serum creatinine concentration of 1000mmol/L on an isolated organ perfusion system.

**Results:** The AQIX® RS-I group flushed significantly faster than the hyperosmolar citrate group, 20.6±2.3 vs 10.0±1.63min/millL0g respectively (p<0.0022). Oxygen consumption, renal blood flow and resistance were all significantly bet-

**PO-507 COMPARISON OF RIGHT AND LEFT LAPAROSCOPIC LIVE DONOR NEPHRECTOMY**

Mark D. Kay, Nicholas R. Brook, Monika Kaushik, Simon J.F. Harper, Atul Bagul, Michael L. Nicholson. Cardiovascular Sciences - Transplant Group, University of Leicester, Leicester, United Kingdom.

**Purpose:** Laparoscopic live donor nephrectomy (LDN) may reduce some of the disincentives to kidney donation. Many surgeons are reluctant to procure the right kidney laparoscopically because of its short vein. The aim of this study was to evaluate the incidence of CMV disease and its influence on early graft function.

**Methods:** 84 transperitoneal LDN were performed, 66 left and 18 right. Two different right sided LDN techniques were used: initially after laparoscopic dissection of the kidney and renal vessels, the inferior vena cava (IVC) was controlled with a Satinsky clamp introduced through a mid right upper quadrant incision, through which the kidney was removed (n=8). Subsequently, the IVC was completely mobilised by laparoscopic retrocaval dissection (n=12). This allowed use of a linear stapler-cutter, including the caival oristum with the renal vein. The right kidney was then removed through a short Pfannenstiel incision. All left kidneys were removed through a Pfannenstiel incision.

**Results:** Left kidneys had longer renal veins (38 vs 27 mm; P<0.05), but there were no differences in arterial length (32 vs 31 mm). Three right kidneys required renal vein lengthening using recipient saphenous vein grafting. Two left LDN were converted to open operation for bleeding. Operating time was shorter for right sided LDN (132 vs 182 min; P<0.05). Operating time was not different right or left renal veins. The functional results of right and left kidneys are equivalent.

**Conclusions:** Despite shorter operating times suggesting that right LDN is technically easier, there is a greater need for back-table reconstruction of the left kidney.

**PO-507 THE INCIDENCE AND OUTCOME OF TRANSPLANT RENAL ARTERY STENOSIS (TRAS) – SINGLE CENTER EXPERIENCE**

Wojciech G. Polak, 1 Dominika Jezior, 2 Jerzy Garcapek, 2 Pawel Chudoba, 1 Dariusz Patrzalek, 1 Maria Boratynska, 2 Piotr Szyber, 1 Marian Klinger 3. 1Department of Vascular, General and Transplant Surgery, Wroclaw Medical University, Wroclaw, Poland; 2Department of Nephrology and Transplantation Medicine, Wroclaw Medical University, Wroclaw, Poland; 3Department of Radiology, Wroclaw Medical University, Wroclaw, Poland.

**Introduction:** The incidence TRAS varies from 1% to 23% depending on the definition and diagnostic techniques.

**Purpose:** The aim of this study was to determine the incidence of TRAS in our institution and to analyze the treatment options, and the outcome.

**Material and methods:** Retrospective analysis of all medical records of 896 kidney allograft recipients transplanted between 1998 and 2004 was performed to find patients with TRAS.

**Results:** The incidence of TRAS in our institution over the last 17 years was 1.0% (9 patients). Time from KTx to first symptoms of TRAS ranged from 5 weeks to 4 years (median 4 months). In three patients refractory hypertension occurred and six patients developed allograft dysfunction. Screening color-Doppler ultrasonography showed hemodynamic changes associated with TRAS in six patients and the definitive diagnosis of TRAS was confirmed by angiography in all patients. Two patients with anastomotic stenosis underwent surgery and seven patients had percutaneous transluminal angioplasty (PTA) with stenting in 3 cases. Both surgical as well as PTA treatment was successful in all but one patients. One patient treated with PTA alone developed chronic insufficiency of the renal allograft and finally he lost his graft. In the remained patients all symptoms resolved after treatment.

**Conclusions:** In our material TRAS was an uncommon complication after KTx. If recognized properly, it can be treated by surgery or PTA with a high success rate.

**PO-507 LEFT VERSUS RIGHT KIDNEY IN LAPAROSCOPIC LIVING DONOR KIDNEY TRANSPLANTATION**

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**Introduction:** The choice of laparoscopically harvested kidneys is usually determined by the surgeon’s optimal access and fear of a short right renal vein.
KIDNEY TRANSPLANTATION AND THE INNATE IMMUNE SYSTEM – THE ROLE OF TLR-POLYMORPHISMS

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Background: The impact of the innate immune system on kidney transplantation is the subject of intense research. The recently recognized TLRs are involved in acute rejection through their ability of generating proinflammatory cytokines, or maintaining chronic inflammation. Therefore we hypothesise that genetic variations in the TLR-system may affect clinical outcome of kidney transplantation through different activation pathways of the innate immunity. We determined several polymorphisms (SNPs) in the TLR2, TLR3, TLR4 and TLR9 gene.

Methods: In 281 patients receiving their first kidney transplant, the following SNPs in the TLR-system were analyzed (TLR2: R677W, del -196/-174; TLR3: F412L, T737S; TLR4: T399I, D299G; TLR9: P545P , -1237T/C) by real-time PCR. Statistical analyses were performed using the SPSS statistical package.

Results: Every SNP was in Hardy-Weinberg Equilibrium except TLR3 T737S, which was monomorphic in our population. For the F412L-TLR3-polymorphism (CC-allele) we found a significantly higher rate of acute rejection (43.6% vs. 22.7%, p=0.002), as well as a significantly higher rate of delayed graft function (21.4% vs. 12.1%, p=0.04). Interestingly there was no effect on graft survival, 

Conclusions: Lapsoscopic harvesting of right kidneys did not increase vascular complications. Symmetric kidneys on CT or MRI showed significant differences in preoperative scintigraphies, allowing the team to respect the rule "keep the best kidney for the donor".

PO-514 STATIC NORMOTHERMIC PRESERVATION OF RENAL ALLOGRAFTS USING A NOVEL NON-PHOSPHATE BUFFERED PRESERVATION SOLUTION

Mark D. Kay 1, Sarah A. Hesgood 1, Simon J.F. Harper 1, Douglas Rees 2, Michael L. Nicholson 1, 1Cardiovascular Sciences - Transplant Group, University of Leicester, United Kingdom; 2Rees-Del International Ltd, London.

Purpose: The aim of this study was to assess the viability and function of renal allografts under normothermic conditions using a novel non-phosphate buffered preservation solution AQIX®-RS-I.

Methods: Porcine kidneys were flushed at 30°C with AQIX®-RS-I at 100mmHg pressure after 5-10 minutes warm ischaemic time, and stored statically at either 4°C or 30°C for 2 hours (n=6 per group). Assessment of renal function by physiological and biochemical parameters was performed by perfusing the organs with autologous blood at 37°C, with an initial circulating serum creatinine concentration of 1000µmol/l on an isolated organ perfusion system for 6 hours.

Results: Although the hypertrophied group demonstrated overall superior renal function, the normothermically stored kidneys displayed a statistically comparable ability to recover post-ischaemia. Furthermore renal function was still evident after 6 hours perfusion with increasing oxygen consumption, renal blood flow and reduced renal vascular resistance.

Conclusions: The effectiveness and versatility of AQIX®-RS-I as a preservative buffer for both normothermic and hypothermic organ preservation has been demonstrated. Renal viability was maintained after 2 hours static normothermic storage. This study provides a foundation for further analysis utilising normothermic preservation.

PO-515 IMMUNOSUPPRESSIVE REGIMENS AND THE RISK OF CANCER AFTER KIDNEY TRANSPLANTATION: A 32-YEAR EXPERIENCE

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Background: New potent immunosuppressive regimens (IR) have prolonged kidney transplant survival (KTx) survival, but their impact on the development of de novo malignancies has not been completely defined. We report incidence and type of neoplasias arising following KTx, based on the different IR employed over a 32-year period.

Methods: The study included data from 807 recipients undergoing 816 KTx between 1972 and 2003. For every patient the follow-up was prolonged until death or tumor diagnosis. Recipients were stratified into 5 groups based on the IR employed: Era-1: azathioprine/stereoids (n=29); Era-2: cyclosporine/stereoids (n=197); Era-3: calcineurin inhibitors (CNI)/azathioprine/stereoids (n=185); Era-4: CNI/MMF/stereoids (n=373); Era-5: sirolimus/MMF/stereoids (n=12).

Results: After 5,928 person-years follow-up, 65 recipients were diagnosed with 73 tumors (9.0%); 28 non-melanoma-skin-cancer (n-MSC), 30 carcinomas, 9 PTLD, 5 sarcomas and 1 pheochromocytoma. Mean age at diagnosis was 57.4 years for n-MSC and 51.5 years for other tumor types (n-SC). The interval between KTX and tumor diagnosis was 58.0 months for n-MSC and 86.9 months for n-SC. No recipient died due to n-MSC; mortality rate for n-SC was 1.4%. Relative risk (RR=observed/expected in general population) for n-SC was 1.8. Significant risk factors at multivariate analysis were: recipient age, prolonged immunosuppression, donor type, IR-Era. Stratifying RR according to IR-Era, showed increased tumor risk (RR-Era 1=1.06;RR-Era 4=1.85;p=0.02). In Era-5 no tumor has been recorded. Use of T-cell-depleting antibodies was not associated to increased PTLD risk.

Conclusions: Powerful IR allow extended graft survival but is associated to increased tumor risk. Melanocytic oncological screening and individualized immunosuppression might be both beneficial.

PO-516 SERUM AND URINARY EXPRESSION PROFILES OF THE IMMUNOMODULATORY ENZYME INDOLEAMINE 2,3-DIOXYGENASE IN PATIENTS AFTER KIDNEY TRANSPLANTATION

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Purpose: Indoleamine 2,3-dioxigenase (IDO) via tryptophan depletion inhibits T-cell proliferation and leads to T-cell anergy. The role of IDO in solid organ transplantation has not been clarified yet.

Methods: 35 renal transplant recipients were followed during the first 4 post-operative weeks. Immunosuppression consisted of calcineurin-inhibitor based triple therapy. Serum and urine concentrations of kynurenine and tryptophan were analysed by HPLC. Kynurenine per tryptophan ratios (kyn/trp) were calculated as an indirect estimate of IDO activity. Intragraft expression of IDO was assessed by immunohistochemistry. Neopterin levels were assessed using radioimmunossay.

Results: Patients with an uncomplicated postoperative course showed a significant decrease of serum kyn/trp by the end of the first week (day 5: 4.6±2.5; day 15: 4.1±1.9; day 19: 4.7±2.4) when compared to pretransplant levels (153±21). However, there was a slow increase of serum kynurenine and a decrease of tryptophan concentrations in patients with acute rejection episodes (113±35; p<0.05). In parallel urinary kyn/trp was significantly higher during rejection (186±56) than in cases of stable graft function (67±34; p<0.05). Serum and urinary kyn/trp correlated significantly with neopterin concentrations suggesting an INF-γ induced increase in IDO activity. Intragraft IDO staining was...
localised predominantly in renal tubular epithelial cells in Banff II biopsies, whereas normal renal biopsy did not stain for IDO.

Conclusion: Acute rejection is associated with simultaneously increased serum and urinary kynurenine in patients after kidney transplantation. ABO activity may thereby serve as a novel, reliable marker of allo-immune activation.

CASE REPORT: GIANT ARACHNOID CYSTS IN THE MAN WITH POLYCYSTIC KIDNEY DISEASE (ADPKD) AND CEREBELLMUM STROKE

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ADPKD is frequently associated with cyst formation of different extrarenal localisation. However, the unique occurrence of giant arachnoid cyst was infrequently reported. The 40-year-old man, with ADPKD and kidney transplant since 3 years, was admitted to the hospital because of facial asymmetry, speaking disorders, dizziness, nausea, vomiting, buzzing in the right ear, and double vision. The extent ischaemic stroke of lower part of right hemisphere of cerebellum and brain trunk was diagnosed. Moreover MRI examination revealed two giant arachnoid cysts. The larger one was 6.0 x 9.5 cm and the second one was 1.5 x 5.0 cm in diameter with no indications for neurosurgical treatment. The supratentorial vascular was narrowed on the left side. In clinical examination the horizontal and circumcircular nystagmus, signs of peripheral paresis of right facial nerve as well as slight signs of right-side paresis were observed. Kidney graft function was well preserved, with no signs of inflammatory status. Blood count revealed posttransplant erythrocytosis. Before that incidence the patient have no symptoms of cerebral disorders and actively worked. The triple immunosuppressive therapy based on CsA (blood through level - 80 - 100 ng/ml), azathioprine (1 mg/kg) and prednisone (5 mg QD). Because of erythrocytosis ACE inhibitor was introduced. After one month of treatment patient was self-reliant but exhibited paresis of right facial nerve and right side partial deafness and vision disturbance.

Conclusion: The giant intracranial arachnoid cysts was accidentally discovered in the ADPKD man with independent neurologic disorder. The peculiarity relies on the dimension of the cyst (9.5 cm), comparing to the previously reported.

ABDOMINAL AORTIC ANEURYSM IN PATIENTS WITH RECENT ALLOGRAFT: EXPERIENCE OF ENDOVASCULAR OR OPEN REPAIR IN 6 RECIPIENTS

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Purpose: Wider indications for kidney transplantation (KT) and increasing survival, increase the number of renal transplant patients (RTPs) undergoing aortic reconstruction. The purpose of the study deals on indications to endovascular vs open abdominal aortic aneurysm (AAA) repair and on the use of temporary aorto-femoral shunt (AFS), as the safer, less invasive and cheaper technique.

Patients and Methods: 6 consecutive patients, out of our 2555 transplants, were submitted to AAA reconstruction at our institution. All RTPs had received their graft from a cadaver. Their mean age at transplantation was 35.1±11.1 years (range: 18-50 yrs). The mean interval between KT and aortic reconstruction was 20.3±11.0 years (range 4 to 31 years). Heavy comorbidities was assessed in 83% of the patients. Aortofermal extracorporeal perfusion was adopted in one patient, AFS was placed in 3 cases. A modular bifurcated endovascular stent graft was inserted by a transfemoral route in another patient.

Results: All patients had an uneventful postoperative course; hospital stay was 8.3±3.7 days after the operation: the renal function was unchanged at discharge. One patient died from sudden myocardial infarction 37 months later. 5 patients are alive with a normal renal function for more than 10 months to 13 years after the AAA repair. The patient operated on by endovascular repair is alive from 64 months.

Conclusions: Although RTPs have an increased risk of vascular complications in the postoperative period, an individualized approach for repairing AAA offers the same prognosis of success, if compared to that of non transplanted population.

THE PREDICTIVE VALUE OF BANFF SCORE OF EARLY KIDNEY ALLOGRAFT BIOPSY ON OUTCOME AFTER COMBINED LIVER-KIDNEY TRANSPLANTATION

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The aim of the study was to evaluate Banff criteria scores of acute rejection of early kidney allograft biopsies. We analyzed data of 71 patients who had renal allograft biopsy within the first posttransplant month. All biopsies were performed in case of delayed or deteriorated graft function. One year after transplantation 16 patients exhibited excellent renal function (group I, Scr ≤ 1.4 mg/dl), 30 patients had preserved renal function (group II, Scr 1.51-1.99 mg/dl), 18 patients had deteriorated renal function (group III, Scr ≥ 2.0 mg/dl). Seven recipients lost their grafts within one year after transplantation (group IV).

Results: Mean “g” and “v” scores were significantly higher in group IV comparing to group II, and also Banff index was significantly higher in group IV in comparison to group I. Positive correlations were observed between: “ah” and Scr (39, 90, 180 day); “g” or Banff index and Scr (90, 180 day) (p<0.05).

Conclusion: Our data shows that the deterioration of renal function was connected with higher Banff score index, glomerulititis and vasculitis. Glomerulititis, arteri hyalinosis and Banff index were correlated to graft function one year after transplantation.

OUTCOME AFTER COMBINED LIVER-KIDNEY TRANSPLANTATION

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Combined Liver-Kidney Transplantation (CLKTx) is the best and definitive solution for patients suffering from concurrent irreversible liver and renal failure or for some hereditary disorders. Between February 1987 and July 2004, 14 adult patients (8 women, 6 men, mean age: 38 ± 18 y) received a CLKTx in our institution. Indications for Liver Tx were: Primary Hyperoxaluria (3), APKD (1), PPKD associated to Caroli disease or hepatic fibrosis (2), cirrhosis (post HCV:3, post HBV:2, Wilson disease:1, autoimmune:1), chronic first liver Tx resection:1). Renal failure required haemodialysis in 7 patients, and was severe in 7 patients (mean creatinin clearance: 26 ml/min). Mean waiting time was very variable: 196 days (from 7 to 670). Immunosuppressive regimen was: MMF+Tacrolimus+steroids (CS) in 9, Azathioprine+ciclosporine+CS in 4 and Azathioprine+CS in 1. Three patients died within the first 3 months postCLKTx because of sepsis. Patient survival rate is 78% and remain unchanged still now. Today, eleven patients are alive with a median follow-up of 36 months (8 to 180); 10 with both liver and renal functioning graft, the last one needed a liver retransplantation for post-HCV cirrhosis recurrence 38 months after CLKTx. Acute renal rejection occurred in 2 patients and no liver rejection was observed.

Conclusion: CLKTx offer an excellent survival rate of both liver and kidney graft with a very low acute rejection rate. High initial mortality requires new strategies in order to choose the best timing for CLKTx.

ENTERIC-COATED MYCOPHENOLATE SODIUM (EC-MPS) IS EFFECTIVE AND SAFE IN DE NOVO RENAL TRANSPLANT HIGH-RISK RECIPIENTS

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The safety and efficacy of myfortic® (EC-MPS) in combination with Neoral (CSA; cyclosporine microemulsion) has been proven in several studies. The percentage of high-risk patients in these studies was low while this population
is increasing. In our analysis we assessed the safety and efficacy of EC-MPS in de novo kidney, high-risk transplant recipients.

**Methods:** In a previously published de novo study 164 renal transplant patients were treated with EC-MPS in combination with CsA (monitored by C2), Simulect (basiliximab), and steroids. High-risk patients were selected and had at least one of the following criteria: black recipients, recipients <60yrs, donors >55yrs, >4 HLA mismatches, prior transplantation, non-heart beating donors (NHBD), and PRA >35%.

**Results:** 113 out of 164 patients were high-risk patients (38.1% black, 19.5% >60yrs, 9.7% donors >55yrs, 62.8% >4 HLA mismatches, 5.3% prior transplant, 3.5% NHBD, 0.9% PRA >35%). The BPAR rate of 20.4% was low, the graft loss was 6.2% and the patient survival was 100% at 12 month. Following AE's were reported: hematological 15%, infectious 12%, and gastrointestinal 25% (12% diarrhea). The EC-MPS median dose was maintained at the recommended 1.44 g/dl at M, 6, 9, and 12.

**Conclusions:** EC-MPS in combination with CsA, Simulect, and steroids in high-risk patients provides a favorable therapeutic effect as demonstrated by a low BPAR rate and an excellent tolerability of EC-MPS. The majority of patients having been maintained at the therapeutic EC-MPS dose through 12 months. Prospective de novo studies in this patient population are necessary to confirm this data.

1 Cibrik et al. (2004)AJT,Supp8,Vol 4,220,p218

**PO-522 HYPERURICEMIA - A MARKER OF RENAL VASCULAR INVOLVEMENT IN KIDNEY TRANSPLANT RECIPIENT**

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**Background:** Hyperuricemia in kidney transplant recipients is believed to be due to the side effect of Cyclosporine A (CyA). However neither the potential predisposing factors nor the mechanisms of hyperuricemia have been clearly elucidated. It has been reported that hyperuricemia in patients on CyA is associated with lower GFR or reduced clearance. Hyperuricemia is commonly encountered in patients with renal vascular involvement such as IgA nephropathy. The transient hyperuricemia in pregnancy endotheliosis and its abrupt onset countered in patients with renal vascular involvement such as IgA nephropathy. This retrospective analysis of data suggests that hyperuricemia is increasing. In our analysis we assessed the safety and efficacy of EC-MPS and well regulated blood pressure resulted in improved gastrointestinal QoL. The immunosuppressive regimen seems to influence QoL, however a higher number of patients might be required to achieve statistically significant results. We will continue to routinely evaluate QoL in our patients. Updated results will be presented at the meeting.

**PO-524 PREDICTORS OF CARDIOVASCULAR EVENTS AND ASSOCIATED MORTALITY OF KIDNEY TRANSPLANT RECIPIENTS**

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**Purpose:** Cardiovascular disease is the most common cause of death after renal transplantation. Furthermore, acute coronary syndrome (ACS) attributable to coronary artery disease (CAD) accounts for the majority of deaths due to cardiovascular disease posttransplant. While renal transplantation is the treatment of choice for end-stage renal disease, understanding the causes of graft and patient loss is exceedingly important to improve outcomes.

**Methods:** This observational study included 1200 patients who underwent a kidney transplant between 1988 and 2003. The outcome was the occurrence of an ACS event within average of 15 years after renal transplantation.

**Results:** Of all 215 deaths, 28.3% were caused by complications of CAD which was the most common cause of death in our center. On multivariate analysis, diabetes (P = 0.005), prior transplant (P = 0.047), body mass index (BMI) at the time of transplant (P=0.01), cholesterol level (P=0.012) and LDL (P=0.007) during 3 years after transplant were associated with early ACS.

**Conclusion:** Diabetes, prior transplant, BMI, cholesterol and LDL were significantly associated with early ACS highlighting the importance of improved screening and perioperative management.

**PO-525 POST-TRANSPLANT DIABETES MELLITUS CAN NOT BE PREDICTED BY KNOWN RISK FACTORS**

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Post-transplant diabetes mellitus (PTDM) is frequent complication after renal transplantation. PTDM is a consequence of reduced insulin secretion and/or increased insulin resistance but the exact processes underlying this metabolic disturbance are still unknown. The aim of our study was to detect transplant recipient - dependent risk factors of new-onset diabetes mellitus after renal transplantation.

We compared patients who received the kidney from the same donor. Thirty two pairs of renal transplant patients were analysed. In every analysed pair the diabetics mellitus occurred only in one recipient. Number of factors that could have had the influence on the occurrence of diabetes mellitus including age, blood group, diagnosis of renal disease, time and type of renal replacement therapy, HLA, number of HLA mismatches, anti-HLA antibodies (PRA), cold ischemic time, the incidence of acute tubular necrosis, graft function, graft rejection, treatment (applied medications), the SM index, BMI, the weight at the moment of transplantation and at weight increase at the moment of diabetes occurrence, TG and cholesterol levels, co-morbidity (hyper tension, hepatic lesion, presence of proteinuria etc.) and HCV, HBV, CMV, herpes and other infections was evaluated. For the statistic analysis EPINFO Ver.3.2 PC-programme was used.

**Conclusion:** The analysis of the pairs of recipients allowed us to exclude donor - dependent risk factors and any analysed recipient feature did not combine with the diabetes occurrence. Despite the factors responsible for developing diabetes mellitus are still unknown, it may be suggested that the issue is impaired glucose tolerance undetected before transplantation. The matter requires further research.

**PO-526 LIVING DONOR KIDNEY TRANSPLANTATION:**

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**Purpose:** The lack of cadaveric donors for kidney transplantation (KTX) has led to an acceptance of suboptimal donors. Kidneys with multiple arteries are accepted for donation although vascular reconstructions may prolong warm and cold ischemia (WIT/CIT). We report our experience with 8 recipients where
elaborate arterial reconstruction was necessary due to multiple or polar arteries.

**Methods:** Between 1995 and 2004 111 consecutive living donor kidney transplants (LDKTX) were performed in our centre. Preoperative evaluation of the donors consisted of detailed medical work-up, scintigraphic evaluation of side specific kidney-function and CT/MR-angiografie to detect vascular abnormalities. The kidney with less function and less arteries was selected for donation.

**Results:** Pola are arteries were anastomosed to inferior epigastric artery (n=4) after reconstruction of main renal artery with neither prolonged CIT nor WIT. A substantial pola artery was anastomosed to internal iliac artery (n=1), equivalent diameter of renal arteries were anastomosed in ostium commune technique (n=1). Two cases presented with triple arteries which were anastomosed via venous interposition of a saphenal vein segment. Operative time was signific- antly longer with need for arterial reconstruction: 184 ± 39 min vs 136 ± 37 min. Mean CIT in cases with arterial reconstruction was 156 ± 35 min versus 145 ± 32 min in grafts with single arteries. After reconstruction all grafts showed primary function, patency of arteries was documented by doppler-ultrasound.

**Conclusion:** Vascular reconstruction of additional renal arteries prolongs CIT and operative time. However as this does not harm primary function rate, re- construction is worth it as nephron mass can be saved.

**PO-527 THE ANTIOXIDANT HYDROXYTYSROLO PROTECTS THE KIDNEY FROM THE CYCLOSPORINE INDUCED OXIDATIVE STRESS BUT NOT FROM THE HAEMODYNAMIC ALTERATIONS**

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**Background:** Cyclosporine A (CsA) is the first-line immunosuppressant used in transplantation and autoimmune diseases. Nephrotoxicity is the major limita- tion of CsA. Several evidences suggest that reactive oxygen species (ROS) play a role. This study aimed to investigate hydroxytyrosol (DOPET) effects, an antioxidant component of olive oil, on CsA-induced oxidative stress and haemodynamic alterations in a rat model of chronic CsA nephrotoxicity.

**Methods:** Sprague-Dawley rats were treated i.p. with CsA (15 mg/kg) alone or in combination with DOPET (20 mg/kg) for 3 weeks. Glomerular filtration rate (GFR) was assessed by inulin clearance; blood pressure was monitored by the tail method. At the end, the animals were sacrificed and the superoxide concentra- tion within the abdominal aorta and the renal artery cells was quantified from the oxidation of dihydrothidium (DHE) using fluorescence microscopic imaging analysis. On kidney tissues, lipid peroxidation was measured as thio- barbituric acid-reacting substances (TBARS) and superoxide dismutase activity. Urinary MCP-1 as well as CD3+ and HLA-DR+ cells can provide a potential renal transplant recipients.

**Results:** CsA increased superoxide concentration in the aorta and in the renal artery; DOPET inhibited this effect. CsA-treated rats showed higher levels of TBARS in their kidneys, a decrease of GSH and HO-1 mRNA up-regulation in comparison with controls. DOPET reversed these CsA effects. After CsA treat- ment GFR decreased and blood pressure increased; DOPET did not improve renal haemodynamics and hypertension.

**Conclusion:** DOPET protection from CsA induced oxidative stress is not asso- ciated with a parallel action on haemodynamics. Therefore free radicals seem not to be completely responsible for the haemodynamic CsA toxicity.

**PO-528 INCIDENCE OF CARDIOVASCULAR RISK FACTORS AND COMPLICATIONS BEFORE AND AFTER KIDNEY TRANSPLANTATION**

Mohammad Ali Ostovan, Alineh Mehdizadeh, Afsoon Fazeldazeh, Ali Razmok, Ganbar Ali Rais-Jalali, Seyed Ali Malek-Hosseini. Nemazee Hospital, Shiraz Transplant Research Center, Shiraz, Fars, Islamic Republic of Iran.

**Purpose:** Cardiovascular disease is a leading cause of death after renal trans- plantation (RTx), and the incidence is considerably higher than in the general population. Aim of this study was to evaluate the incidence of atherosclerotic cardiovascular complications after RTx.

**Methods:** Analysis of atherosclerotic cardiovascular diseases and cardiovas- cular risk factors before and after transplantation in 500 renal transplant recipi- ents between 1987 and 1992.

**Results:** Following RTx 11.7% developed atherosclerotic cardiovascular dis- ease, primarily coronary artery disease (9.8%). The comparison of risk factors before transplantation showed: The prevalence of systemic hyperten- sion (67% to 86%), diabetes mellitus (7% to 16%) and obesity (26% to 48%) had increased significantly whereas the number of smokers halved to 20%. The number of hyperglycemies decreased significantly (235 ± 144 to 217 ± 122). The total and HDL cholesterol rose significantly (232 ± 65 to 273 ± 62 and 47 ± 29 to 56 ± 21, respectively). The LDL cholesterol increase was insignificant (180 ± 62 to 189 ± 53). In the univariate analysis, cardiovascular diseases were significantly associated with male gender, age over 50 years, diabetes mellitus (DM), smoking, total cholesterol > 200, LDL cholesterol > 180, HDL chole- sterol < 55, fibrinogen > 350, body mass index > 25 kg/m2, and more than 2 antihypertensive agents per day.

**Conclusion:** The high incidence of cardiovascular disease following renal transplantation is mainly due to a high prevalence of classical risk factors be- fore and following transplantation. The treatment of the risk factors must be introduced early in the course of renal failure, further, they must be continued following transplantation.

**PO-529 PRETRANSPLANT CARDIAC INVESTIGATIONS IN THE IRANIAN RENAL TRANSPLANT POPULATION—THE EFFECTIVENESS OF THE CLINICAL HISTORY AND THE CURRENT SCREENING METHODS IN PREDICTING CARDIAC EVENTS**

Mohammad Ali Ostovan, Alineh Mehdizadeh, Ali Razmok, Afsoon Fazeldazeh, Ganbar Ali Rais-Jalali, Seyed Ali Malek-Hosseini. Nemazee Hospital, Shiraz Transplant Research Center, Shiraz, Fars, Islamic Republic of Iran.

**Purpose:** Coronary artery disease (CAD) is prevalent among end-stage re- nal failure patients and remains the major cause of mortality following renal transplantation. Death with a functioning transplant institute remains the most common cause of kidney graft failure. In this study we attempt to evaluate the effectiveness of the clinical history and current screening techniques available in predicting pretransplant CAD and also assess the role of coronary angiogra- phy as a pretransplant screening technique.

**Methods:** Clinical data of 190 renal transplant patients was analyzed. Any clinical history of cardiac disease and all preoperative cardiac screening data was recorded for each patient. The study endpoints were the subsequent develop- ment of myocardial infarction (MI), undergoing coronary artery bypass graft (CABG) or death.

**Results:** Factors that were significantly associated with reaching a study end- point included: age at transplant [Hazard Ratio (HR) 1.91, P < 0.001], history of heart failure (HR 8.62, P < 0.001), presence of CAD on coronary angiography (HR 5.55, P = 0.033), anterior Q wave on electrocardiogram (ECC) (HR 8.6, P < 0.001) and history of a cerebrovascular accident (HR of 4.32, P = 0.008). The screening techniques of myocardial perfusion scan and echocardiography were conclusive as predictive variables of outcome.

**Conclusion:** Clinical history, ECC results and echocardiography are good, practical and low-cost screening methods. Coronary angiography is appropri- ate in certain high-risk groups but not necessary as part of screening in all potential renal transplant recipients.

**PO-530 ELEVATION OF MONOCYTE CHEMOTACTIC PEPTIDE-1 (MCP-1) AND ACTIVATED CELLS IN URINE—SENSITIVE REJECTION MARKERS IN RENAL GRAFT RECIPIENTS**

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Cytokines produced during acute immunological allosresponse induce chemokines what results in the infiltration of the allograft. These chemokines and cells are excreted with urine. The aim of the study was to assess the diag- nostic utility of urinary excretion of MCP-1 and CD3+, CD14+ and HLA-DR+ cells. The study enrolled 35 patients with acute renal rejection and 65 with stable graft function. Urinary sediments, were prepared by means of cytospin and stained with anti-CD3, anti-CD14, anti-HLA-DR labeled monoclonal antibod- ies and expressed as counts per 10 high power fields. Urinary MCP-1 was assayed by ELISA and expressed as ng per mg of creatinine.

In patients with acute rejection MCP-1 level was ten-fold higher than in pa- tients with stable graft function (6.13 ± 3.38 vs 0.60 ± 0.35 ng/mg creatinine). The number of CD3+ cells was approx. four times higher than in the non- rejection patients (9.0 ± 4.6 vs 2.0 ± 2.2). The number of DR+ cells was 8 times higher in the acute rejection patients (16.0 ± 7.2 vs 2.0 ± 2.7). The counts of CD3+ and DR+ cells correlated with Banff score.

The assessment of MCP-1 as well as CD3+ and HLA-DR+ cells can provide a useful noninvasive device for diagnosis of acute rejection. The number of CD14+ cells was significantly increased in patients during acute rejection (p < 0.0001). CD3, DR+ and CD14 cell counts strongly correlated with urine excretion of MCP-1.
BK AND JC POLYOMAVIRUS REACTIVATION ASSOCIATED WITH IMPAIRMENT RENAL TRANSPLANT FUNCTION

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Up to date only BK polyomavirus (PV) was related to graft nephropathy. The aim of the study was to estimate the risk factors and incidence of BK and JC polyomavirus infection, and their influence on development nephropathy after kidney transplantation.

Since the year 2001, a number of 174 renal transplant recipients have been screened for evidence of decoy cells (DC) in urine sediment. Moreover, 45 selection recipients were screened with associated creatinine, were assessed by PCR for PVDNA in urine and plasma. The primer pair amplified a 176-bp sequence from BKV genome and a 173-bp sequence from JCV genome.

DC were found in 17 out of 174 patients (9.8%). PVDNA was found in plasma of 2 out of 45 recipients (4%). Analysis of urine revealed of total of 8 patients with PVDNA (18%). JC polyomavirus was evidenced in one patient plasma, and 4 urine samples. All the patients with reactivated polyoma were treated with MMF. Additionally 6 patients received tacrolimus, and 2 patients cyclosporine. Biochemical proven PV nephropathy was found in four patients. At the time of diagnosis creatinine was 2.2 mg/dL. The all patients’ immunosuppression was reduced. One patient was treated with ciclofivir and one with cyclophosphamide. The former successfully eliminated the viral disease, the latter died with functioning graft, while others maintain stable renal function.

BK as well as JC polyomavirus may cause nephropathy in renal transplant patients. The impairment of renal function proceeds slowly. The major risk factor of PV reactivation is an immunosuppressive regimen based on MMF and tacrolimus.

IMMUNOHISTOCHEMICAL URINARY ANALYSIS AND MONOCYTE CHEMOTACTIC PEPTIDE (MCP-1) IN RENAL TRANSPLANT RECIPIENTS WITH POLYOMAVIRUS REACTIVATION

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Reactivation of PV may induce chronic tubulointerstitial inflammation of the transplant kidney. The aim of the study was to investigate the influence of PV reactivation on the set of cells in the urinary sediment and MCP-1 excretion. A total of 1189 urine sediments from 174 renal allograft recipients were analyzed. Papanicolaou method and lectin stainings were used for identification of epithelial urinary tract cells. Decoy cells were identified by immunofluorescent method, using specific antibodies (JCBK Monoclonal antibody). Similar method was used to detect CD3, CD4, CD8, CD14. Moreover urinary excretion of MCP-1 was assessed. The results of urine sediment analysis and MCP-1 concentrations were compared between patients with decoy cells and stable graft function (reference group n=65). In seventeen patients (10%) decoy cells were identified in urine. These patients had higher serum creatinine levels, in 4 patients biopsy proved PV nephropathy, in 2 PCR revealed PV infection. Patients with reactivation of PV had significantly greater excretion of CD3+, CD4+, CD8+, CD14+, HLA-DR+ and distal tubule cells, as well as higher urinary MCP-1 concentration (ng per mg of creatinine).

CHEMOTACTIC PEPTIDE (MCP-1) IN RENAL TRANSPLANTATION

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Gastrointestinal (GI) complications commonly occur following renal transplantation. No effective GI medications prescribed or assessed with higher cost, poorer graft outcomes. We examined whether certain immunosuppression (IS) regimens were associated with increased use of GI medications, and assessed IS and non-IS medication costs.

Methods: US commercial administrative claims for 1,957 kidney recipients were linked to data from the Organ Procurement Transplant Network. All recipients had ≥1 pharmacy claim post-transplant for either tacrolimus (tac) or sirolimus (sirol) IS claim.

Data was analyzed as a matched cohort study, with each IS regimen pooled with a control group (n=65). IS regimens were associated with increased use of GI medications, and assessed IS and non-IS medication costs.

Conclusion: US commercial administrative claims for 1,957 kidney recipients were linked to data from the Organ Procurement Transplant Network. All recipients had ≥1 pharmacy claim post-transplant for either tacrolimus (tac) or sirolimus (sirol) IS claim. IS regimens were associated with increased use of GI medications. GI medications comprised 34% of non-IS drug costs.

EPIDEMIOLOGIC RISK FACTORS FOR DIARRHEA FOLLOWING RENAL TRANSPLANTATION

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Diarrhea is a common complication following renal transplantation. Minimization of MMF is a strategy employed to alleviate post-transplant diarrhea. We investigated the consequences of MMF dose reductions following diarrhea di- agnosis following kidney transplantation.

Methods: Adult patients were included in the study if a diarrhea diagnosis was recorded following transplantation with a MMF prescription at the time of diagnosis. Patient records for all adult renal transplant recipients were drawn from the United States Renal Data System (USRDS) between 1995 and 2001. Diagnosis of diarrhea was identified from ICD-9-CM codes in USRDS supplied Medicare billing data. The study interval began within three days of the diagnosis and ended at graft failure, censoring at 3 years post-transplant, last follow-up, or last prescription record. Associations were estimated using multivariate adjusted time varying methods.

Results: 1,121 patients were identified with a MMF prescription at diarrhea diagnosis. 25 patients experienced graft failure during the study interval. MMF primary insurance at transplant were included. The study began with transplant and ended at graft failure, censoring at 3 years post-transplant, last follow-up, or end of Medicare coverage. Risk factors were identified with product limit time-to-event methods estimating diarrhea incidence during transplant function.

Results: 18,617 patients were included. Overall incidence of diagnosed diarr- eha through three-years post-transplant was 30.5%. Patients with type 1 dia- betes experienced the greatest risk of diagnosed diarrhea (40.4% vs. p<0.0001). Diarrhea diagnosis was more common in females than males (36.3% vs. 26.7%, p<0.0001). Diarrhea incidence decreased with age (32.7% age≥30 to 26.9% age≥60; p=0.0002). Diarrhea diagnosis was more common with CMV D/R sero- pairings (39.3% p=0.0009), Caucasian race (31.8%, p=0.0009), and pre- transplant congestive heart failure (34.7%, p<0.0001). Immunosuppression at transplant discharge was associated with diarrhea diagnosis: diarrhea was more common with tacrolimus than cyclosporine (32.2% vs. 30.2%, p=0.01) and more common with MMF than azathioprine (32.5% vs. 27.3%, p=0.01).

Conclusions: Diarrhea is commonly diagnosed following renal transplanta- tion. Patient characteristics, diseases, and treatment choices are associated with differential risk. Pre-emptive management strategies for patients at higher risk of diarrhea could permit avoidance of the adverse outcomes associated with immunosuppression modification.

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DE NOVO DIABETES WITH COMPLICATIONS AFTER PROTEINURIA DEVELOPMENT AFTER CYCLOSPORINE EFFECTS OF LOSARTAN AND CARVEDILOL ON

University of Gdansk, Poland.

with hypertension.

blocker, losartan on the surrogate marker of kidney injury, albuminuria in rtr

cross-over study to evaluate the influence of AT-1 angiotensin II receptor

In general, incidence of urological complications in our center is significantly lower in living-unrelated cases. Moreover, such a rate in the cadaveric group is as low as the living-related group. This is a positive point for the fearless usage of cadaver-source organs.

PO-536 DE NOVO DIABETES WITH COMPLICATIONS AFTER KIDNEY TRANSPLANTATION

Thomas Burroughs, Jason Swindle, Mark Schnitzer. Medicine, Saint Louis University, USA.

We sought to estimate the incidence of major diabetes complications from new onset diabetes mellitus (NODM) after kidney transplantation (KTX) to determine whether complication rates differed by immunosuppression (cyclosporine (CyA) or tacrolimus (Tac)).

Methods: We used registry data from the United States Renal Data System to investigate rates of NODM complications among adult Medicare beneficiaries transplanted in 1995-2001 without pre-transplant evidence of DM. We ascertained NODM and its complications from inpatient and outpatient billing records, and estimated incidence of first events by the product-limit method, censoring at: loss of Medicare, three-years after KTX, death, or end of observation (12/31/2001). Complication classes included neuropathy, retinopathy, ketoacidosis, hyperosmolarity, diabetes coma, peripheral vascular disease and nephropathy among patients diagnosed with NODM after transplantation.

Results:

| Condition | Overall incidence Standard error | Overall incidence with Tac vs Cys - mol | Relative Hr with Tac vs Cys - mol | 95% Cl | p value |
|-----------|---------------------------------|---------------------------------------|---------------------------------|-------|---------|
| Diabetes  | 27.35%                          | 0.0031                                | 1.382                           | 1.299 - 1.471 | p < 0.0001 |
| Total complications | 6.16%                          | 0.0016                                | 1.306                           | 1.133 - 1.508 | p < 0.002 |
| Metabolic complications | 3.43%                          | 0.0012                                | 1.466                           | 1.215 - 1.769 | p < 0.0001 |
| Ketoacidosis | 1.75%                          | 0.0092                                | 1.273                           | 0.963 - 1.683 | p = 0.09 |
| Coma with ketoacidosis | 0.12%                          | 0.00023                               | 1.936                           | 0.781 - 4.797 | p = 0.15 |
| Hyponatremia/shock | 1.13%                          | 0.0075                                | 1.590                           | 1.165 - 2.171 | p < 0.001 |
| Hyperosmolar coma | 0.79%                          | 0.0062                                | 1.738                           | 1.141 - 2.335 | p < 0.01 |
| System-based complications | 3.65%                          | 0.00133                               | 1.171                           | 0.966 - 1.420 | p = 0.10 |
| Neurological manifestations | 2.48%                          | 0.001130                              | 1.155                           | 0.908 - 1.469 | p = 0.23 |
| Peripheral circulatory disorders | 1.01%                          | 0.00073                               | 1.347                           | 0.927 - 1.918 | p = 0.11 |
| Ophthalmic manifestations | 1.50%                          | 0.00085                               | 1.084                           | 0.794 - 1.479 | p = 0.6115 |

Conclusions: Among 28,307 eligible KTX recipients, the cumulative incidence of NODM was 23.27% at 36 months. The incidence of any DM complication was 6.16% among all eligible recipients and 20.05% among recipients with de novo DM. Tac was significantly associated with metabolic complications and trended toward significance for systems-based complications.

PO-537 EFFECTS OF LOSARTAN AND CARVEDILOL ON ALBUMINURIA IN A DOUBLE BLIND, RANDOMIZED STUDY IN RENAL TRANSPLANT RECIPIENTS

Leszek Tylcik 1, Bogdan Biedunkiewicz 1, Andrzej Chamienczyk, Klaudiusz Wojnarowski, Wieslawa Lysiak-Szydlowska 2, Zbigniew Zdrojewski, Boleslaw Rutkowski 1. 1 Department of Nephrology Transplantology and Internal Medicine, Medical University of Gdansk; 2 Department of Clinical Nutrition and Laboratory Diagnostic, Medical University of Gdansk, Poland.

Background: The renoprotective effects of agents inhibiting renin-angiotensin system in renal transplant recipients (rtr) is supposed but not finally proven. To gain more light on this issue we performed double-blind, placebo-controlled, cross-over study to evaluate the influence of AT-1 angiotensin II receptor blocker, losartan on the surrogate marker of kidney injury, albuminuria in rtr with hypertension.

Patients and Methods: 14 of 16 patients (9M, 5F), 44.38±12.32 years old, 63.19±36.55 months after kidney transplantation, with hypertension, stable serum creatinine 1.39±0.17 mg/dl, without proteinuria completed the protocol. The dosages of cyclosporin and calcium channel blockers were not changed during the study. Patients received randomly either losartan (50-100 mg daily) or carvedilol (12.5-50 mg daily) for 8 weeks, allowing a 8-week placebo washout between treatments. The target office trough blood pressure was below 130/80 mmHg.

Results: Systolic and diastolic ambulatory blood pressure did not differ between the treatment periods. Losartan significantly reduced albuminuria relative to placebo and carvedilol (27.62±6.39 vs. 34.89±7.01 vs. 44.77±8.99 mg/ creatinine, p < 0.01). Losartan was well tolerated and free of adverse effects. Significant but not clinically relevant decrease of hemoglobin after losartan was observed (losartan: 12.9±1.15 g/dl, placebo: 13.42±1.21, carvedilol: 13.71±1.32, p<0.001). Serum potassium, creatinine and trough blood cy closporin level was unaffected.

Conclusion: Losartan decreases albuminuria in rtr and this effect is independent for blood pressure lowering. Losartan therapy seems to be free of adverse effects but is accompanied by slight decrease of hemoglobin level.

PO-538 EFFECT OF ORGAN SOURCE ON UROLOGICAL COMPLICATIONS IN RENAL TRANSPLANT RECIPIENTS

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Purpose: To determine the effect of organ source (cadaver versus living donors) on major urological complications in renal transplant recipients.

Methods: This study concerns the effect of organ source on major urological complications occurring as a result of operative procedure in 1003 consented (50-300 mg/24h) and 1500 mg/24h before conversion Uprot was compared before (Uprot0) and after 3 months. Twenty four hours Uprot was compared before (Uprot0) and after 3 months. Twenty four hours Uprot was compared before (Uprot0) and after 3 months. Twenty four hours Uprot was compared before (Uprot0) and after 3 months.

Conclusion: Among 1003 cases, 421 (42.0%) have been living-related, 471 (47.0%) living-unrelated and 111 (11.5%) cadaveric. 126 (6%) and 311 (31%) were male and female, respectively. 45 complications in 45 patients (76% male, 24% female; no graft loss) were diagnosed, including 5 cases of obstruction (0.49%), 21 urine leaks (2.0%), 10 fluid collections (0.9%), 5 cases of hematomata (0.49%) and 4 cases of stone (0.39%). Incidences of urine leak and obstruction have been significantly higher in males. 6.3% of cadaveric transplants, 6.4% of living-related and 2.3% of living-unrelated cases have had one major urological complication.

Conclusion: In general, incidence of urological complications in our center is significantly lower in living-unrelated cases. Moreover, such a rate in the cadaveric group is as low as the living-related group. This is a positive point for the fearless usage of cadaver-source organs.

PO-539 PROTEINURIA DEVELOPMENT AFTER CYCLOSPORINE CONVERSION TO SIROLIMUS IN KIDNEY TRANSPLANTATION

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Proteinuria (Uprot) increase after sirolimus (SRL) initiation has been reported in kidney transplantation. The aim of our study was to analyze the factors associated with Uprot development after SRL treatment. We reviewed 78 renal transplant (RT) patients (pts) submitted to cyclosporine (CYA) conversion to SRL. 43±50 months after RT. Mean follow-up after conversion was 21.1±2 months. Twenty four hours Uprot was compared before (Uprot0) and after 3 months (Uprot3) conversion. De novo Uprot0-300mg/24h was evident in 18 pts; 22 pts showed Uprot increase from 1017±0.664 mg/24h to 2038±2460 mg/24h (p=0.04). By binary regression, the risk of Uprot0-1500mg/24h was 10 fold higher in patients that had already protU0-300 mg/24h before conversion (p<0.001). Lower risk of developing proteinuria was observed in patients who switched to SRL owing to CYA adverse effects (p=0.009). In the 55 patients with 1 year follow-up, 29 pts (53%) presented a decrease and 26 pts (47%) showed a increase in creatinine (Cr) levels. The absence of Cr decrease was 10 fold higher in pts with Uprot0-300mg/24h (p=0.007), 20 fold higher in pts with Uprot0-1500 mg/24h (p=0.02) and was associated with a later onset of SRL (after RT (p=0.001). In summary, after conversion to SRL, we verified appearance or increase in proteinuria, respectively, in 23% and 28% of pts. The risk of developing Uprot0-1500 mg/24h in patients with previous Uprot0-300mg/24h was evident. A later onset of SRL and the presence of Uprot before conversion or Uprot after conversion were associated with an increased risk of higher creatinine levels 1 year after conversion.
PO-541 PRIMARY STENTING TO REDUCE URETERAL COMPLICATIONS AFTER KIDNEY TRANSPLANTATION: A SINGLE CENTER EXPERIENCE IN 500 CONSECUTIVE PATIENTS

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Purpose: Ureteral complications after kidney transplantation (KT) are the leading cause for unplanned returns to the operating room. This study aimed to define the best surgical technique of ureteral implantation and to evaluate the impact of ureteral stenting in KT.

Methods: 500 consecutive KT from 1996-2003 were analyzed for ureteral complications requiring surgical or interventional treatment within one year after transplantation. Three different surgical techniques were used: 79 Polya-Leadbetter (PL) 1996-1998, n=157; Lich-Gregoir (LG) 1999-2000, n=150; LG with primary stenting for six weeks (LGS) 2001-2003, n=193. Primary end-point was necessity for interventional or surgical treatment. Statistical analysis included chi-squared-test with Bonferroni correction. Significance was set at p<0.05.

Results: Surgical and interventional treatments did not differ significantly between PL and LG (p=0.26, and 0.51, respectively). A significant decrease was found in overall complications in LGS as compared to PL or LG (p<0.001 and p<0.001, respectively). While revisional surgeries occurred less frequently in LGS as compared to PL or LG (p=0.04). Every isolated strains was tested to know antibiotics resistance.

PO-544 CONSTITUTIONAL CHANGES FOLLOWING NON-HEART-BEATING DONOR (NHBD) KIDNEY TRANSPLANTATION

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Purpose: A rise in serum alanine aminotransferase (ALT) without other evidence of liver dysfunction has been proposed as a marker of ischaemic injury to the kidney. A syndrome consisting of elevated ALT, thrombocytopenia and impaired initial function (“The Asystolic Donor Syndrome”) has been reported in a single series of NHBD kidney recipients. We aimed to determine whether this occurred in our patients, and if so what the long-term consequences were.

Methods: We reviewed clinical data from 100 consecutive NHBD kidney recipients and recorded post-operative blood results, delayed graft function (DGF), primary non-function (PNF) and survival data. A peak ALT > 80 IU/L (double the upper limit of normal in our laboratory) in the first 3 post-operative days was considered a marker of significant ischaemic injury. Results: Of the 100 recipients, 45 had peak ALT > 80 IU/L in the first 3 days (high ALT group). None had other evidence of liver dysfunction. The high ALT group had longer primary warm ischaemia (23.6±6.8 vs 18.8±7.8 mins, p<0.001). Results of Maastricht category (MC) II kidneys.
PO-545 REPAGLINIDE IS A SAFE AND EFFECTIVE TREATMENT OPTION OF NEW-ONSET DIABETES MELLITUS AFTER RENAL TRANSPLANTATION

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Objective: The glinides, a new class of short-acting insulin secretagogue, have not been studied in patients after organ transplantation. It was the purpose of this study to assess the safety and efficacy of the short-acting insulin secretagogue repaglinide in patients with new-onset diabetes mellitus (NODM) after renal transplantation.

Patients and Methods: 16 patients with NODM after renal transplantation were selected to receive repaglinide therapy. All patients received prednisone, 9 patients were treated with tacrolimus, six patients received cyclosporine A and 7 patients received mycophenolate mofetil.

Results: For 11 of the 16 patients treatment with repaglinide therapy was successful. Mean fasting blood glucose decreased from 154±59 mg/dl to 117±36 mg/dl (p=0.05). Five patients were not treated successfully with repaglinide and needed insulin. Mean HbA1c decreased from 7.7±2.5% to 6.5±1.5% (p=0.05). There were no side effects causing withdrawal of repaglinide therapy. There were no changes in serum creatinine concentrations, and modifications of the dosages of cyclosporine and tacrolimus in association with repaglinide therapy were not necessary.

Conclusion: Treatment with repaglinide appears to be safe and effective for a majority of patients with NODM after renal transplantation.

PO-546 PROGNOSTIC VALUE OF THE RESISTANCE INDEX IN THE POSTOPERATIVE PERIOD OF KIDNEY TRANSPLANT

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Purpose: The aim of this paper is to investigate if an abnormal pattern of RI fluctuations may forecast postoperative complications from any cause in kidney transplantation.

Patients and methods: The study group consisted in 34 consecutive kidney transplantations performed at our institution from February 1st to June 30th, 2003. 29 kidneys came from a cadaver donor (CD) and 5 from a living donor (LD). 41% of grafts had major vascular anomalies. RI was measured intraoperatively, 24 hours, 3 days, 6 and 9 days post transplant, using an Aloka 2000 unit with a probe of 7.5 MHz. A RI-value lower than 0.8 was considered as normal.

Results: Mean intra-operative R.I. value of the all study group was 0.63 ± 0.06 (range 0.5-0.7), with no significant differences between CD and LD recipients. 35 patients with an uneventful post-transplant course (Group I), had a mean postoperative R.I. value of 0.73 ± 0.04 (range 0.62-0.80). A significant increase of the postoperative R.I. was found in 10 patients (Group II), whose mean value was 0.82 ± 0.06 (range 0.7-0.96). An early statistical significant difference from the baseline value was found in the Group II between intraoperative RI and RI calculated 24 hours after the transplant (0.62 ± 0.07 vs 0.76 ± 0.04; p = 0.0004).

Conclusion: Authors conclude that according to their data, the value of R.I. in the early phase of the post-transplant period has to be considered an important aid for forecast early complications of the post transplant course.

PO-547 THE EFFECT OF FASTING RAMADAN ON KIDNEY TRANSPLANT RECIPIENTS

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Purpose: Adult Muslims renal transplants often ask their doctors whether fasting is safe. Scanty studies addressed this question with controversial results. This prospective study was undertaken to look for any clinical or biological changes during the month of the fast.

PO-548 RENAL TRANSPLANT RECIPIENTS RECEIVING MMF WITH TACROLIMUS CAN BE CONVERTED TO ENTERIC-COATED MYCOPHENOLATE SODIUM WITHOUT COMPROMISE IN TOLERABILITY AND EFFICACY

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Aims: Enteric-coated mycophenolate sodium (EC-MMPS, myfortic®) is a novel formulation designed to release mycophenolic acid (MPA) in the small intestine, and therefore to improve the GI tolerability of MPA. It has been shown earlier that EC-MMPS and mycophenolate mofetil (MMF) are therapeutically equivalent in de novo kidney recipients. This is the first reported multicenter trial investigating the safety of converting maintenance renal transplant patients receiving a tacrolimus based regimen from MMF to EC-MMPS.

Methods: 63 Caucasian patients with stable renal graft function were analysed. Patients receiving MMF and tacrolimus were converted to EC-MMPS 37.9±27.6 months after transplantation. Patients receiving MMF 250-2000mg/day were switched to equimolar doses of EC-MMPS 180-1440mg/day.

Results: 93.7% of the patients completed the study, 3 discontinued due to adverse events and 1 due to administrative problems. After conversion to EC-MMPS, BPAR have been observed in 1 patient and none has experienced a chronic rejection; no graft loss or deaths were reported. Renal function in terms of creatinine clearance (Nankivell) was 64.0±21.3 vs 62.6±20.0ml/min and serum creatinine was 125.5±4.1 vs 127.5±46.5µmol/l at baseline vs end of treatment, respectively, demonstrating no deterioration of renal function after conversion from MMF to EC-MMPS. The overall incidence of adverse events was 79.4%.

Conclusions: In summary, these data indicate that renal transplant patients receiving MMF in combination with tacrolimus can be converted to EC-MMPS with no compromise in efficacy and tolerability.

PO-549 NUMBER OF HLA-B MISMATCHES AS INDEPENDENT RISK FACTOR FOR POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE

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Background: Uncontrolled Epstein Barr virus related clonal expansion of B-cells after transplantation may lead to post transplant lymphoproliferative disease (PTLD). Although several risk factors for PTLD development after solid organ transplantation have been identified, their exact pathogenic role and relevance is still unclear. The degree of HLA mismatching has been identified as a risk factor for PTLD after haematopoietic stem cell transplantation.

Purpose: To analyse the relation between HLA-matching and development of PTLD in kidney transplant recipients.

Patients and methods: PTLD observed in cadavere kidney recipients, transplanted between January 1985 and December 2002 at our center, were reviewed and re-classified according to the WHO classification. PTLD-risk was assessed in a multivariable Cox regression model, including immunosuppressive therapy and HLA mismatches.

Methods: twenty two kidney transplant patients with stable kidney functions, who were transplanted for more than one year, and voluntary chose to fast during Ramadan in 1425 H (Oct.-Nov.,2004), were studied. There were 10 men and 12 women, mean age 47±11.6 years (25-69 y). Mean age of graft 78.8±61.7 months (14-250 m). The etiology of ESRD was unknown in 13 (59%) patients. Eighteen (82%) recipients had living unrelated donors.19 patients were on triple immunosupressor regimen. Comorbide conditions were hypertension, dyslipidemia and diabetes mellitus found in 20, 9 and 5 patients respectively.

Clinical and biological assessment was done once during the month preceding Ramadan, during Ramadan, and in the month following the fast. Medications were taken in two divided doses at sunset (time of breaking the fast) and pre dawn (before the fast). Patients fasted with p. 0.05 was considered significant.

Results: All the transplant recipients tasted the whole of the month of Ramadan, none of them experienced any undue fatigue, or any other symptoms compared to the period before the fast. Body weight, blood pressure, kidney function tests, blood sugar, lipid profile, and drugs levels were all stable without any significant difference during Ramadan compared to pre or post the fast.

Conclusion: The fast of Ramadan is safe and has no adverse effects in renal transplant recipients after one year of transplantation with stable graft function.
CADAVERIC KIDNEY TRANSPLANTATION UNDER CURRENT IMMUNOSUPPRESSIVE REGIMENS: A COMPARISON OF OUTCOME WITH LIVING RELATED AND UN RELATED TRANSPLANT

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Introduction & Objectives: Live donors have been the main source of kidney donation in Iran. Since the year 2000 a new legislation allowed organ retrieval from cadaveric. The aim was to compare the outcome of kidney transplantation (TX) and recipient who received graft from cadaveric or live donor.

Material, Methods: From January 2001 to September 2004, 290 patients underwent TX. 90 PT received grafts from cadaveric donors (CG), 31 from related (LRD) and 169 from unrelated donors (LURD). Immunosuppressive included cyclosporine, steroid, MMF. Graft survival, rejection, function and surgical complications after TX have been compared between 3 groups. Survival was estimated by the Kaplan-Meier method.

Results: The incidence of delayed graft function was higher in recipient of CG (5%) than the LRD group (1.3%) p < 0.02. Acute rejection developed in 4.5% of LRD, 6% of LURD and 6.5% of CG recipients (p < 0.05). Infectious hernia and lymphocele were higher in CG than the LRD and LURD recipients (p < 0.003). Other complications were similar.

Serum creatinine at 1 week, 3 months and 1,2,3 years post TX were lower in the LRDs compared with the others. No difference in the serum creatinine was observed between LUR and CG recipient.

The one, 2, 3 years survival rates were higher in the LRD (95%, 93%, 90%) than the LURD (89%, 84%, 80%) and the CG recipients (87%, 80%, 80%, p < 0.05). No significant difference was present the survival rate of the other two groups (p < 0.05).

Conclusion: under the current immunosuppression the survival rates of graft in CG and LURD were similar. Cadaveric donors in developing countries can be excellent source for kidney transplantation.

PO-551 WHY LOCAL ORGAN PROCUREMENT IS ASSOCIATED WITH LESS RENAL TRANSPLANTATION COMPLICATIONS

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Introduction: In France, renal procurement teams generally keep for their own hospital one of the kidney for transplantation. Is this policy beneficial to the patients and why?

Patients and methods: Between 12/08/1970 and 04/08/2000 we performed 2000 renal transplantation. We locally harvested 804 kidneys and we received 1196 kidneys from other centers. 1496 kidneys were preserved in Eurocollins solution and 504 in UW-CSS solution. 477 kidneys yielded one or more arteries, 595 were removed without any aortic patch. 81 kidneys presented an arterial injury. Cold ischemic time (CIT) was 30.5 ± 12 hours.

Results: see Table 1

Table 1. Results

| n | Arterial injuries (%) | CIT (h) | UW Median survival (ATN) (months) | Ureteral stenosis (%) |
|---|------------------------|--------|----------------------------------|-----------------------|
| Local Kidneys | 804 | 2.4 | 47 | 123 | 36 | 2.6 |
| Other Kidneys | 1196 | 4.7 | 121 | 121 | 4.4 | 4.8 |

| p | <0.01 | <0.01 | <0.001 | <0.01 |

ATN: acute tubular necrosis.

Conclusions: Local transplantation team who harvested kidneys yielded less surgical complications (especially lower vascular injuries), preserved their kidneys with UW solution and transplanted it with a short CIT. Moreover the transplant surgeons committed with the organ procurement keep a close watch to see that all goes well and are carefully for the kidneys.

PO-552 RISK OF CANCER IN PATIENTS FOLLOWING RENAL TRANSPLANTATION

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Objectives: The high incidence of cancer development after renal transplantation is critical since the graft survival has been improved and the age of donors and recipients increased. We review our experience of cancers occurring in kidney transplanted patients over the last twenty years.

Materials and methods: From 1979 to 2000, 2000 patients were transplanted in our department. We reanalyzed our data in order to determined the incidence and risk factors of cancer development in transplanted patients.

Results: During the follow-up period (mean: 124 months), 242 patients (12%) developed a malignant tumor. The most frequent cancers were pulmonary (43%), breast (42), lymphoma (23) and cutaneous (20). Twenty two patients (19 men and 3 women) were diagnosed as having a urological cancer (1%), 12 renal, 6 prostate, 3 bladder and 1 testicular cancer. 76 patients died of the cancer 99.6 months after transplantation. The risk of cancer is in correlation with age at transplantation: 5% in the third decade, 10% in the fourth, 13% in the fifth, 20% in the sixth and 25% in the seventh.

Conclusion: The risk of cancer is correlated with the age at transplantation and needs a specific information and surveillance especially in patients transplanted after 50 years old.

PO-553 CONSEQUENCES OF ILLAC ARTERIAL ATRHEROSOMA ON RENAL TRANSPLANTATION

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Objectives: As the age of recipients has significantly increased over the last 15 years, surgeons sometimes need to deal with atherosclerotic lesions of the iliac arterial system. Arterial reconstruction during renal transplantation should now be less frequent due to better preoperative screening and prevention of hyperparathyroidism, but in some cases external iliac artery (EIA) atheroma may require an additional surgical vascular procedure during renal transplantation. This paper describes the role of iliac artery atherosclerosis and technical aspects of arterial restorations performed in patients undergoing renal transplantation since 1985.

Patients and Methods: In a series of 1,110 renal transplantsations performed between 1985 and 2000, 107 patient have moderate to severe atherosclerosis of the external iliac arteries. 38 patients required endarterectomy during renal transplantation and 69 patients were considered not to require any special procedure.

Results: Among the 38 patients requiring endarterectomy, 12 end-to-end arterial anastomoses were performed and 6 (50%) arterial stenoses (AS) were observed, and 26 side-to-end arterial anastomoses were performed with only one AS (4%). Patients and grafts survival curves showed a significant negative correlation with severity of atherosclerosis.

Conclusion: Preoperative assessment of the EIA is mandatory before renal transplantation. Renal transplantation can be performed in patients with an atheromatous EIA, if the artery can be clamped for endarterectomy. In our experience, side-to-end anastomosis using a donor patch onto the EIA gave better results by avoiding AS after endarterectomy. However, even despite vascular repair, graft survival is significantly lower in patients with atheromatous lesions requiring endarterectomy.

PO-554 ABSTRACT WITHDRAWN

PO-555 LONG-TERM BENEFIT OF MYCOPHENOLATE MOFETIL (MMF) RESCUE THERAPY IN CADAVERIC KIDNEY TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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In a retrospective we analyzed the benefit from the addition of MMF as maintenance immunosuppressive therapy after withdrawal of cyclosporine A (CsA) in patients with chronic progressive allograft dysfunction. Data from 35 renal transplantsations performed between March 1987 and August 1997 were reviewed. For induction therapy all patients received CsA and steroids (n=24) or CsA, azathioprine (AZA) and steroids (n=11). MMF (1,500 - 2,000 mg/day) was substituted for CsA and/or AZA for the following reasons: increasing cre-
atine levels caused by biopsy-proven Ca toxicity (n=11), altered peripheral flow-resistance index (FLI) in the kidney, and/or instable blood pressure. Other reasons for an allograft nephropathy like acute rejections or urinary tract infections were excluded by urinary cytology methods.

Improved renal function as detected by standard laboratory monitoring could be shown after 1 month of onset therapy, in 9 cases after 2 months (p<0.01).

Within 3 months 2 patients must be switched back because of gastrointestinal symptoms. In 2 patients an acute rejection episode (BANFF III) was observed after 23 and 31 months, respectively. Two patients died with functioning graft because of myocardial infarction. Five years after onset of MMF rescue therapy 6 out of 31 patients lost their transplant, in all other cases creatinine levels remained stable (95% had optimal AUC levels between 30 - 60 mg/L/h).

In conclusion, renal transplant recipients with progressively deteriorating organ function may be safely switched to MMF resulting in an excellent graft and patient survival.

**PO-556**

**HOW INFLUENCE THE OF ANURIA IN PATIENTS BEFORE KIDNEY TRANSPLANTATION THE OUTCOME OF POSTOPERATIVE COMPLICATIONS?**

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**Objectives:** How influence the of anuria in patients before kidney transplantation the outcome of postoperative complications?

**Material:** From 1/95-12/2004 433 patients were transplanted in our department. At the time of transplantation 42% of the patients were (with anuria: women, age 46.3 years).

The anuria was detected 1/2 to 12 years before (average 2.8 years) transplantation with a waiting time approximately 5 years.

**Results:** 42% of the patients had a really 0-diuresis. The reason the dialysis was in 78% a glomerulonephritis.

**Conclusions:** patients with a short range of anuria during the dialysis time had a quicker normalization of the diuresis without medical therapy. When the range was longer than 10 years and an high miktionfrequency with small urinevol- umes persist

**PO-557**

**MYCOPHENOLIC ACID IN MANAGING CHRONIC ALLOGRAFT NEPHROPATHY**

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Chronic allograft nephropathy is the leading cause of transplant kidney loss at the present. Its pathogenesis involves both immunological and non-immunological mechanisms. This implies that factors beyond T cell activation play active role in inducing chronic graft failure. Recent, publication shows that almost 100% of the kidney transplant will have CNI toxicity if they are put on calcineurin inhibitor for more than 10 years.

**Purpose:** We test if CNI minimization plus increment of MPA could improve chronic allograft nephropathy.

**Material/Method:** 145 kidney transplant patient followed in a single clinic were survey for chronic allograft nephropathy, which is defined as gradual creatinine increment for more than 0.5mg/dl in 3 months or 1 mg/ml in 6 month. Their CNI were minimized to keep tacrolimus trough level around 3-4 ng/ml, and cyclosporine C2 level around 500-600 ng/ml. Meanwhile, their MPA dosages were increased varing from 500mg/day to 1500mg/day.

**Result:** Nine patient were enrolled (M: 5, F:4) and followed up for more that one year. None of them showed sign of acute rejection or heavy proteinuria for more than 3.5 g/dm2. After CNI minimization and increment of MPA dosage, most of the patient showed improvement of the graft function when compared with the peak creatinine level during follow up. Their creatinine clearance increased by 11.3 ± 4.1 ml/min, while creatinine decreased by 0.8 ± 0.3. Decrease of the hemoglobin (1.4±0.7) and leucocyte count (866±407.9) were the most affected.

**Conclusion:** Our preliminary results suggested that CNI reduction with MPA increment is a simple and effective measure to treat chronic allograft nephrapathy.

**PO-558**

**PRETRANSPLANT AND POSTTRANSPLANT PREDICTOR OF KIDNEY GRAFT AND PATIENTES SURVIVAL – A SINGLE CENTER ANALYSIS OF 600 CASES (CROATIA, ZAGREB)**

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This retrospective study reviews risk and pitfalls for graft survival based on 32 years experience of single transplant center in Zagreb, Croatia. Four hundred and fifteen primary cadaveric kidneys (CD) transplant recipients and 102 living related (LR) recipients whose graft survived for more than six months were analyzed in the period 1982-2005. In LR transplantation, recipients of HLA haploidentical grafts had lower rejection risk and better graft survival, with half-estimate of 20 years 38%. CD first transplants matched graft had lower incidence of rejection and better survival (42% half-life) than haploidentical LR grafts. Expected half-life is 13.6 years for LR and 16.4 years in group of CD recipients. However in this analysis we shall consider different parameters that may contribute to graft and patient's survival. It will be analyzed: original disease, serum creatinine, relationship (graft type), rejection episodes, long term survival, recipient/donor age, gender, ischaemia time, and presensitiza- tion. The data were analyzed using Kaplan-Meier estimates. Good survival rate is depending on different immune and non-immune factors, which have stronger and more accurate impact in single center graft and patients survival.

**PO-559**

**PARATHYROIDECTOMY IN PATIENTS ON RENAL REPLACEMENT THERAPY: A 10-YR SINGLE CENTER EXPERIENCE**

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**Objective:** To assess long term results and efficacy of parathyroidectomy for treatment of renal hyperparathyroidism.

**Background:** Secondary hyperparathyroidism in patients with chronic renal failure refractory to medical treatment is often treated with parathyroidectomy. Total parathyroidectomy without autotransplantation produces favourable results.

**Patients and Methods:** Complete electronic data from 64 patients with hyperparathyroidism who underwent parathyroidectomy from August 1994 to De- cember 2004 were retrospectively collected. Generalized bone pain, persist- ent hypercalcemia, pathological fractures and muscle weakness formed indi- cations for surgery. Parathyroid gland localization techniques included: thyroid ultrasound, sestamibi scintigraphy and fine needle biopsy in some. S- rial biochemical parameters (calcium, phosphate, alkaline phosphatase) and serum parathormone levels after surgery were compared with preoperative values to assess the durability of procedure. Main outcome measures studied were postoperative morbidity, mortality, symptomatic relief, normalization of biochemical parameters and recurrence.

**Results:** At the end of follow-up (mean 5.4 yr) 88% patients had symp- tomatic relief. The mean preoperative PTH level of 134 pmol/L dropped to 5.5 pmol/L after surgery. The mean postoperative calcium was 2.38±0.08 mmol/L which was significantly lower than the mean preoperative value. Three patients (4.6%) had persistent hypocalcemia and 4 (6.2%) developed recurrent hyper- parathyroidism requiring surgery. None of the patients developed permanent recurrent laryngeal nerve palsy. One (1.5%) patient died of aspiration syn- drome after surgery. Hyperplasia of parathyroid glands was the commonest pathology noted (92%).

**Conclusion:** Parathyroidectomy effectively treats secondary and tertiary hyperparathyroidism in more than 90% patients. The morbidity related to the pro- cedure is low with occasional mortality possibly related to co-morbid conditions in these otherwise high-risk cases.
EFFECTS OF ILOPROST ADMINISTRATION BEFORE UNILATERAL NEPHRECTOMY ON LIPID PEROXIDATION: AN EXPERIMENTAL STUDY

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Living kidney donation represents a great source for end stage renal disease patients. Under various stress conditions lipid peroxidation is increased. Iloprost is a chemically stable derivative of a naturally-occurring prostacyclin which has vasodilator and antithrombotic effects. Unilateral nephrectomy can induce oxidative stress, we aimed to detect the lipid peroxidation parameters after unilateral nephrectomy and also evaluate how the iloprost administration before unilateral nephrectomy would affect oxidative stress. The adult male Wistar albino rats weighing 200-250 g were divided into 3 weight-matched groups. Sham group (S) (n=7), Unilateral nephrectomized group (N) (n=7), an hour before unilateral nephrectomy 1mg/kg iloprost administered group (IN) (n=7). Under anesthesia left posterior intercostal incision was performed and left kidney removed. The rats were sacrificed after 24 hours from operation. The blood samples were collected by intracardiac puncture after one day from operation. We measured MDA as a lipid peroxidation parameter, intraerythrocytic GSH and SOD as antioxidants.

Our results are shown in table.

|          | S (n=7) | N (n=7) | IN (n=7) |
|----------|---------|---------|----------|
| Plasma MDA (nmol/mg protein) | 1.42±0.16 | 2.09±0.21 | 1.58±0.23 |
| Intraerythrocytic GSH (g/mg protein) | 3.57±0.29 | 2.82±0.15 | 3.09±0.25 |
| Intraerythrocytic SOD (U/mg protein) | 24.23±3.28 | 24.01±1.61 | 22.73±1.34 |

a: S vs. N; b: N vs. IN; ***p<0.001; **p<0.01; *p<0.05.

Unilateral nephrectomy is a condition that causes oxidative stress for organism. Iloprost administration before unilateral nephrectomy reduces lipid peroxidation which increased after nephrectomy and supports antioxidant activities.

LAPAROSCOPIC LIVING DONOR NEPHRECTOMY IN THE REPUBLIC OF MACEDONIA:FIRST FOUR CASES

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Background: Laparoscopic surgery has been gaining more popularity among transplant surgeons especially in the countries with predominantly living donor transplantation(TR) as Balkan area is. We report our first four kidney grafts harvested by laparoscopic procedure.

Material and methods: In the last 2 years we performed 4 laparoscopic (hand-assisted and three full left-sided) live donor nephrectomies(LDN), two transperitoneal and two extraperitoneal. Mean donor and recipient’s age was 54 (range 38-62) and 25.4 (range 18-40) respectively. The mean operative time was 220±29 while mean warm ischemia time (WIT)was 7±21.min. The recipients and donor survival, DGF, the graft function, intra and postoperative complications were analyzed.

Results: There were no major complications during the laparoscopic procedure. Despite the long WIT there was no significant delayed graft function. Only one case required open conversion. The mean length of stay for the donors was 4.2 days. The mean recipient’s serum creatinin was 1.6±0.8,12-24 months after the surgery.

Conclusion: The authors consider the laparoscopic surgery safe for the donors and yields kidneys with excellent function. The further use of the procedure is fully recommended.

IS THERE A DIFFERENCE IN DEMOGRAPHIC CHARACTERISTICS OF LIVING DONOR SUB GROUPS AND DOES IT AFFECT THE OUTCOME IN RENAL TRANSPLANTATION?

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Living donor renal transplantation is being promoted worldwide due to its high success rate and to meet demand of kidney donation. Strategies to increase living donation need to focus on demographic characteristics of potential donors. Outcome in subgroups of living donor transplantation should also be evaluated critically to balance its benefits against potential risks. We report a retrospective analysis of living donor renal transplantation done in our unit since 1993, looking at donor characteristics and its impact on outcome. Kaplan-Meier and Cox proportional hazards model were used for graft survival. There were 310 living donor transplants-252 (81%) living related and 58 (19%) unrelated. Donors’ mean age was 44 (range 17-75) being less in related than in unrelated. Recipients of parents’ kidneys were younger. Siblings were the commonest donors (n=79) followed by mothers (n=75), fathers (n=60), wives (n=31), husbands (n=8), male partner (n=4) and female partner (n=2). Ethnically White related donors were 76% (n=191) and unrelated 56% (n=55). Respective figures for Non Whites were 13% (n=30) and 2% (n=1).

Graft survival for recipients of unrelated donors was 98.4% and 92% at 2 and 5 years respectively. It was 98.2% and 97% for those of unrelated donors. 10 recipients of related donor kidneys died (7 with functional graft) and 2 of unrelated donors (1 with functioning graft). Thus first degree relatives are the predominant living donors under current arrangement of donor selection in all ethnic groups and the outcome is similar irrespective of the donor type.
lively. Patients with a sepsis (pneumonia) onset pre-transplantation cost an extra $27,400 ($22,800) during the year of the onset. Patients with a sepsis (pneumonia) onset post-transplantation cost on average $48,400 ($38,400) extra. Regression analyses controlling for recipient, donor, and transplant characteristics confirmed the magnitude and significance of the AAMP results.

Conclusions: Episodes of sepsis and pneumonia have a strong and independent impact on graft survival and costs.

**DETERMINATION OF BK VIRUS LOAD IN URINE AND PLASMA IN RENAL TRANSPLANT RECIPIENTS**

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BK virus is an important pathogen in renal transplant recipients associated with interstitial nephritis (BKVAN) and ureteric stenosis in renal transplant recipients. We therefore devised a method to detect the virus using real-time PCR in our unit.

**Materials and Methods:** Plasma and Urine samples from 34 patients were randomly tested for the presence of cell free BK virus using Real time PCR. Similarly serial monitoring was done on 20 renal allograft recipients. BKV-V1 plasmid was used as standard. A quantitative PCR was performed using dual-labelled TAMRA probes. The results were expressed as mean genome copies per ml of plasma or urine. Variation in plasma and urine levels were compared with clinical state and level of immunosuppression. The effect of intervention in cases of high BK virus load was also assessed.

**Results:** BK virus was detectable in all patients in urine or Plasma at some stage following transplant. However the majority had low levels. Three patients had high load detectable in both urine (-10^7 ml) and plasma (-10^5 ml). One of these had a biopsy proven BKVAN that responded partially to immunosuppression reduction with antiviral therapy. In other two, the high titres were detected first by Real-time PCR. In both, this was associated with graft dysfunction that was reversed following reduction in immunosuppression.

**Conclusion:** Quantitative Real-time PCR is a sensitive rapid method for detection of BK virus in both urine and plasma. Early detection of high viral copy and prompt restoration of immunity by reduction in immunosuppression helps prevent further damage by the virus and thus help preserve graft function.

**PO-565**

A CLINICAL DECISION MODEL OF INFECTION WITH MODERN QUADRUPLE IMMUNOSUPPRESSION

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This study developed a robust clinical decision model to examine the incidence, nature and consequences of infection in patients receiving anti-CD25-based quadruple immunosuppression after renal transplantation.

**Methods:** Case and event incidence, cumulative probabilities, frequency distributions, and outcomes under conditions of normal clinical practice were examined in 270 sequential patients receiving anti-CD25 based quadruple immune suppression.

**Results:** The overall case incidence of infection was 72.6%, with a mean event incidence of 1.58/patient/year. Principal pathogens were bacterial (46.7%), fungal (10.4%) and viral (51.5%) and unknown (8.5%). The case incidence of CMV infection was 34.4% (93/270 patients), declining from 53% in D+/R+ pairs, to 27% in D+/R- pairs and 7% in D-/R- pairs. 58% of cases were diagnosed in Q1, 33% in Q2, 5% in Q3, and 1% in Q4. 25.9% of patients (70/270) exhibited CMVpp65 antigenemia only, and 8.5% (23/270) developed symptomatic disease which was proportionally most common in D+/R- pairs (12%). Symptomatic disease was associated with a significantly higher maximum level of pp65 expression (80±187 vs 9±12 cells, p<0.001). No graft losses or patient deaths were attributed to CMV.

**Conclusion:** CMV infection remains an important consequence in patients receiving quadruple immune suppression and effective anti-viral therapy. The combination of frequency and resource utilization data provides a robust model for rapid analysis of clinical and economic outcomes and comparison of therapeutic strategies.

**PO-567**

EFFICACY AND SAFETY OF A COMBINED POLYCYCLONAL-MONOCYCLONAL INDUCTION WITH TACROLIMUS AND MMF IN HIGH-RISK CADEVERIC RENAL TRANSPLANTATION

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**Background:** An increasing number of renal transplant patients present for repeated transplant, frequently with increased panel reactivity (PRA). Literature demonstrates significantly lower GS rates, compared to non-sensitized patients undergoing first transplant. This study examines the efficacy and safety of tacrolimus in combination with MMF, steroids and a combined polyclonal-monoclonal induction, in immunological high-risk cadaveric renal transplantation.

**Patients and Methods:** A series of 20 renal allograft recipients with PRA>30% or history of previous immunological graft loss were enrolled in this study (10 male, 10 female, mean age 44.5 years) and were followed for a period of 1 year. Assessments were performed at 1, 3, 6 and 12 months. Besides 1-year-GS, functional parameters, as well as adverse events, complications and graft loss were observed.

**Results:** Patient survival after 12 months was 100%. Over all, 1-year-GS was 96%. 1 graft was lost due to technical problems (graft vein thrombosis) no graft loss accounted to immunological reasons. During the first year, the total number of biopsy proven acute rejection episodes (ARE) was only 20%. Delayed graft function was found in 8 patients (40%). Two patients had to be discontinu-}

**Conclusion:** The combined polyclonal-monoclonal induction with the use of tacrolimus, MMF and steroids, provides a very effective and safe regimen in high-risk cadaveric kidney transplantation.

**PO-568**

A DECISION ANALYTIC MODEL OF CMV INFECTION WITH MODERN QUADRUPLE IMMUNOSUPPRESSION

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**Purpose:** To develop a robust clinical decision model to investigate the determinants, detection, and consequences of CMV infection following renal transplantation in patients receiving anti-CD25 based quadruple immune suppression.

**Methods:** Case and event incidence, cumulative probability, and outcomes of CMV under conditions of normal clinical practice were examined in 270 sequential patients receiving current quadruple immune suppression, and were incorporated into a population-based probabilistic decision analytic model of renal transplantation.

**Results:** Patients were allocated to four risk strata according to donor (D) and recipient (R) CMV serostatus pre-transplant. High risk D+/R- received 3 months of VGGV prophylaxis, and all patients were monitored by CMVpp65 expression. The overall case incidence of CMV detection was 34.4% (93/270 patients), declining from 53% in D+/R+ pairs, to 27% in D+/R- pairs and 7% in D-/R- pairs. 58% of cases were diagnosed in Q1, 33% in Q2, 5% in Q3, and 1% in Q4. 25.9% of patients (70/270) exhibited CMVpp65 antigenemia only, and 8.5% (23/270) developed symptomatic disease which was proportionally most common in D+/R- pairs (12%). Symptomatic disease was associated with a significantly higher maximum level of pp65 expression (80±187 vs 9±12 cells, p<0.001). No graft losses or patient deaths were attributed to CMV.

**Conclusion:** CMV infection remains an important consequence in patients receiving quadruple immune suppression and effective anti-viral therapy. The combination of frequency and resource utilization data provides a robust model for rapid analysis of clinical and economic outcomes and comparison of therapeutic strategies.

**PO-569**

TACROLIMUS VERSUS CYCLOSPORINE MICROEMULSION: IMMUNOSUPPRESSIVE REGIMEN MAKES A DIFFERENCE IN LIVING RENAL TRANSPLANTATION

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Living donation now accounts for over 50% of kidney transplants in the US. We investigated whether there are differences in terms of graft outcome or cost between tacrolimus (TAC)- and cyclosporine (CSA)-based immunosuppression in living donor transplantation recipients (LDTx).
IMMUNOSUPPRESSIVE REGIMEN MAKES A DIFFERENCE IN CADAVERIC RENAL TRANSPLANTATION: TACROLIMUS VERSUS CYCLOSPORINE MICROEMULSION

Robert S. Woodward1, Andrea Kulinvna1, Daniel C. Brennan2, 1HMP, UNH, Durham, NH, USA; 2Washington University, St. Louis, MO, USA.

We compared 2-year costs and 3-year graft survival between subgroups of patients receiving cyclosporine microemulsion (CSA)-based versus tacrolimus (TAC)-based immunosuppression.

Methods: We analyzed USRDS data on first, single-organ deceased donor renal transplant recipients (DDTRs) transplanted in 1998-2000 with Medicare as the primary payer. We compared patients on CSA+MMF+steroids (n=5,445) against patients on TAC+MMF+steroids (n=1,854), controlling for the receipt of induction. We calculated Medicare's average per patient savings at 2 years post-tx associated with the use of the CSA+steroids without Azα or MMF had superior outcomes compared to recipients of TAC+MMF+steroids (HR=0.957, P=0.026). Costs: At 2 years post-transplantation, Medicare payments were the highest ($70,511) for patients on TAC+MMF+steroids, followed by patients on CSA+steroids ($63,632), patients on CSA+Azα-steroids ($58,729), and patients on CSA+MMF+steroids ($58,772). Patients on the standard TAC regimen accured significantly higher cost than all other cohorts (p<0.001).

Conclusion: Use of CsA, MMF, and steroids when compared to TAC, MMF, and steroids in LDRs was associated with superior graft outcome and lower costs at 2 years post-transplantation.

PO-571 BASILIXIMAB VS. ANTITHYMOCYTE GLOBULIN IN CADAVERIC RENAL TRANSPLANTATIONS

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Purpose: In cadaveric transplantation, induction therapy is induced with either polyclonal or monoclonal antibody preparations. We compared the drugs basiliximab and antithymocyte globulin (ATG) in induction therapy; in terms of rates of acute rejection (AR), chronic allograft nephropathy (CAN), patients and graft survival.

Patients and Methods: We performed 47 cadaveric renal transplantations between May 2001 -Dec. 2004. ATG (2.5 mg/kg) and basiliximab (20 mg in days 0 and 4) in 31 and 16 patients, respectively. All of the patients received triple immunosuppressive combinations. The mean follow-up period was 27 months. Both groups were similar in terms of recipients' age, gender and tissue mismatch.

Results: AR episodes were seen in 2 (12.5%) in basiliximab and 5 (16.1%) in ATG groups (p=0.74), while there were found to be in 1 (5%) and 3 (9.3%) cases in the basiliximab and ATG groups, respectively. In the basiliximab group, the mean serum creatinine levels in the 1st and 6th months, 1st and 2nd years were 1.6, 1.4, 1.8 and 1.3 mg/dl, respectively. In the ATG group, the mean serum creatinine levels in the 1st and 6th months, 1st and 2nd years were 1.7, 1.4, 1.4 and 1.4 mg/dl, respectively. No statistical differences were seen between the two groups in terms of serum creatinine levels.

The rates of 3-year graft and patient survival were 78.7 and 93.7 percent in the basiliximab group, while 80.9 and 96.7 percent in the ATG group (p<0.05).

Conclusion: Although we did not obtain late results; the rates of AR, the early graft and patient survival rates were similar in both groups. Thus, basiliximab can be used as effectively and securely as ATG.

PO-572 SCLEROSING ENCAPSULATING PERITONITIS (SEP) AND RENAL TRANSPLANTATION: FAVOURABLE OUTCOME IN 2 CASES IN OUR CENTER

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SEP is an uncommon (3.5-4.2/1000 pts/yr) complication of peritoneal dialysis (PD), rarely reported in renal transplanted patients (RT); we describe 2 cases out of 1870 RT in our center.

Case 1: 26 year old male, PD treated since 1997 transplanted in 2001. Immunosuppression (IS): tacrolimus (TAC), mycophenolate mofetil (MMF) and steroids (S). After 2 years: 25% body weight loss, anorexia, vomiting and abdominal pain; AT CT scan: ascites and peritoneal calcifications. At laparotomy: encapsulating peritonitis with bioplastic picture. S surgery consisted of enterolysis. IS: TAC and MMF unchanged, S dose increased (2.5 to 5 mg/day), 1 year after body weight and well being resumed; sCr unchanged.

Case 2: 47 year old female, PD treated for 5.5 years and subsequently with haemodialysis because of multiple peritoniats, transplanted in 2003 with the same IS as in case 1. 6 months later: 15% weight loss, vomiting and epigastric pain. AT CT scan: encapsulating mass and dilated bowel loops. At laparotomy: ileal loops encased, inflammatory cocoon and loculated ascites. At biopsy: SEP IS: S boluses and switching from TAC to sirolimus (biopsy proven nephrotoxicity and tubulitis), 6 months later; sCr unchanged; the patient’s well being restored.Conclusion: 1) SEP should be investigated in RT previously PD treated, with cachexia and subacute small bowel obstruction of uncertain origin despite of no favouring PD and of adequate IS. 2) Surgery is mandatory in serious cases. 3) Good outcomes may be achieved with any immunosuppressive drugs when therapy includes S.

PO-573 CENTRAL BIOPSY ANALYSIS CONFIRMS RESULTS OF LOCAL BIOPSY ANALYSIS: RE-ASSESSMENT OF THE ATLAS STUDY EFFICACY DATA

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Purpose: The ATLAS study was a 3-arm, 6-month, open, prospective study comparing two steroid-free regimens - basiliximab/tacrolimus (B/Tac) and tacrolimus/MMF (Tac/MMF) - with triple tacrolimus/MMF/steroid therapy as control. Incidence of biopsy-proven acute rejection (AR) was the primary end-point.

If clinical or laboratory signs indicated the occurrence of a rejection, a renal biopsy was to be performed. Rejection was diagnosed and graded by the local histopathologists. The results were presented previously: incidences of AR were 26.3% (B/Tac), 30.5% (Tac/MMF) and 3.6% (control). The estimated 6-month AR-free rates (Kaplan-Meier method) were 72.0% (B/Tac), 69.0% (Tac/MMF), and 91.5% (control).}

Methods: To verify the study results a central re-evaluation was performed in a blinded manner. Biopsies were again graded according to the Banff (1995) score.

Results: The full analysis set comprised 153 (B/Tac), 151 (Tac/MMF), and 147 patients (control). As in the previous local biopsy analysis, steroid-free groups had statistically significant higher incidences of AR than the control; differences

-PO-570 IMMUNOSUPPRESSIVE REGIMEN MAKES A DIFFERENCE IN CADAVERIC RENAL TRANSPLANTATION: TACROLIMUS VERSUS CYCLOSPORINE MICROEMULSION

Robert S. Woodward1, Andrea Kulinvna1, Daniel C. Brennan2, 1HMP, UNH, Durham, NH, USA; 2Washington University, St. Louis, MO, USA.

We compared 2-year costs and 3-year graft survival between subgroups of patients receiving cyclosporine microemulsion (CSA)-based versus tacrolimus (TAC)-based immunosuppression.

Methods: We analyzed USRDS data on first, single-organ deceased donor renal transplant recipients (DDTRs) transplanted in 1998-2000 with Medicare as the primary payer. We compared patients on CSA+MMF+steroids (n=5,445) against patients on TAC+MMF+steroids (n=1,854), controlling for the receipt of induction. We calculated Medicare's average per patient savings at 2 years post-tx associated with the use of the CSA-based regimen. and used multivariate Cox Proportional Hazards regressions to estimate the relative risk of graft failure at three years post-transplantation for the CsA+steroids regimen and used multivariate Cox Proportional Hazards regressions to estimate the relative risk of graft failure at three years post-transplantation.
between B/Tac and Tac/MMF were not significant: The incidences of biopsy-proven AR were 19.6% (B/Tac), 26.5% (Tac/MMF), and 7.5% (control). The estimated 6-month AR-free rates (Kaplan-Meier method) were 79.1% (B/Tac), 73.0% (Tac/MMF), and 92.2% (control).

Conclusion: Central biopsy assessment resulted in slightly lower incidences of AR than the analysis based on local assessments. Overall, the study results were confirmed: With the tacrolimus/MMF/steroid combination a very low AR rate was achieved. Steroid-free therapy was feasible but the incidences of AR were higher in these arms, with the B/Tac combination appearing to be more efficacious than Tac/MMF.

PO-574 EZETIMIBE FOR TREATMENT OF HYPERCHOLESTEROLEMIA AFTER KIDNEY TRANSPLANTATION

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The majorities of patients newly develops or experiences an aggravation of hypercholesterolemia after kidney transplantation. This major risk factor for cardiovascular mortality and mortality after kidney transplantation is often not sufficiently controlled by the single treatment with statins. The aim of this study was to prospectively investigate the safety and efficacy of ezetimibe, a new inhibitor of intestinal cholesterol absorption, in addition to a treatment with statins in patients after kidney transplantation.

Twelve kidney transplant recipients, treated with fluvastatin (n=10), pravastatin (n=1), or simvastatin (n=1), but not meeting the target lipid level according to AHA criteria, additionally received 10 mg ezetimibe per day. Their mean age was 53±9 years (8 male/4 female), transplanted 1-18 years ago. Immunosuppressive therapy consisted of prednisone (all patients), cyclosporine A (CyA, n=7), and tacrolimus (Tac, n=0). Two patients additionally received azathioprine and 3 mycophenolate mofetil.

Blood samples for determination of total cholesterol (TC), LDL cholesterol, HDL cholesterol, serum creatinine, creatine kinase (CK), CyA and Tac concentrations were drawn on day 0, 7, 42 and 84. As early as one week after the beginning of ezetimibe treatment, an additional effect on serum lipids could be observed (TC -56±13 mg/dl, LDL -58±21 mg/dl). This effect persisted throughout the study period (day 84: TC -54±13 mg/dl, LDL -58±21 mg/dl). There were no changes in transplant function and CyA and Tac concentrations, respectively. Side effects were not observed.

PO-575 NEW-ONSET DIABETES IN THE FIRST YEAR AFTER KIDNEY TRANSPLANTATION – INCIDENCE AND RISK FACTORS

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New-onset diabetes mellitus (NODM) is an increasing and clinically relevant complication after kidney transplantation (KTx).

We studied all 620 patients receiving a kidney transplant at our institution between January 1996 and December 2002. After excluding patients with combined transplantation, diabetes prior transplantation, graft failure and death within 1 year after KTx and missing data, 363 adult kidney transplant recipients were eligible for further analysis. NODM was diagnosed according to international consensus guidelines (Transplantation 2003;75:SS3).

The mean incidence of NODM was found to be 11.8% during the first year after KTx. NODM increased over time from 4.0% in 1996 to 17.8% in 2002.

We found an increasing incidence of NODM, especially in recent years. Besides the choice of immunosuppression, an increasing number of retransplantations may contribute to this fact.

PO-576 A RANDOMIZED OPEN-LABEL STUDY TO COMPARE THE SAFETY AND EFFICACY OF TWO DIFFERENT SIROLIMUS REGIMENS WITH A TACROLIMUS + MYCOPHENOLEATE MOFETIL REGIMEN IN DE NOVO RENAL ALLOGRAFT RECIPIENTS: 6 MONTH INTERIM ANALYSIS

Frank Pietruck,1, Marian Klinger2. 1The ORION Study Group; 2Nephrology, University Hospital, Essen, Germany; 2Nephrology and Transplantation, Medical Academy of Wroclaw, Poland.

Objectives: To compare the safety and efficacy of sirolimus monotherapy with tacrolimus/mosteridines in de novo renal allograft recipients in the first year after transplantation.

Methods: A randomized, open-label, multicenter study to compare two monotherapy regimens in de novo renal transplantation recipients: Group 1: a combination of sirolimus and corticosteroids (sirolimus 8 mg/m² per day plus corticosteroids (2 mg/kg per day); Group 2: tacrolimus (10 mg/m² per day) plus corticosteroids (2 mg/kg per day).

Results: The primary endpoint, renal function, will be reported after 6 months. A total of 111 patients from 19 centers were randomized. At 6 months, no significant differences were found between the two groups with regard to graft function.

Conclusion: The two monotherapy regimens were equally effective and safe in the treatment of renal transplantation recipients in the first year after transplantation.

PO-577 KIDNEY TRANSPLANTATION IMPROVES THE EXERCISE CAPACITY OF THE END-STAGE RENAL FAILURE PATIENTS

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Purpose: To study effects of kidney transplantation on exercise performance in end-stage renal failure patients.

Methods: A prospective, randomized, controlled, crossover study. TN 87 patients on hemodialysis were enrolled in two groups.

Results: The VO2max of the patient group was significantly higher than that of the control group (p<0.01). The VO2max of the patient group was 20.3±6.3 ml/kg/min, and that of the control group was 17.1±5.9 ml/kg/min.

Conclusion: Kidney transplantation improves exercise capacity in end-stage renal failure patients.
PO-578 NON-INVASIVE METHODS TO PREDICT KIDNEY FUNCTION IMMEDIATELY AFTER TRANSPLANTATION
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We have investigated the utility of the guidelines for the diagnosis and classification of CKD based on the estimated GFR (MDRD equation) elaborated by the Kidney Disease Outcomes Quality Initiative of the National Kidney Foundation of renal transplant patients, namely, 23.9%, and 11.3%, respectively. The mean cold ischemia time was 1880 min. Kidneys with IF showed significantly lower weight (211.28 vs. 281.36 g; p < 0.001). Neither RBF nor VR were different between the IF and DF groups. However, CBF was significantly greater in the IF than in the DF group at Smr: 29.98 vs. 23.56 mL/min/100g tissue (p < 0.001). The difference was even more significant at 35 min: 33.94 vs. 15.47 mL/min/100g tissue (p < 0.0001). The DF group showed an average reduction in CBF of 8 mL/min/100g between 5 and 35 min. The maximum cortical blood flow at 5 min after reperfusion in DF was 34.5 mL/min/100g tissue, at 35 min all kidneys in this group had CBF values not greater than 22 mL/min/100g tissue, whereas there was no significant change in CBF among the IF group.

Conclusion: The evaluation of CBF after transplantation predicted the occurrence of immediate allograft function: a CBF value of less than 22 mL/min/100g tissue at 35 min after revascularization was significantly associated with delayed/slow graft function.

PO-579 CHRONIC KIDNEY DISEASE CLASSIFICATION IN RENAL TRANSPLANT RECIPIENTS
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To investigate the efficacy and safety of mycophenolate mofetil (MMF) for prevention and treatment of rejection in renal transplant recipients.

Methods: A total of 124 renal transplant recipients were randomly divided into MMF group: oral MMF 20 to 25 mg kg⁻¹ day⁻¹ (n=48), or Aza group: Azathioprine 50 mg/d (n=76). All of the patients generally administered ATG, CsA and Pred as basic immunosuppression. The morbidity of acute rejection (AR), corticosteroid-resistant rejection (CRR) and complication in the patients of the two groups 2 months after transplantation were observed.

Results: There was no significant difference in morbidity. 3-month graft loss between two groups. Morbidity of acute rejection and CRR was 31.2% and 6.2% respectively in MMF group, significantly lower than in Aza group (both p < 0.05). The efficacy of MMF 3.0g/d to treat CRR was similar to that of OKT3. The side effects related to MMF and Aza included vomiting, diarrhea, leukopenia, pancytopenia, panhematopenia, infection and medicamentous liver lesion, and its morbidity in MMF group and Aza group was 8.3% vs 2.6% (p < 0.05), 62.5% vs 39.5% (p < 0.05), 31.2% vs 13.2% (p < 0.05), 6.3% vs 6.0% (p < 0.001), 50.0% vs 46.0%(p < 0.05), 4.2% vs 11.8%(p < 0.05), respectively. 58.3% of the patients experienced at least one adverse events and 25.0% of the patients had to reduce or withdraw MMF in MMF group compared with 19.7% and 9.2% in Aza group (p < 0.001 and 0.05 respectively).

Conclusion: MMF could significantly decrease the incidence of early AR and CRR respectively. Large dose of MMF (3.0g/d) to treat CRR had a good efficacy. The side effects of MMF were more severe than those of Aza and one fourth was compelled to decrease or withdraw MMF in MMF group.
POLYOMA BK VIRUS NEPHROPATHY (BKVN). THE EFFECT OF EARLY DIAGNOSIS ON RENAL FUNCTION OR GRAFT LOSS

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Purpose: BKVN produces a high incidence of renal function deterioration or graft loss. We analyzed the evolution of renal function in patients with BKVN. Methods: 664 consecutive renal transplant patients were followed from February 1998 to July 2003. All patients with unexplained renal function worsening underwent kidney biopsy and from August 2003 to February 2005 the patients were monitored intensively for BK viruria and urine cytology (decoy cells). If positive, PCR in blood and a kidney biopsy were done. Diagnosis was confirmed by PCR in biopsy tissue.

Results: Twenty patients developed BKVN, 15 (75%) male and 18 (90%) treated with tacrolimus and mycophenolate mofetil. The mean age was 40.5±16.7 vs 52.5±10.1 years. The mean time from transplant to diagnosis was 60.4±46.4 vs 18.2±10.5 weeks and serum creatinine at diagnosis was 2.5±0.7 vs 20.0±6.0 mg/dL. The 12 patients treated with cidofovir had serum creatinine of 3.1±2.2 mg/dL vs 5.0±3.3 in the non-treated patients. Follow-up was 21.8±20 vs 5.2±3.3 months. At diagnosis, 17 patients had viral inclusions (13 PCR positive). In 14 biopsy was repeated (5.1±2.4 months), in six of which the inclusions persisted (five PCR positive), with higher serum creatinine (5.8 vs 2.6 mg/dL). Five patients had acute rejection after immunosuppression reduction. PCR in urine remained positive in all cases tested.

Conclusions: Follow-up with urinary cytology enables earlier diagnosis of BKVN. This plus treatment with cidofovir delays loss of renal function.

MUCORMYCOSIS INFECTION AFTER KIDNEY TRANSPLANTATION

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Mucormycosis is a rare opportunistic fungal infection that occurs in kidney recipients. The most frequent form of presentation is rhino-cerebral. We, however, report pulmonary involvement of this infection in four patients who received kidney transplantation at our center. Three patients were male and two cases were female. Post-transplant diabetes mellitus were seen in three cases. The immunosuppressive regimen in all patients was cyclosporine, Aza-thioprine/MMF and prednisolone. Two cases were given pulse of Methylprednisolone (40 mg/kg) due to acute rejection. In spite of early diagnosis and high dose treatment by amphotericin B in all patients, and extensive debridement in one, all died. Kidney Transplantation, invasive immunosuppressive therapy, and diabetes mellitus were major risk factors for pulmonary mucormycosis in our patients. It is interesting that there was only once rhino-cerebral involvement in all cases. Thus, pulmonary infiltration in kidney recipient can result from mucormycosis and early diagnosis by tissue biopsy and culture, high dose of amphotericin B and extensive debridement (lobectomy in pulmonary involvement) are essential in treatment of this infection.

IMPACT OF KIDNEY TRANSPLANTATION ON HEARING LOSS IN PATIENTS UNDERGOING HEMODIALYSIS

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We carried out serial autoscopy and audiological test ( tympanometry, pure-tone, speech audiometry) in 72 patients with chronic renal failure undergoing hemodialysis before and two weeks after kidney transplantation; patients with histories of chronic otitis, ototoxic drug treatment, Aport's syndrome and auditory trauma were excluded. Intensity of hearing was expressed in decibel from 0-90 dB and band of audiorefrequency in Hertz from 250-6000 HZ. Normal intensity was considered in the range 0-20 dB. We divided hearing loss to five groups: 1) slightly hearing loss (20-30 dB), 2) mild hearing loss (30-40 dB), 3) moderate hearing loss (40-60 dB), 4) severe hearing loss (>-60 dB), 5) high frequency sensory-neural loss was considered hearing loss above 2000 HZ.

The results obtained indicate that the incidence of hearing loss before and after kidney transplantation was 47.2% (34 cases) and 33.3% (24 recipients), respectively. Seven patients out of group 1 and three patients group 5 returned to normal states (group 1). There was significant difference in mean age between normal and hearing loss groups (P<0.05). However, age and sex had not impact on severity of hearing loss before and after kidney transplantation.

The results of audiometric tests indicated significant improvement of kidney transplantation on hearing, especially in high and high frequency ranges. No correlations with blood pressure, weight changes and biochemical parameters (Ca, P, Na, K, Hct and Hb) were found. It is assumed that uremic toxins are responsible for sensory-neural hearing loss in patients undergoing hemodialysis and therefore it can be influenced favorable by a normal renal allograft function.

ANGIOTENSIN GENE POLYMORPHISM IS ASSOCIATED WITH DEVELOPMENT OF POST RENAL TRANSPLANT HYPERTENSION

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Development of hypertension after kidney transplantation depends upon allo-graft function, type and doses of immunosuppression, presence of native kidney, recurrent glomerulonephritis and transplant renal artery stenosis. Presence of hypertension pre-transplant is the most important risk factor for persistence of hypertension after transplant. Several parameters modifying the lipid related donors. Polymorphism of the angiotensin converting enzyme (ACE) gene has been implicated in the development of essential hypertension in the general population and the DD genotype of the ACE gene is associated with poorer allograft functions in renal transplant recipients. The association of ACE gene polymorphism with post renal transplant hypertension is far from clear.

We studied the ACE gene polymorphisms in 42 patients with post transplant hypertension on maintenance doses of immunosuppression, normal allograft functions with no proteinuria and no evidence of renal artery stenosis. The DD genotype was seen in 93%, ID genotype in 5% and II genotype in 2% as compared to 40%, 52% and 8% respectively in patients with essential hypertension and 31%, 47% and 22% respectively in normotensive control Indian population (p<0.05). We conclude that the DD genotype of the ACE gene is associated with occurrence of post transplant hypertension in patients with normal allograft functions on maintenance doses of immunosuppression. This genotype may be an important factor predicting persistence of hypertension after transplant.

POST-TRANSPLANT DYSLIPEMIA: WHICH ARE THE RISK FACTORS? A ONE YEAR FOLLOW-UP AFTER RENAL TRANSPLANTATION

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Introduction: Dyslipidemia, a major cardiovascular risk factor, is a common complication of renal transplantation. Several parameters modifying the lipid levels have been reported but as many patients are already dyslipidemic before transplantation, the true incidence of post-transplant dyslipidemia is not well established.

Methods: All records of 222 non-diabetic cadaveric renal transplant patients performed between January 1996 to 2000 in our center were reviewed. Clini-cal and biological data including: lipid levels(total cholesterol (TC), triglycerides (TG), HDL and LDL) were collected before and one year after transplantation. We sought to determine the incidence and the independent risk factors of hypercholesterolemia and hypertriglyceridemia as well as the prevalence and the independent risk factors of abnormal HDL and LDL levels one year after transplantation. A univariate statistical analysis followed by a multivariate statistical analysis using a step-by-step logistical regression were used.

Results: Before transplantation, 30.7% and 29.7% of patients had elevated TC and TG respectively. One year after transplantation, the incidence of de novo hyperTC and hyperTG were 20% and 15.6% respectively; the prevalence of increased LDL and decreased HDL levels were 55% and 37% respectively. The independent risk factors identified after the multivariate statistical analysis were for TC: pretransplant TG (OR: 3.07; CI: 1.04/21.65) and for TG: pretransplant TG (OR:2.75 CI: 1.67/4.72) and ramipracyl (OR: 7.57 CI: 1.53/38.4). Prevalence of dyslipidemia was significantly lower in patients receiving tacrolimus vs those receiving other immunosuppressants.

Conclusion: In our population, pre-transplant dyslipidemia and treatment with ramipracyl were the major risk factors of post-transplant dyslipidemia. Patients treated with tacrolimus showed less dyslipidemia than those receiving other immunosuppressive treatments.

COMPLICATIONS IN ELDERLY RENAL TRANSPLANT RECIPIENTS

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Elderly renal transplant recipients are frequently reported to have poor patient and graft survival statistics compared to younger controls. This is often at-
tributed to the higher mortality among elderly persons in general, as illustrated by comparatively favourable graft survival censored for death with a functioning graft (DWFGr). However, detailed reports of post-operative course and complications necessary to substantiate this interpretation are lacking.

Consequently, we conducted a detailed retrospective analysis of 55 recipients aged 65 and over, and compared outcomes to 55 younger patients aged 18-64, all undertaken at Guys hospital between 1997 and 2004 with a mean follow-up of 31 months. Actual patient and graft survival statistics were significantly lower among elderly patients (P<0.001 and 0.009 respectively) whereas graft survival censored for DWFGr was not (P=0.175). Mortality was due to cardiac causes (5 vs 1), cancer (3 vs 0), malignancy (3 vs 2) and cerebral abscesses in one elderly patient. Severe infections necessitating admission were more common amongst controls (45%) than elderly patients (35%) (P>0.05). Similarly, while equal proportions in each group experienced rejection (35%) and episodes among controls where more often steroid resistant (25% vs 33%, elderly vs controls P>0.05). Both groups experienced a similar range and frequency of complications, most commonly infection and transplant-related diabetes. Median length of hospital stay differed between the elderly and controls (27 ± 15 vs 12 ± 4 days; P<0.001) with a longer hospital stay for the elderly. This may imply that the elderly group has a higher frequency and severity of complications. Inclusion criteria were all undertaken at Guys hospital between 1997 and 2004 with a mean follow-up of 31 months.

Conclusion: Exclusion of elderly patients from renal transplant waiting lists on the grounds of age alone is not justified by the findings of this study. Overall survival expectancy is lower among these patients, transplantation was reasonably well tolerated.

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### PO-598 BONE HISTOPATHOLOGY AND MINERAL DENSITY IN KIDNEY TRANSPLANT RECIPIENTS AFTER ONE-YEAR OF ALENDRONATE TREATMENT

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**Background:** Bisphosphonates were shown to be effective in prevention of bone loss, but only few data are available about bone histopathology after bisphosphonate treatment.

**Methods:** Sixteen patients with kidney graft (11 men, 5 women, from 33 to 64 years old, treated with dialysis for 74±37 month) were included in the preliminary analysis of prospective clinical study. Inclusion criteria were bone mineral density (BMD) in the range of osteopenia or osteoporosis immediately after transplantation and serum creatinine under 150 µmol/l. They were treated with anti-IL2 monoclonal antibodies, methylprednisolone, cyclosporine and mycophenolate mofetil. Alendronate treatment 70 mg/week was introduced in the first month after transplantation. Bone mineral density (BMD) of lumbar spine and femoral neck was measured with dual energy x-ray absorptiometry immediately after transplantation, after 6 and after 12 month. Iliac bone biopsy was done one year after transplantation.

**Results:** BMD of the lumbar spine decreased by 6.3% (from 0.853 to 0.797 g/cm², p<0.05) and of the femoral neck by 6.5% (from 0.679 to 0.635 g/cm², p<0.01). Intact PTH decreased from 422±520 ng/l at the time of transplantation to 120±95 ng/l at 12th month. Bone biopsy confirmed adynamic bone in 9 cases (56.3%) and mixed uemic osteodistrophy in 7 cases (43.7%).

**Conclusions:** The study shows that alendronate treatment in the early period after transplantation does not completely prevent decrease of bone mineral density of lumbar spine and femoral neck. Treatment is associated with adynamic and mixed bone histology.

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### PO-599 SUPPORTING MEDICATION ADHERENCE IN RENAL TRANSPLANTATION (SMART): A RANDOMIZED CONTROLLED TRIAL TO IMPROVE ADHERENCE WITH THE IMMUNOSUPPRESSIVE REGIMEN

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**Objective:** To investigate the immunosuppression effect of Chinese herb Tripterygium wilfordii hook f. in Chinese renal allograft recipients

**Background:** The feasibility of the routine use of Chinese herbs in the immunosuppressive regimen of organ transplant recipients is being discussed. This randomized controlled trial was performed to examine the effect of the introduction of the Chinese herb on the immunosuppressive regimen in Chinese renal transplant recipients.

**Methods:** The randomized controlled trial included 249 eligible patients. Patients were randomly allocated to the control group (n=123) or the intervention group (n=126). The intervention group used Tripterygium wilfordii hook f. in addition to the immunosuppressive regimen. The control group received the same immunosuppressive regimen without the herb. The primary endpoint was the incidence of acute rejection as defined by the Banff classification. Other endpoints included the incidence of other adverse events, patient and graft survival.

**Results:** The incidence of acute rejection was lower in the intervention group compared to the control group (13.3% vs 24.7%, p=0.01). The incidence of other adverse events was similar in both groups. There were no significant differences in patient and graft survival between the two groups.

**Conclusion:** The introduction of Tripterygium wilfordii hook f. as an additional component of the immunosuppressive regimen in Chinese renal transplant recipients is safe and may improve the incidence of acute rejection.
SIROLIMUS IN COMBINATION WITH MYCOPHENOLATE MOMETIL FOR ELIMINATION OF CALCINEURIN INHIBITORS FOR STABLE RENAL TRANSPLANT RECIPIENTS IN TAIWAN

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Purpose: We tested a hypothesis that elimination of CNI could promote renal allograft function in stable renal transplant recipients (>6 months posttransplant).

Methods: Patients and methods: A single-arm prospective study was conducted in a transplant center. From June to August 2004, 17 male and female patients who did not have recent acute rejection or deterioration of renal function (>30%) were enrolled from June to August 2004. The age ranged from 19 to 67 (43.5 ± 12.4) years, and the baseline serum creatinine from 1.0-2.8 mg/dl. The target MMF dose was 2g/day unless WBC < 4000/mm³, and the target trough level of sirolimus was 8-12 ng/ml. The primary endpoints were incidence of acute rejection and renal function after CNI elimination. The secondary endpoints were graft and patient survival, side effects and infectious complications.

Results: The follow-up periods ranged from 7 to 9 months. The average MMF and sirolimus doses were 1.50 ± 0.44 g/day and 2.38 ± 0.81 mg/day at the 6th month, respectively. There was no acute rejection nor deterioration of renal function after elimination of CNI. The serum creatinine level dropped from 1.50 ± 0.40 to 1.39 ± 0.39 mg/dl, and the graft survival was 100% 6 months post-CNI-elimination. 4 patients resumed CNIs (cyclosporine in 2 and tacrolimus in 2) because of elevation of liver enzymes in 2, leukopenia in 1 and ventral hernia in 1. However, 2 patients had pulmonary TB at the 3rd and 4th months after CNI elimination.

Conclusion: CNIs could be successfully eliminated with a combined sirolimus and MMF regimen in stable renal transplant recipients. Better renal function was noted after CNI elimination, though long-term follow-up for the risk of infection seemed necessary.

THE ROLE OF FREE RADICALS IN ISCHAEMIA-REFUSION INJURY OF THE TRANSPLANTED KIDNEY

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Introduction: Reactive oxygen species (ROS) are considered to be important factors involved in the pathophysiology of renal ischemia/reperfusion injury. ROS induce alterations of proteins, carbohydrates, DNA, lipid membranes and lead to cell and organ dysfunction. Several different antioxidant defense mechanisms operate to prevent or limit oxidant injury.

Aim: An assessment of oxidative stress after the reperfusion of the cadaveric transplanted kidney.

Material and methods: The study has been carried out on the group of 57 cadaveric kidney transplant recipients (mean age 42.5 ± 12.3 years). Venous blood samples were taken on heparin during transplantation procedure from cubital (before reperfusion) and graft renal vein (5 and 15 minutes after reperfusion). Following factors were measured: glutathione level, activities of glutathione peroxidase (GSH-PX), catalase (CAT) and superoxide dismutase (SOD) and oxidant anion production by neutrophils in whole blood before and after reperfusion without and after stimulation with opsonized zymosan according to Bellavite et al. method.

Results: The mean superoxide anion levels increased from [0 [mmol/15 min x 10⁸ granulocytes] to 43.1 ± 18.37 [mmol/15 min x 10⁸ granulocytes] 5 minutes after reperfusion (p < 0.03) and to 69.46 ± 42.74 [mmol/15 min x 10⁸ granulocytes] 15 minutes after reperfusion (p < 0.01).

The differences in glutathione levels and enzymes activity were not significant.

Conclusion: Restoration of oxygen supply to ischemic kidney results in the production of ROS, which may cause renal injury by lipid peroxidation.

Superoxide anion measurement can be used effectively as a marker of oxidative stress resulting from ischemia - reperfusion injury of the transplanted kidney.

CAN ALLOCATION ALGORITHMS IMPROVE WAITING TIME AND SURVIVAL OF RENAL TRANSPLANT RECIPIENTS AT IMMUNOLOGICAL RISK?

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Renal transplant candidates at immunological risk (with anti-HLA antibodies or previous transplants) have lower transplantation chances and their transplant outcomes are generally less satisfactory when compared with standard recipients. Aim of the study was to evaluate the efficacy of the renal allocation algorithm used in our setting in improving transplantability and transplant outcome of recipients at immunological risk.

Methods: From 1/1/1998 to 31/12/2002, 1972 renal transplants performed in 10 transplant Centers were included in the study. 1712 transplants were performed in standard patients (group A) and 260 (13.2%) in recipients at immunological risk (group B). Kidneys were allocated following an algorithm, which foresees priority to patients at immunological risk with a number of HLA-A, -B, -DR mismatches up to 2 and proven that the recipient does not have specific antibodies against donor HLA antigens. All pre-transplant donor-recipient crossmatches were negative. Mean patient follow-up was 42.6 ± 21.3 months. Analysis was supported by the use of the SAS statistical package.

Results: 17 transplant centers were included in the study. From 1998 to 2002 median waiting time of group B patients decreased from 5.5 to 4.3 years. In group B patients, 3-year graft survival rate was not statistically different according to number of previous failed transplants, HLA-DR mismatches and recipient % PRA.

PO-597 EVALUATION OF SOLUBLE CD30 IN PERTRANSPLANT SERUM SAMPLES OF 242 PATIENTS WAITING KIDNEY TRANSPLANTATION

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Background: Sensitivity and specificity of current assays for CD30 are not sufficient for high throughput analysis.

Recent studies suggest that high pretransplant serum levels of soluble CD30 (sCD30) are a risk factor for acute rejection after kidney transplantation. The aim of our study was to correlate sCD30 serum levels in local patients awaiting kidney transplantation with the allograft function after transplantation. We retrospectively analyzed pretransplant sera (median of 6 sera obtained with intervals of 3 months) from 242 patients of whom 214 (88%) were transplanted with a cadaveric kidney whereas 28 patients received an allograft from a living donor. For sCD30 analysis we used an ELISA kit (Bender, Vienna) validated using 47 local controls. In parallel, all sera were tested for HLA antibodies by lymphocyte toxicity test (LCT) and ELISA (BmT, Meersburg).
In patients with 4 or more pretransplant sera analyzed (n=119) our study re-
vealed mean sCD30 levels ranging from 34.4 U/ml (SD 7.9) to 803.4 U/ml (SD 123.5). A high sCD30 level was defined as the highest value of the local 
controls plus 2 SD = 300 U/ml. Persistent high mean level of sCD30 values 
was identified in 12 patients, whereas in 20 patients only isolated samples 
contained such high sCD30 level. However, regarding the incidence of acute 
rejections there was no correlation with pretransplant sCD30 levels > 300 U/ml 
in patients with cadaveric and living transplants, but the complete analysis of 
the clinical data is currently ongoing. 
Thus, our still preliminary results do not support a predictive effect of sCD30 
determination for kidney allograft rejection.

PO-598
RAPAMYCIN IMPAIRS THE HEALING OF THE URETERIC ANASTOMOSIS
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The immunosuppressive properties of rapamycin are well documented and it is 
used routinely in renal transplant recipients. Rapamycin also inhibits fibroblast 
which may be important for proper healing of the ureteric anastomosis after 
renal transplantation. In this study we investigated the effect of rapamycin on 
the healing of the ureteric anastomosis.

Large White/Landrace pigs (n=12) weighing 22-30kg were subjected to laparo-
tomy and mobilization of both ureters. Each ureter was divided, spatulated 
and re-anastomosed using continuous 6/0 PDS. The animals were randomly allo-
cated to receive either rapamycin 2mg orally per day, or no treatment. On the 
5th postoperative day the anastomoses were excised and examined histologi-

cally and biochemically. Thin strips of ureter were used to measure the tensile 
strength of the anastomosis.

The ureteric anastomoses were all healed and patent, although the proximal 
ureters were markedly dilated. The serum creatinine levels were similar in the 
two groups (1.57 and 1.55). The breaking strength of the ureteric anastomo-
sis was lower in the rapamycin treated animals compared to the control group 
(221+24g versus 261+16g). The hydroxyproline levels in the ureter were lower 
in the rapamycin treated animals (12.8+2.7 versus 22.4+5.3). Histological ex-
amination showed no difference.

Thus in summary, healing of the ureteric anastomosis appears to be impaired in 
animals treated with rapamycin.

PO-599
LONG –TERM OUTCOME OF CADAVERIC KIDNEY 
TRANSPLANTATION IN PRUNE-BELLY SYNDROME
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Purpose: To retrospectively assess the long term outcome of cadaveric kidney 
transplantation in prune-belly syndrome patients with renal failure

Methods: Between January 1988 and December 2003, 11 consecutive ca-
daveric kidney transplants were performed in 8 male patients with prune-belly 
syndrome. Median age was 11 years (range 4-32). Patient and graft survival 
were assessed. Cause of death and graft failure was also reported. These 
outcomes were compared in other patients transplanted for other causes of renal 
failure in our centre.

Results: Median follow-up time was 11 years (range 1-16). Urinary diversion 
 prior to transplant was done in 2 patients, an ileal conduit following bilateral na-
tomy nephrectomy in 1 and a cutaneous vesicostomy in 1 that was taken down 
following the transplant. In none of the patients abdominopelvis was manda-
tory prior to transplant. Actuarial survival rate up to 10 years post transplant 
was 100%. Actuarial 1, 3, 5 and 10 graft survival was 91%, 76%, 76% and 57% 
respectively. One patient died from renal failure complication following failing 
graft 11 years post transplant. Five grafts failed. Cause of failure was acute 
rejection in 1 patient and chronic allograft nephropathy in 4. Median serum 
creatinine in the remaining functioning grafts was 89.9 mmol/l (range 47-149).

There was no difference in patient or graft survival between prune-belly syn-
drome patients and those transplanted for other causes of renal failure (p=0.49 
and 0.96 respectively).

Conclusions: Our results clearly show technical feasibility as well as encour-
aging patient and graft survival following kidney transplantation in prune-belly 
syndrome patients.

PO-600
RISK FACTORS OF POSTTRANSPLANT HYPERPARATHYROIDISM AND HYPERCALCEMIA
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August 2000 and August 2001 were studied. Before transplantation and 3 
months and 1 year after that, calcium, phosphorus, albumin and creatinine 
were checked using UV kinetic method and iPTH was measured using IRMA 
method for the patients. For the purpose of this study, hypercalcaemia was de-

defined as serum calcium > 10.8 mg/dl and high iPTH was defined as iPTH> 60 
g/ml. Results were analyzed by SPSS – 10 software for statistical interpreta-
tion of results, pair T-test, independent T-test were used when indicated.

This 121 patients (Male= 84, Female= 37) with mean age of 35.5 years (SD= 
12.5 years) were on dialysis for an average period of 17.4 months (SD= 6 
months) prior to their transplantation. An increase in the serum calcium and 
a decrease in serum phosphorus and iPTH level was seen in the patients (P<0.001).

Hypercalcaemia was seen in 21 (17.4%) and 75.7%) patients there 
months and 1 year after transplantation respectively. Patients with longer his-
tory of dialysis before their transplantation had an increased risk of developing 
post transplant hyperparathyroidism and hypercalcaemia in the first year post 
transplant period. (P<0.001).

Patients of older age group has an increased risk of developing post transplant hyperparathyroidism (P< 0.05).

Age and the patients time on dialysis before transplantation seems to be 
important risk factors for development post transplant hyperparathyroidism.

We should care more of these factors in transplant patients to decrease the 
risk of post transplant hyperparathyroidism and hypercalcaemia.

PO-601
COMPARISON OF SPOUSAL WITH OTHER DONOR 
GROUPS; A SINGLE CENTER STUDY
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In coping with the shortage of living related and cadaveric donor groups for re-

nal transplantation, and in the fear of organ marketing, spousal donors are con-
sidered as an invaluable potential source. Survival rates have been reported to 
be as high as even some related groups. In this study, 1093 consecutive renal 
transplantations performed in Shiraz (Southern Iran) Organ Transplant center 
till 2003 were studied and patient survival rates in different donor groups were 
calculated using Kaplan-Meier analysis.

The three-year survival rates were 93% for kidneys from 61 spouses, 92% 
for kidneys from 473 living related donors, 91% for kidneys from 427 living-
related (excluding spouses) donors, and 83% for 118 cadaveric kidneys. 
Such results are the same as many other similar reports that consistently show a 
10% lower three-year survival for cadaveric transplants, in addition to the fact 
that spousal donors are at least as good as living related donors, and are a 
reliable source in cases of organ shortage.

PO-602
RENAL TRANSPLANTATION IN THE ELDERLY; 
A SINGLE-CENTER EXPERIENCE
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The increasing number of the aged population in the world has put forward 
the issue of renal transplantation for elderly recipients. However, most studies 
in developed countries have demonstrated a lower graft survival, and patient 
death as a cause of graft loss in elderly patients. This study presents results of 
elderly renal grafts among 1041 consecutive operations in Shiraz (South-
ern Iran) organ transplant center. Surgical techniques and immunosuppressive 
protocols have been the same in all age groups.

Among 1041 consecutive recipients, 120 (11.5%) were 50 or more years old 
(the elderly group); most recipients (56.5%) belonged to the 16-40 age group. 
The elderly group consisted of 76.7% males and 23.3% females; donors in this 
group were 56.7% living-unrelated, 33.3% living related and 10.0% cadavers; 
the number of living-unrelated donors is significantly higher than other age 
groups.

Rejection rate was significantly less in the elderly group (6.6% vs. 12.5%) 
which confirms other studies. However, ATN, major urological complications 
needs intervention, infectious complications (mainly UTI) and cardiovascu-
lar problems occurred significantly more in the aged group. The 1-, 2-, and 
3-year patient survival rates in the elderly group were 93%, 91%, and 88%, re-
spectively. Corresponding data in other age groups were 95%, 92%, and 91%.

Most common causes of death were ATN and infectious complications. The 
data show a lower patient survival in the elderly; however, in contrast to other 
studies, patient death due to factors other than those considered to be the 
cause occurred not more than in other groups. Lower incidence of rejection may 
allow reducing immunosuppression which can help in minimizing infectious 
complications as a major cause of death.
**PO-603** CELLULAR IMMUNITY FOLLOWING VACCINATION AGAINST INFLUENZA VIRUSES IN KIDNEY TRANSPLANT RECIPIENTS

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As kidney transplant recipients are at risk of infections due to their immunosuppressive therapy (cyclosporine A, tacrolimus, azathioprine/mycophenolate mofetil (MMF), prednisone), we performed vaccinations against influenza viruses (Influvac SSW® 2, SmithKline Beecham Pharma) in 65 of these transplant patients and monitored their cellular influenza immunity pre and post one month post vaccination by lymphocyte transformation test (LTT) and ELISPOT. By LTT we observed a significant increase of proliferative responses towards influenza B/Yamanashi, the most recent component of the vaccine (median 1233 vs. 3157 cpm increment, p<0.0001). The ELISPOT was more sensitive and detected significant, 3-fold increases (p<0.0001) in interferon γ production using all three influenza splits (A/Beijing, A/Sydney, and B/Yamanashi). Furthermore, as compared to the other immunosuppressive drugs mentioned above, cyclosporine A treated transplant patients (n=37) displayed significantly higher vaccination-induced increases in ELISPOT reactions (p<0.05). In addition, prednisone treatment appears as a factor significantly influencing LTT but not ELISPOT responses. LTT reactions towards influenza B/Yamanashi were negatively correlated with prednisone dose both at baseline and at month 1 (n=0.32, p=0.01, and n=−0.38, p=0.002, respectively). On the contrary, creatinine level (median 1.3, range 0.6-5.4 mg/dl), interval to transplantation (median 6 years, range 4 months - 19 years), and presence of hypertension or diabetes could not be defined as significant influencing factors. Thus, in kidney transplant recipients under routine immunosuppression influenza-specific cellular immunity can be achieved by vaccination. Here, the ELISPOT assay appears more sensitive to detect immunity than the LTT.

**PO-604** EXPERIENCE WITH CALCINEURINIC-FREE IMMUNOSUPPRESSION IN KIDNEY TRANSPLANTATION WITH MARGINAL DONORS

Federico Oppenheimer, Nuria Saval, Alex Gutiérrez, Nuria Esforzado, Federico Cofan, Vicente Torregrosa, Maria Jose Ricart, Fritz Diekmann, Marta Crespo, Esther Rossich, Josep Maria Campistol. Renal Transplant Unit, Hospital Clinic de Barcelona, Barcelona, Spain.

Kidneys from marginal donors -Non-heart-beating-donors (NHBD), acute renal failure (ARF) and elderly donors- usually show prolonged delayed graft function (DGF) and consequently are at higher risk for acute rejection. Therefore, the use of a strong non-nephrotoxic immunosuppression may be beneficial.

**Aim:** The aim of the present study was to present the results of a pilot study using non-nephrotoxic sirolimus-based therapy in kidney transplantation using marginal donors from November 2002 to October 2004.

**Patients and Methods:** Sixty-seven patients received kidneys from forty-five marginal donors. Cold storage (67) or pulsatile machine (6) was employed. Patients were divided in two groups: Group I: NHBD (n = 22), Group II: ARF and elderly donors (n = 45). Immunosuppression consisted of MMF 2g/day, prednisone at standard doses, sirolimus initiated on day 5 (three loading doses of 6 mg/day, followed by 2mg/day) and rabbit-ATG 1.25 mg/kg for 7 days for group I or Basiliximab for group II. The mean follow-up was 12.4 months.

**Results:** See table 1

| Group I (n=22) | Group II (n=45) |
|---------------|---------------|
| Donor Age (years) | 39 ± 13 | 60 ± 13.4 |
| Recipients age (years) | 49.6 ± 11.2 | 59.5 ± 12.2 |
| Cold ischemia time (hours) | 12.9 ± 3.8 | 16.1 ± 6.2 |
| DGF (%) | 72.7 | 22.7 |
| Graft survival at 1 year (%) | 90.1 | 95.8 |
| Non-primary function (n) | 1 | 0 |
| Patient survival at 1 year (%) | 95.4 | 97.8 |
| Acute rejection at 1 year (%) | 1.9 | 2.4 |
| Renal function (Cr:6mg) (mg/dl) | 1.8 ± 0.7 | 1.7 ± 0.6 |

**Conclusions:** Immunosuppression with ATG or Basiliximab in combination with sirolimus and MMF is effective for recipients of marginal kidney transplants. The excellent renal function and graft survival are the most remarkable results.

**PO-605** LONG TERM RENAL GRAFT SURVIVAL ACCORDING TO THE LIVING DONOR TYPES

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**Purpose:** To know the distribution of living donor types in the kidney transplantation and search their long term survivals. Methods: Materials: 1229 kidney transplantations were performed at our center from November 28, 1989 to December 27, 2003, 86.41% of which were done with living donors. We analyzed the 10 years graft survival rates in many subsets of the cohort. Donor age, sex, ABO compatibility and donor types were considered as risk factors.

**Results:** Genetically related living donors composed of 710 parents (group A: 57.77%), 174 siblings (group B: 14.16%), and 19 others (1.55%). Genetically unrelated were 134 husbands or wives (group C: 10.90%) and 11 others (0.90%). 14 (1.14%) were unknown. The 10 years graft survival rates of each group were 64.82% in group A, 71.19% in group B and 72.93% in group C with no significant difference. A subset of group A who are older than 60 and ABO incompatible revealed significantly low graft survival rate when compared with subsets of both group B and group C who are younger than 60 and ABO compatible.

**Conclusions:** In Japan, three out of four living donors are parents and some of them are aged. If a donor has multiple risk factors with other living donors relevant, prognostic factors should not be neglected in the donor selection.

**PO-606** TRANSPORT TO TRANSPLANT: ARE WE QUICK ENOUGH?

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**Background:** Renal transplant cold ischaemic time (CIT) is well recognized risk factor for poor graft outcome. British Transplant Society guidelines are to keep the cold storage times of the kidney to below 24 hours whenever possible. While our average CIT in last 4 years remained below 19 hours, we believe that there is still scope for reduction in that time.

**Aim:** Identify factors which influenced the CIT in 2003 at our centre in order to reduce this time to the shortest possible.

**Method:** We recognized following periods as components of total CIT: Retrieval & Transport: Time from retrieval of the kidney till it reaches our centre Cross matching time: Time from arrival of sample to tissue laboratory till reporting of cross match result. Gaining access to the operating theatre: Time from report of cross match to take the kidney to the theatre. Procedure time: Time from gaining access to the theatre to perfusion of the organ in the recipient.

**Results:** Total CIT: 18 hours 37mins. Mean times for factors expressed as percentage of Total CIT were as follows: Retrieval and transport: 49% Cross matching time: 19% Gaining access to theatre: 23% Procedure time: 9%

**Conclusion:** The time for retrieval and transport can be reduced but will need a review of the national procedure in place. There is also a possibility of not performing crossmatch when the recipient immunization history is well known. A dedicated transplant theatre will have a salutary effect on the CIT in our institution. Starting Anaesthesia during organ bench preparation could have an effect on CIT.

**PO-607** CLINICAL FEATURES AND LONG-TERM OUTCOME OF BLOOD TRANSMITTED HEPATITIS (B, C, D) IN HEMODIALYSIS PATIENTS

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**Purpose:** All consensus recommendation for the most critical need in hepatitis C and B research is to study the course and treatment of hepatitis in certain groups of population. The aim of this research is to study the clinical features and the long-term outcome of viral hepatitis in hemodialysis patients.

**Methods:** 38 patients with acute hepatitis HBV and/or HCV were involved. 22 patients with chronic renal insufficiency were included.
studied for 36 months. The control group – 50 patients with hepatitis of the similar etiologic structure without chronic renal failure. Activity of the patholog-
ical process, the time and intensity of immune response, duration of viremia and the incidence of hepatitis developing into a chronic form were compared. Results: The incidence of anicteric forms of hepatitis in dialysis patients and in a control group was 16,6% and 6,25% correspondingly. Hépibillrubinemia level in those groups was correspondingly 116,9mcml/l against 269,3 mcml/l and activity of GPT 8.5 mmol/l against 15,3mmol/l. Developing into a chronic hepatitis were observed in both investigated group more often (29% against 12%).

Conclusion: The clinical course of hepatitis in patients with chronic renal fail-
ure are changed by a high incidence of subclinical forms and a milder course of the disease with a tendency to develop into the chronic form. This can be due to a significant immune deficiency inherent to such patients, in-
cluding delayed and weakened humoral response to the causative agents antigens.

PO-608 IMMUNE CELL FUNCTION ASSAY – A NEW PARAMETER FOR MONITORING OF IMMUNOSUPPRESSION

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Background: The survival of transplanted organ is dependent on mainte-
nance immunosuppression. However, it is difficult to distinguish between profiles of over and under-immunosuppression.

Aim: Aim of this pilot study was to evaluate novel, Immuknow assay in char-
acterization of clinically relevant immune status of renal transplant recipient.

Method: 13 kidney recipients were monitored for first six post-transplantation weeks. The immune function was determined by quantitative measurement of intracellular ATP level in CD4+ lymphocytes after PHA stimulation, FK or CSA blood levels, graft function and histology, and parameters of infection, were correlated with assay results.

Results: ATP release and FK/CSA blood level values were measured for each patient at baseline (13 instances), during quiescence (26 instances), acute re-
jection (4 instances) and infection (4 instances). During quiescence, ATP devi-
ation from the baseline of ± 50% (350-600 ng/ml) was much smaller than that of –100% to +200% scatter of calcineurin (CNI) blood levels (150-600 ng/ml and 5-20 ng/ml for CSA and FK). Elevation of ATP of ± 50% of baseline was positively correlated with biopsy proven rejection in 3/4 of instances. Such cor-
relation with CNI levels could not be found. Likewise, decrease in ATP >50% below baseline, but not the elevation of CNI levels, was correlated with infec-
tion in 2/4 of instances.

Conclusion: Immuknow is better correlated with the clinical status than mea-
surement of CNI blood levels and therefore could be recommended for post-
transplant monitoring of immunosuppression.

PO-609 MYCOPHENOLATE MOFETIL AND TACROLISUM HAVE AN INFLUENCE ON ISCHAEMIA-REPERFUSION INJURY IN KIDNEYS PROCURED FROM NON-HEART-BEATING DONOR (NHBD) – AN EXPERIMENTAL STUDY

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Purpose: The aim of our study was to evaluate the application of tacrolimus and mycophenolate mofetil (MMF) to the NHBD just before kidney procure-
ment for decreasing ischaeemia-reperfusion injury (IRI) after kidney transplanta-
tion.

Material and method: The influence on the development of IRI of an early intravenous application of tacrolimus and MMF to the donor was monitored on an animal (landrace pigs) NHBD model (N=20). Animals were divided to the 4 groups (each group - N=5).GI with MMF, GII with tacrolimus, GIII with MMF and tacrolimus and GIV with placebo application 30 minutes before NHBD model creation. The intensity of IRI was evaluated by examination of malondi-
aldehyde, reduced glutathione and tumor necrosis factor α in the venous blood renal vein of NHBD kidneys in -20, 0, 20, 60 and 90 minutes after reperfusion. The statistical analysis was done by ANOVA test (Kruskal-Wallis test).

Results: The study demonstrated that particularly MMF reduces the produc-
tion of malondialdehyde as an indicator of reactive oxygen species production (p < 0.02). MMF alone has no positive influence on the level of inflammation after kidney reperfusion (Tabl). Combination of MMF and tacrolimus consid-
ernally reduces the plasma levels of tumor necrosis factor α (p < 0.05) as an indicator of the degree of inflammatory reaction after reperfusion of a kidney from a NHBD (Table 1).

Conclusion: Pre-treatment of NHBD with combinations of MMF and tacrolimus improve the immediate functions of the transplanted kidneys via significant reduction of inflammatory response rate after kidneys transplant-
lation.

LIVER AND INTESTINE POSTER PRESENTATIONS

Table 1. TNFα plasma levels (ng/l)

| Time (min) | G1  | GII | GIII | GIV | Kruskal-Wallis |
|-------------|-----|-----|-----|-----|---------------|
| -20         | 12.1±9.9 | 31.6±20.8 | 13.5±4.4 | 46.9±11.8 | p<0.02         |
| 0           | 27.5±9.9 | 47.5±14.7 | 20.1±8.9 | 50.7±13.6 | p<0.01         |
| 20          | 23.9±6.5 | 35.5±5.6  | 14.5±8.2 | 50.4±23.9 | p<0.02         |
| 60          | 169.9±308.1 | 49.8±58.9  | 66.1±38.2 | 191.5±78.7 | p<0.01         |
| 90          | 183.8±124 | 39.7±24.2 | 41.1±33  | 215.6±83.4 | p<0.01         |

PO-610 NEOANGIOGENESIS IN THE LIVER TISSUE MICROFRAGMENTS TRANSPLANTED INTO THE SMALL INTESTINAL SEGMENT

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The aim of this study was to demonstrate neoangiogenesis in the transplanted liver tissue. For this purpose we transplanted liver from syngeneic rats defi-
cient in dipetidyl peptidase 4 enzyme activity, into 10 normal F344 rats into the small intestinal segment. The intestinal segment used was 2 centimeters long to accommodate 0.3-0.5 gram liver, which constituted 5% of the native liver mass. The intestinal mucosa was denuded before liver fragments were placed in the container, which had an intact vascular pedicle. Staining of transplanted tissues for dpdp showed, dpdp-positive capillaries were observed at the edges of transplanted liver tissue in the immediate vicinity of the intestinal wall of the container within 2-3 days following liver transplantation. At later times, an oc-
casional dpdp-positive blood vessel was observed even in the parenchyma of the transplanted liver. Staining of tissues for desmin, as well as α-smooth mus-
cle actin verified that mature blood vessels were present in the intestinal wall, as well as the auxiliary liver parenchyma, throughout the duration of the exper-
iments. Tuc, use of the dpdp-deficient F344 rats was effective for this demon-
stration. The dpdp-deficient rat has been valuable for analyzing the biology of transplanted liver cells. Thus, the additional use of this animal for analyzing angiogenesis in the auxiliary liver should permit further detailed analysis of underlying mechanisms.

PO-611 EFFECTIVE RESCUE OF PATIENTS WITH UNRESECTABLE HEPATOBLASTOMA BY LIVER TRANSPLANTATION. FROM HIGH RISK TO STANDARD RISK PROGNOSIS

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Background: 30% of hepatoblastomas (HB) are still unresectable after chemotherapy. Therefore the prognosis of high risk HB without transplantation (OLT) is poor. We aimed to review the outcome of patients transplanted for HB comparing them to those who underwent a simple resection of the mass.

Patients and methods: The notes of patients diagnosed with HB at our centre in the last 20 years were retrospectively reviewed. We divided patients who received a OLT (Group A) from those who underwent tumour excision (Group B). We recorded: demographic features, pre-treatment extent of the tumour (Pretext), alpha-fetoprotein (AFP) level, chemotherapy, liver, cardiac and renal function, overall survival.

Results: Group A comprised of 9 patients, 6 males, median age at presen-
tation 6,3 years (range 0,2-35), 7 classified Pretext 4, 2 Pretext 3, none with

Pretext 2. We recorded: demographic features, pre-treatment extent of the tumour (Pretext), alpha-fetoprotein (AFP) level, chemotherapy, liver, cardiac and renal function, overall survival.

Results: Group A comprised of 9 patients, 6 males, median age at presen-
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Pretext 2. We recorded: demographic features, pre-treatment extent of the tumour (Pretext), alpha-fetoprotein (AFP) level, chemotherapy, liver, cardiac and renal function, overall survival.
COMPARISON OF TWO DIFFERENT TECHNIQUES OF REPERFUSION IN ADULT ORTHOTOPIC LIVER TRANSPLANTATION
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To determine the impact of two reperfusion techniques on perioperative hemodynamic changes and postoperative graft function of patients undergoing liver transplantation. Fifty consecutive transplants were performed and divided into two groups: Group A, 25 patients, portal vein flush without vena cava venting. Group B, 25 patients, vena cava venting, no portal vein flush. 64 parameters analyzed: Recipient sex, age, blood type, primary disease, MELD score, UNOS status. Donor age, macrosteatosis, ICU stay, pressor requirements, and serum sodium, recipient arterial pressure, core temperature, heart rate, central venous pressure, and pulmonary artery pressure before reperfusion and at 1, 5, 15, and 30 minutes after reperfusion. Cardiac output and systemic vascular resistance before and after reperfusion. Potassium levels, pH, and lactate levels 5 minutes before reperfusion and at 30 seconds and 5, 15, and 30 minutes after reperfusion. Warm and total ischemia time. Post-reperfusion syndrome (PRS) defined as a decrease in mean arterial pressure >30% below the baseline value. Early graft function defined by measurement of liver function tests in the first three postoperative days. Donor and recipient characteristics were similar in both groups. Pearson Chi Square test and T test used for statistical analysis. One patient (4%) in group B experienced a PRS. Pearson Chi Square test found no significant relationship between the two different techniques. T test analysis showed significant difference between the two groups in favour of Group A for 11 of the 64 parameters analyzed.

THE CORONARY VEIN, SUPERIOR MESENTERIC VEIN: AN ALTERNATIVE SOURCE OF PORTAL INFLOW IN LIVER TRANSPLANTATION
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Introduction: The Piggy-back technique has been proposed as an alternative procedure to the conventional technique in orthotopic liver transplantation. However, there is controversy over advantages and specific complications. We present a retrospective analysis over the last seven years with Piggy-back technique.

Methods: From July 1998 to March 2005, 95 liver transplantsations in 90 patients were performed. In all cases, Piggy-back technique was done. Therefore, hepatectomy was carried out with preservation of the vena cava inferior and the hepatic veins were closed with running sutures. The retrohepatic donor vena cava was converted to a single hepatic vein and the Piggy-back anastomosis was performed as end-to-side anastomosis to a sagittal incision of the recipient vena cava. In no case the use of veno-venous bypass was necessary.

Results: Intraoperative complications due to Piggy-back technique did not occur and a switch to the conventional technique was not indicated in any case. Early postoperative complications occurred in 2 patients (2.2%). Both of them showed a suprahepatic vena cava stenosis, which required immediate surgical correction. Late postoperative complications were thrombosis of a single hepatic vein with temporary restriction of the liver function (3.3%), which were managed with conservative therapy. None of our patients died as a result of complications related to the Piggy-back technique. No postoperative renal failure or gastrointestinal complications were observed in our patients.

Conclusion: Piggy-back technique without veno-venous bypass is possible in all of our patients. The potential advantages were hemodynamic stability during the anhepatic phase and preserved renal and intestine perfusion. We suggest that the Piggy-back technique can be used as an alternative to the conventional technique in liver transplantation.

PORTAL VEIN ARTERIALIZATION INCREASES LIVER REGENERATION IN ACUTE LIVER FAILURE INDUCED BY EXTENDED HEPATECTOMY OR TOXIN ADMINISTRATION IN THE RAT
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Purpose: To determine whether the increase of oxygen supply in the portal system by statistical analysis of oxygenator (L.E.O.NARDO) device is effective in treating suines with acute liver failure (ALF).

Materials and Methods: Eight suines with ALF induced by 80% liver resection were randomly divided in two groups: four animals received L.E.O.NARDO treatment and four suines were not treated (control group). Blood was withdrawn from iliac artery and reversed in the portal venous system. An extracorporeal device was interposed between the outflow and the inflow in order to monitoring the haemodynamic and biochemical parameters. Each treatment lasted 6 hours. Serum and liver samples were collected in both groups.

Results: L.E.O.NARDO treatment yielded beneficial effects for liver resection-induced ALF suines with survival and decreased plasma ammonia, transaminase and bilirubin. There was an expected decrease in PT level. In contrast, for the suines with ALF of non treated group (control group), there were no significant changes in ammonia, transaminases and bilirubin. Three suines of L.E.O.NARDO group survived at 1 week while none suine of control group lived.

Conclusion: The L.E.O.NARDO device may represent a novel approach for ALF suine induced by partial liver resection.

PORTAL VEIN THROMBOSIS IN ADULT LIVER PARTIAL LIVER TRANSPLANTATION USING RIGHT LOBE
In Sung Moon, Dong Goo Kim, Myung Duk Lee, Suk Gee Hong, Sun Cheol Park, Surgery, Kang Nam St. Mary's Hospital, The Catholic Univ. of Korea, Seoul, Republic of Korea.

In the presence of complete occlusion or stenosis of the recipient portal vein secondary to portal vein thrombosis, the portal vein reconstruction could be made from well developed collaterals. We had two cases of portal vein reconstructions from distended coronary vein and superior mesenteric vein using cadaveric iliac vein in partial liver transplantation in adult using right lobe. Here, we report two cases of our experience.
INCISIONAL HERNIA AFTER ORTHOTOPIC LIVER TRANSPLANTATION: PREDISPISING FACTORS, SURGICAL TREATMENT AND OUTCOMES

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A retrospective analysis was performed of both the nature of and management of incisional hernia (IH) in adult orthotopic liver transplant (OLTx) recipients of our programme. All data was obtained from the liver transplant database and chart review.

Forty-five of 538 (8.3%) patients were diagnosed with IH after OLTx (16 (35%) males, 29 females; mean age 28 years; age range 23-27 years). The median patient follow-up was 7.9 years (range: 1.9 – 17.5). The median time to diagnosis of IH was 12 months (range: 4 - 128) post OLTx, with 30/45 (66%) of IH occurring within 2 years following OLTx. At the time of OLTx 12/45(26%) recipients were diabetic, 8/45(18%) were smokers, and 9/45 (20%) developed wound infection or peritonitis. Reoperation via the transplant incision occurred in 5/45(20%) of patients.

Operative repair IH was performed in 37/45 (82%) patients. Primary operative repair consisted of suture repair in 16, polypropylene mesh in 13, polypropylene/péTFE in 5, and péTFE in 3. Conservative management of IH in 8 patients was due to allograft dysfunction 4, patient refused surgery 2, small IH 2.

Prior to 2000 primary surgery was performed in 82% of cases, versus 18% since [p=0.00]. In 5/17 (13.5%) patients IH recurrence occurred [3/16 (19%) post primary surgery repair and 2/10 (20%) post primary mesh repair]. (p=0.49).

Following mesh repair an inflammatory reaction in the abdominal wall occurred in 5/21 (24%) cases.

Conclusion: IH occurs in 8.3% OLTx patients and surgical repair is reasonably effective. Mesh repair has become more common with time and may be associated with a lower IH recurrence rate.

LIVER TRANSPLANTATION IN HIV-HCV INFECTED PATIENTS

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The aim of the study was to evaluate the feasibility of Liver Transplantation (LT) in HIV co-infected patients (pts). Eight pts (8 male, mean age 44 years) underwent LT between September 2002 and July 2004. Seven pts were HIV-HCV positive and one had hepatitis B plus a HCC. Pre-LT plasma HIV 1-RNA levels was undetectable and CD4+ T-cell count was > 200 cells/mL for at least 3 months in all pts. Five pts received Highly Active AntiRetroviral Therapy before LT. LT was performed using the piggy-back technique. Immunosuppression was a combination of tacrolimus-stereoids-MMF.

Five pts are alive at a mean follow-up of 13 months (6-23 months). All alive pts have low levels of HIV RNA and CD4+ T-cell count increased after LT. None developed acute rejection or opportunistic infections. One patient died of liver failure 18 months after LT due to portal vein (PV) thrombosis; One patient died 8 days after LT of massive PV system thrombosis. Another patient died soon after LT of PNF. Six pts developed early recurrence of hepatitis C (1 fibrosing cholestatic hepatitis) requiring combination therapy of interferon plus ribavirin in 4. Significant improvement of quality of life was observed in 6/8 pts. LT in HIV-HCV coinfected pts is feasible and results in the short and medium term are good. Early and severe HCV recurrence occurred after LT. In this study PV thrombosis was a main complication.

ANTIVIRAL LONG-TERM MAINTENANCE THERAPY WITH INTERFERON AND RIBAVIRIN FOR RECURRENT HEPATITIS C AFTER LIVER TRANSPLANTATION–IMPACT ON ALLOGRAFT MORPHOLOGY AND LONG-TERM SURVIVAL

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Background: The aim of this study was to evaluate feasibility and efficacy of an antiviral long-term maintenance therapy (AMT) using interferon-α 2b (IFN) and ribavirin (RB) for recurrent hepatitis C after liver transplantation. Patients and methods: 21 HCV-positive liver transplant patients with recurrent hepatitis C underwent a 12-months basic antiviral therapy, consisting of IFN (3X3 MIU/week) and RB (600mg/day), followed by AMT with the same dosages for an indefinite period. Serial allograft biopsies were scored according to the modified “Hepatitis Activity Index”. Impact of AMT and other clinical and virological parameters on long-term survival was assessed using a cox regression model. Results: After 12 months of basic antiviral therapy, 14 patients (66.6%) had achieved initial clearance of viremia levels, and 17 (81%) participants demonstrated complete normalization of allograft function, respectively. In virological responders (n=14) AMT led to further regression of fibrosis (1.6 at baseline versus 1.1 at 24 months AMT). Persistence of intermittently high viremia levels, AMT prevented progression to severe allograft fibrosis (2.0 at baseline versus 2.3 at 12 months AMT) in virological nonresponders (n=7). Conclusion: Long-term antiviral maintenance therapy with IFN and RB might significantly improve patients’ survival.

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be an effective therapeutic approach for preventing progression to severe allograft fibrosis and thereby for improving long-term survival in liver transplant recipients with recurrent hepatitis C.

**PO-622** HEPATOPULMONARY SYNDROME (HPS): A PROSPECTIVE STUDY ON THE PROBABILITY RATE OF HYPOXEMIA OVER TWO YEARS IN LIVER TRANSPLANT CANDIDATES WITH INTRAPULMONARY VASCULAR DILATATIONS (IPVD)

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**Background and aim:** Hepatopulmonary syndrome, caused by intrapulmonary vasodilatation, when associated with severe hypoxemia has been related to increased morbidity-mortality in liver transplant candidates. The progression of hypoxemia in cirrhotic patients with intrapulmonary vasodilatation is not well known. Our aim was to determine the probability of developing hypoxemia (PaO2<70mmHg) in cirrhotic patients with intrapulmonary vasodilatation over two years.

**Methods:** Thirty-two transplant candidates with intrapulmonary vasodilatation detected by contrast-enhanced echocardiography (CEE) were prospectively studied and the PaO2 was measured at the start and at the end of 12 and 24 months.

**Results:** Paired t test showed that the mean 12-month and 24-month PaO2 were significantly lower than the basal value (p=0.048 and p=0.0004, respectively) and the same was seen when comparing 12 and 24-month values (p=0.044). The Kaplan-Meier estimated ratio for the appearance of hypoxemia was approximately 10%/±5% at 12 months and 28%/±10% at 2 years.

**Conclusion:** We demonstrated a progressive course of hypoxemia in cirrhotics with intrapulmonary vasodilatation. Identification of early hypoxemia can lead to a better understanding of the hepatopulmonary syndrome and may be helpful to optimize timing and to predict outcomes of liver transplantation.

**PO-623** BENEFIT OF SUSTAINED VIROLOGICAL RESPONSE TO COMBINATION THERAPY ON GRAFT SURVIVAL OF LIVER TRANSPLANTED PATIENTS WITH RECURRENT CHRONIC C HEPATITIS

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Recurrent hepatitis C infection is an important cause of progressive fibrosis and graft loss after liver transplantation. Treatment for post-transplant recurrence is often difficult, but results in sustained virological response (SVR) in up to 30% of cases. The aim of this study was to evaluate the positive impact of SVR on patients and graft survival.

**Patients and methods:** 34 patients with a SVR to IFN-ribavirin were included. 46 patients who were non-responders to the combination formed the control group. No difference were observed in the two groups in relation to age, gender, genotype, type of immunosuppression therapy, period of inclusion, and severity of disease at inclusion. Follow-up data were recorded every 6 months and ALT, HCV RNA, and the occurrence of clinical problems (cirrhosis, decompen- sation, hepatocellular carcinoma, death). A graft biopsy was performed every year. The mean follow-up duration was 52 months in responders and 57 months in non-responders.

**Results:** Two patients died in each group of patients. Two patients with SVR developed late virologic relapse. Fibrosis decreased in 38% des patients with SVR, remained stable in 44% and worsened in 18%. In contrast, fibrosis increased in the majority of non-responders patients (74%, p<0.05). At the end of follow-up, no patient without cirrhosis at inclusion developed cirrhosis of the graft versus 9 in non-responders patients (p=0.009). Three patients were re-transplanted and are alive. No difference in patient survival was observed in the two groups.

**Conclusion:** this study shows that HCV eradication has a positive impact on graft survival.

**PO-624** PROSTAGLANDIN E1 ACCELERATES EARLY RECOVERY OF ALLOGRAFT FUNCTION IN LIVER TRANSPLANT PATIENTS WITH RECURRENT HEPATITIS C

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**Background:** The aim of this prospective randomised study was to evaluate the impact of immunomodulation with intravenous prostaglandin E1 for HCV recurrence after liver transplantation.

**Patients and methods:** A total of 25 HCV-positive liver transplant recipients with serologically and histologically confirmed recurrent disease were included in this study. In all of them antiviral treatment consisted of a combination with interferon-α [prop] 2b (IFN, 3x3 MIU IE/week) and ribavirin (RBV, 3x200mg/day) for 12 months, followed by a maintenance therapy. In the PGE1-group (n=11), patients additionally received intravenous therapy with a PGE1 analogue (Al-prostadil, 0.5µg/kg/h) for 7 days. Viremia levels, allograft function and allograft morphology were assessed continuously.

**Results:** In contrast to the non-PGE1-population aminotransferases declined significantly in the PGE1-group during first week of antiviral treatment (AST0: 1,4 mmol/L; ASTT: 0,3 mmol/L; P=0.01). In the PGE1-group, biochemical and virological response 12 months after starting antiviral therapy was 82% and 84%, respectively, compared to 85.7% and 71.4% in the non-PGE1-group (NS). In the PGE1-population grade of necroinflammation declined from 6.0 ± 3.5 to 3.6 ± 1.7 (P=0,04) and stage of fibrosis decreased from 1.8 ± 0.7 to 1.5 ± 0.5 after 12 months of antiviral therapy, which was comparable to the non-PGE1-group. 5-year patient and graft survival was 60% in the PGE1-group and 70% in the non-PGE1-population (NS).

**Conclusion:** Intravenous PGE1 seems to provide beneficial early cytoprotective effects in liver recipients with recurrent HCV disease. If this treatment will finally improve long-term survival has to be evaluated in the future.

**PO-625** SEVERE RECURRENT FIBROUS CHOLESTATIC HEPATITIS C AFTER LIVER TRANSPLANTATION—DIFFERENT CLINICAL PATTERNS AND IMPLICATION FOR TREATMENT

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**Background:** The aim of this study was to analyse possible risk factors and thereby resulting implications for treatment of fibrosing cholestatic HCV recurrence after liver transplantation.

**Patients and methods:** Between 1995 and 2004 a total of 25 patients underwent LT due to HCV-induced liver cirrhosis. Recurrent hepatitis C was treated by an antiviral combination therapy consisting of interferon-α [prop] 2b (IFN, 3x3 MIU IE/week) and ribavirin (RB, 3x200mg/day). Viral loads, allograft function, and allograft morphology were assessed continuously. Clinical and virus-related factors were analysed as potential risk factors for development of cholestatic disease.

**Results:** 23 patients (92%) developed recurrent hepatitis C after a median of 20 weeks. 4 patients (16%) developed FCH. 2 of them primarily 4 and 5 months post-LT, another 2 patients 6 and 24 months posttransplantation as a result of treatment discontinuation in a persistent viremic situation. Patients with (n=4) and without (n=19) development of FCH did not differ regarding basic demographic parameters. However, all patients (100%) with FCH received a MMF-based immunosuppression, compared to 52% of non-cholestatic recipients (p=0.07). Furthermore, viremia levels at HCV disease recurrence were significantly higher in the cholestatic patients (5287 ± 2450 MEQ/ml versus 701 ± 470 MEQ/ml, p=0.02). Mean survival was 26 months in cholestatic course (versus 82 months non-cholestatic, log rank p=0.008).

**Conclusion:** Early posttransplant onset of FCH is associated with fatal disease course. Administration of MMF and high viremia levels seem to be significant risk factors. Treatment discontinuation under viremia carries the risk of severe cholestatic HCV disease progression.

**PO-626** EXPERIENCE WITH ARTERIAL VASCULAR CONDUITS IN ADULT ORTHOTOPIC LIVER TRANSPLANT RECIPIENTS

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**Purpose:** To analyze our unit's experience with arterial vascular conduits using the infra-renal aorta/common iliac artery as inflow in adult orthotopic liver
transplant (OLTx) recipients. Data was obtained from the transplant unit records and database, plus hospital records. Statistics were by SPSS.

Results: From 1/1986–12/2003, 31/582 (5.3%) of OLTx procedures required an arterial conduit for recipient hepatic artery problems. OLTx is the most promising therapy, better than arterial embolization, with good long-term results and normalization of cardiac function. However, OLT for HHT remains a difficult procedure due to the collateral arterial reorganization.

Conclusions: Arterial vascular conduits are required in 5.3% of adult OLTx procedures and are performed more commonly in hospitalized cases and in retransplant procedures. Two thirds of conduits are required for hepatic artery problems. Allograft loss is more common in OLTx recipients requiring conduits, and is significantly associated with retransplant procedures.
The data are presented as the mean (Table 1; *p were compared.

Results: The thickness of the perforated, unsealed gallbladder (20.3 ± 12.1mmHg) could be significantly increased (TachoComb-S: 46.5 ± 15.7; Tis-suicol: 41.2 ± 22.5; Coseal: 24.5 ± 7.2). In liver resection group, a significant 90% reduction of blood loss could be reached. Blood loss: TachoComb-S: 98%; Tissu-cot: 91%; Coseal: 93%). The blood loss in the sealed portal vein anastomosis could be decreased significantly (TachoComb-S: 98%; Tissuocol: 92%; Coseal: 89%). Blood loss after arteriotomy could be decreased more than 98% in the first 20 sec in two-thirds of animals using sealant.

Conclusion: The implementation of sealants in liver and transplantation surgery can lead to a significant reduction of blood loss. TachoComb-S and Tissuocol had the best results for biliary leakage prevention and vascular anastomosis. TachoComb-S and CoSeal had the best results after liver resection. The favorites in arteriotomy were Tissuocol and CoSeal. All three products were identical in handling and application.

PO-634 LIVER TRANSPLANTATION AND LIVER RESECTION FOR SURGICAL TREATMENT OF HEPATOCELLULAR CARCINOMA: A 15-YEAR SINGLE-CENTER EXPERIENCE

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Purpose: Surgical therapy offers the only chance for cure of patients with hepatocellular carcinoma (HCC). The role of liver resection (LRx) or liver transplantation (LTx) was analyzed in a consecutive series of HCC patients. Study aim was to compare both treatment modalities based on clinicopathological prognostic factors including the TNM system of pathological classification.

Materials/Methods: LTx (n=111) and LRx (n=109) were performed for the following histological diagnoses: HCC without co-existing liver disease (44%), associated with various hepatic abnormalities (39%), fibrolamellar carcinoma (11%), and mixed hepatocellularcarcinoma (6%). Different determinants for better outcome were analyzed with regards to the survival rates.

Results: Overall survival rates at 15 years were 51% after LTx and 59% following LRx. For LRx, improved long-term outcome was significantly associated with age of 30-50 years, HCC without coexisting liver disease, fibrolamellar carcinoma, solitary tumor, unilobar location, absence of vascular invasion, portal vein thrombosis or extrahepatic spread, primary tumor categories T2/T3, tumor stages II/III, and curative operation (R0). Regarding LTx, the corresponding determinants were: fulfilled Milan criteria, pT2, absence of portal vein thrombosis or extrahepatic spread (negative regional lymph nodes, no distant metastases), and tumor stage II. The pTNM classification had clinical prognos-tic significance after resection and transplantation. 33 patients had secondary transplantations or resections due to recurrence.

Conclusion: LRx is treatment of choice for primary liver cancer while LTx may be indicated, especially in cases of nonresectable or recurrent lesions. Therapeutic spectrum for HCC should include both LRx and LTx, being integrated into one common concept.

PO-635 LIVER TRANSPLANTATION FOR TREATMENT OF HEPATIC EPITHELIOID HEMANGIOENDOTHELIOMAS

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Hepatic epithelioid hemangioendothelioma (HEH) has a very low incidence with unclear malignant potential. In the present work we analyze 300 published cases and describe 4 female patients with HEH, who were treated curatively in our institution.

Of four patients with HEH, liver transplantation (LTx) was performed (two cadaveric and one living donated) in 3 patients. In one patient a right sided hemi-hepatectomy with partial resection of the diaphragm was performed. All patients were seen in our transplantation and oncology outpatient clinics on a regular basis with follow up periods from 1 to 12 years. No adjuvant chemother-apy was applied. Till present, no tumor recurrences or metastases could be observed.

In the literature, most HEH patients (male to female: 2 to 3) presented right sided upper abdominal pain and/or weight loss. In most cases, the tumor had spread throughout the liver and presented as multiple nodules ranging from 27 to 45% of all tumors metastasized, mostly to the lungs and bones. The keys
toward diagnosis included radiology, histology and detection of cells expressing factor VIII-related antigens. The 5-year overall survival rate varied from 43 to 55% and is significantly higher in comparison to other malignant hepatic tumors.

Early detection and surgical intervention can offer a curative treatment to the patient. First choice treatment is radical liver resection or LTx. Regarding the long waiting lists for LTx, and unclear dignity of this tumor with a progressive growth pattern, living donor LTx represents a potentially important role for patients with a non-resectable tumor.

**PO-636 ADVERSE EFFECTS OF BRAIN DEATH ON THE GRAFT QUALITY AND CLINICAL OUTCOME OF TRANSPLANTED LIVER AND KIDNEY**

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**Purpose:** It has been shown that brain death (BD) is an important risk factor in solid organ transplantation. Our aim was to review the adverse effects of BD on donor organ quality and determine preventive methods to minimize the damage.

**Materials and Methods:** There is lack of information on BD effects on organ quality and its outcome after transplantation because of the nature of risk and the difﬁculty of designing clinical trials. The related articles were analyzed to evaluate previous related data about the role of BD.

**Results:** BD in acute phase results in autonomic storm. Ischemia due to microcirculation disturbances plays an important role in quality of peripheral organs, causing poor renal and hepatic perfusions. BD could induce immunogenicity and inﬂamed organs from BD donors evoke acute host allosensitivity. Polymorphonuclear leukocytes and macrophages enter the graft and may release cytokines. The increased expression of ICAM-1, VCAM-1, and CD45 induces more inﬂammation after implantation of the harvested organ. Apoptosis is another important phenomenon to be accused in BD damage, predisposing the graft for additional ischemia/reperfusion injury.

**Conclusion:** If hemodynamic instability in the brain-dead donor is not corrected, organ dysfunction is increased and immune activation occurs faster. Use of catecholamines (dopamine or noradrenaline) in donor could decrease the damage. The qualitative survival model can predict the short-term survival after ALDLT.

**PO-637 ACUTE RENAL FAILURE AFTER CADAVERIC LIVER TRANSPLANTATION IN IRAN**

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Acute renal failure is a frequent medical complication after liver transplantation and inﬂuences patients’ outcomes.

From 117 orthotopic liver transplantations that were performed between May 1, 1993, and July, 2004, 91 of them were included and analyzed in our retrospective database review. ARF was deﬁned as serum creatinine more than 2mg/dl.

Their mean age was 30.69 years and 63.7% (N= 58) were male. The 91 recipients had the following indications: Cryptogenic N=27 (29.7%), autoimmune N=18 (19.8%), Wilson’s disease N=10 (11.1%), hepatitis B-related N=9 (9.9%), hepatitis C-related N=7 (7.7%), primary sclerosing cholangitis N=8 (8.8%), primary biliary cirrhosis N=3 (3.3%), biliary atresia N=2 (2.2%), drug toxicity N=2, hepatocellular carcinoma N=1(1.1%), Budd-Chiari syndrome N=2 (2.2%), and mixed hepatitis B and C N=1 (1.1%).

85 patients received cyclosporine (CsA), azathioprine/mycophenolate, and steroid, and 18, a combination with tacrolimus (FK506).

Ten (11.94%) patients developed ARF in early (14 days) postoperative period which four of them required renal replacement therapy. The majority of patients (50%) returned to normal renal function at 2 weeks after the diagnosis of ARF. No patient experienced mortality.

Four of these patients had a diagnosis of cryptogenic cirrhosis; two, hepatitis C-related cirrhosis; one, primary biliary cirrhosis and two, autoimmune cirrhosis. The ARF etiology was multifactorial for the majority of patients. ARF treatment included fluid replacement, decreased or altered immunosuppressive agents, avoiding exposure to nephrotoxic drugs, adjusting antibiotic dosages and in four patients renal replacement therapy.

We conclude that the incidence of ARF is relatively low and has good outcomes. The etiology was multifactorial for the majority of patients. We suggest that in the early postoperative period of liver transplantation cases diagnosis and treatment of ARF is important.

**PO-638 INCIDENCE AND RISK FACTORS OF RENAL DYSFUNCTION AFTER LIVER TRANSPLANTATION IN IRAN**

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Renal dysfunction is common among patients awaiting liver transplantation and in early phase after transplantation this might be associated with poor prognosis. Little is known, however, about it in IRAN.

We analyzed cadaveric related liver transplant recipients who had developed ARF in the first month post transplantation. ARF were deﬁned as serum creatinine increased post operatively (p<0.001).

Ten patients (11.1%) developed acute renal failure post operatively (p<0.05) which majority (50%) of them recovered by 30th day. Four of them required renal replacement therapy (CVVHD).

Age was an independent risk factor for development of ARF (p<0.05). Sex, blood group, duration of liver disease and preoperative diabetes did not affect the postoperative renal dysfunction.

Presence of hepatitis C was related to development of postoperative renal failure (p<0.05). ARF etiology was multifactorial for the majority of patients. Conversion to oral immunosuppressive drugs or excluding these drugs decreases ARF. Performing liver transplantation in younger patients have more desirable outcome. Liver transplantation in patients with hepatitis C needs more evaluation. We suggest a prospective study to evaluate the impact of early post-op ARF on long term renal function and graft survival.

**PO-639 A QUALITATIVE SURVIVAL MODEL FOR A SHORT-TERM SURVIVAL AFTER ADULT TO ADULT LIVING DONOR LIVER TRANSPLANTATION**

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The number of adult to adult living donor liver transplantation (ALDLT) has rapidly increased but information on risk factors remain fragmentary. We aimed to establish a qualitative model for 90-day survival incorporating various risk factors. 286 cases which had received primary ALDLT using right lobe grafts from 1998 to 2004 were randomly divided by two groups in the ratio of 2:1; 191 and 95 recipients. The former group of patients was used to develop a model. Outcome was deﬁned as 90-day survival, and a total of 36 preoperative and operative variables including a period of surgery; from 1998 to 2001 and from 2002 to 2004 October. They were studied using Cox’s proportional hazard regression model. HLA DR 2 mismatches (HR = 4.68, CI = 2.06 -11.6), loge (blood loss volume) (HR=2.39, CI = 2.39 -3.57), period of surgery (1998-2001 vs 2002-2004) (HR=2.31, CI = 1.00 -5.31) and loge (serum CRP) (HR=1.52, CI = 1.02 -2.27) were found to be independent risk factors. Based on these results, a survival model was built to calculate a risk score (R) for each patient. R = 1.58 x(HLA DR 2 Mismatches) + 0.87 x Loge(Blood Loss Volume) + 0.42 x Loge(Serum CRP) + 0.82 x(Period of Surgery) + 0.022 x(MELD score). This model applied to another group of remaining 95 patients for cross-validation. The qualitative survival model can predict the short-term survival after ALDLT.

**PO-640 CYCLOSPORINE- AND TACROLIMUS-BASED MONOTHERAPY IMMUNOSUPPRESSIVE REGIMENS ARE COMPARABLE IN TERMS OF IMPACT ON THE NATURAL HISTORY OF HCV RECURRENT IN LIVER TRANSPLANTATION. PRELIMINARY RESULTS FROM A PROSPECTIVE, RANDOMIZED TRIAL**

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**Background:** To date, clinical studies have failed in demonstrating any differ-
ence between CsA- and tacrolimus (Tac)-based regimens, in terms of impact on the natural history of HCV disease recurrence.

**Aim:** To compare CsA and Tac monotherapy in HCV liver transplant recipients.

**Patients and Methods:** Twenty-five patients with a minimum follow up of 1 year from the first transplantation were included in the study population. They were randomly assigned to receive either CsA (12) or Tac (13), since the first postoperative day, as part of a larger prospective trial. Ribavirin with/without interferon was administered. Twenty-one patients (11 CsA, 11 CsA). Endpoint of the study was the progression of HCV disease recurrence, in terms of histology of liver graft, fluctuation of cytology and cholestasis markers, and of HCV RNA. At baseline, the two groups were comparable.

**Results:** Growth, grading and fibrosis progression rate were comparable between the groups. As well, transaminases, GGT and total/direct bilirubine were similar, despite alkaline phosphatases were lower in the Tac group (22.1±2.2 vs. 14.3±5.5, p<0.01). An episode of acute rejection occurred in 3 patients (2 CsA, 1 Tac). HCV RNA was not available in all patients.

**Conclusions:** At the short term, CsA and Tac monotherapy regimens are comparable.

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**PO-641 LONG PERIOD OUTCOME OF ABO-INCOMPATIBLE LIVING DONOR LIVER TRANSPLANTATION IN A SINGLE CENTER EXPERIENCE**

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**Purpose:** The survival rate in ABO-incompatible LDLT was much poorer than in ABO-compatible recipients for the early experiences. But the introduction of novel immunosuppressive regimens and apheresis has yielded excellent short period results in ABO-incompatible transplantations and then long period results also should be discussed.

**Methods:** In our institution we experienced 11 ABO-incompatible patients out of 91 LDLT. Those were 5 infants, 4 children and 2 adults. The titers of IgM or IgG more than 16 was the indication for preoperative apheresis. PE or DFPP was performed consecutive 3 days before transplantation and the patients were also administered azathioprine or MMF 3 days before the transplantation followed by tacrolimus or cyclosporine, as well as methylprednisolone.

**Results:** Titr of IgG more than 16 was the indication for preoperative apheresis. PE or DFPP was performed consecutive 3 days before transplantation and the patients were also administered azathioprine or MMF 3 days before transplantation followed by tacrolimus or cyclosporine, as well as methylprednisolone. Three patients had anti-C20Ab (rituximab) after operation and 2 patients also had intrahepatic artery or intraportal infusion of prostanoid E1 and methyl-prednisolone.

**Conclusions:** A total of 11 cases are survived for a long period (from 5 mo. To 10 y, mean 5 y) and they are leading in good condition at present. Seven patients had preoperative apheresis. Eight patients had acute rejection and 6 patients were steroid resistant rejections followed by DSG and apheresis. One patient who had accelerated rejection was dead due to liver failure. Three patients who were administered rituximab did not have severe rejections and adverse effects. In the peripheral blood of a patient who had rituximab, CD19 positive lymphocytes were less than 1% until 20 month after LDLT.

**PO-642 TWO CASES IN ONE FAMILY OF LIVING DONOR LIVER TRANSPLANTATION FOR HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA**

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**Purpose:** We experienced two pediatric patients homozygous for familial hypercholesterolemia (FH) who received living donor liver transplantation (LDLT) from their parents who were heterozygous for FH.

**Methods:** Case 1: The elder brother presented orange cutaneous xanthomas and was diagnosed homozygous FH at the age of one. The total cholesterol was 898 mg/dl, LDL cholesterol was 756 mg/dl. It was difficult to find a deceased donor in Japan; thus he underwent LDLT with his father as the donor. Case 2: The younger sister was born 2 years after her brother’s LDLT. The total cholesterol was 857 mg/dl just after birth. She was once listed on the brain dead donor series of Japan, but no donor appeared for one year. She underwent ABO-incompatible LDLT with her mother as the donor at the age of 2.

**Results:** Case 1: His cholesterol level has remained controlled at around 280 mg/dl with HMG-CoA reductase for 4.5 years after LDLT. Case 2: We performed plasma exchange twice before LDLT to reduce the IgM and IgG hemagglutinin tilters. One week after LDLT IgG tilters were elevated with weight gain. The immunodepletion of LFT’s, right lobe LDLT and rituximab showed reduced drug induced liver dysfunction. Five months after LDLT the cholesterol of her remained stable at around 240 mg/dl. At present the four patients including the living donor are leading a normal daily life.

**Conclusion:** Living donor liver transplantation from a donor with heterozygous FH is a feasible indication for the treatment of homozygous FH.

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**PO-643 ADULT-TO-ADULT RIGHT LOBE LIVE DONOR LIVER TRANSPLANTATION WITHOUT ABDOMINAL DRAINAGE**

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**Objective:** To evaluate the feasibility of right lobe live donor liver transplantation (RLDLT) without abdominal drainage.

**Methods:** A prospective study was performed on 53 adult patients who underwent RLDDL without abdominal drainage (nondrainage group). The median preoperative model for end-stage liver disease score was 26 (range, 9–52), and 21 (40%) patients were on high-urgency list for liver transplantation. All patients received right lobe grafts with the middle hepatic vein. The operative outcomes were compared with 45 RLDDL recipients with abdominal drainage during the same study period (drainage group).

**Results:** The time of postoperative hospital stay was comparable (median = 18 days in both groups) with a comparable operative morbidity rate (42% in drainage group vs. 38% in nondrainage group, p=0.651). However, 24 (53%) patients in the drainage group had minor wound complications, which was significantly higher than that of 5 (9%) patients in the nondrainage group (p=0.001). Surgical re-exploration was required in 8 (18%) and 4 (8%) patients in the drainage group and the nondrainage group, respectively. Abdominal tapping was not required in drainage group but required in 7 (13%) patients in the nondrainage group for relief of ascites (p=0.014). There was no difference in the liver function and renal function between the two groups on postoperative day 7 and day 30. Graft survival rates were 91% and 96% for the drainage and nondrainage groups, respectively, on follow-up.

**Conclusion:** RLDDL can be performed without abdominal drainage and results in satisfactory operative outcomes. A more selective approach for abdominal drainage can be adopted in RLDDL.

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**PO-644 MIDDLE HEPATIC VEIN THROMBOSIS AS A COMPLICATION OF RIGHT HEPATECTOMY IN LIVING DONOR LIVER TRANSPLANTATION**

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Living donor liver transplantation (LDLT) is a currently available option to increase the donor pool and shorten waiting time in the list. We present a rare donor complication in LDLT that occurred in our program.

**Case report:** A 30-year-old man without a significant past medical history was evaluated for living donation for his father. Donor physical examination, liver function tests and magnetic resonance imaging (MRI) were normal. Donor right hepatectomy was uneventful. The parenchymal transaction was performed without any vascular inflow interruption on either side of the liver and no packed red blood cells were transfused. No thromboembolism prophylaxis was used. Follow-up ultrasound performed routinely 48 hours after the surgery showed a middle hepatic vein thrombosis (HVT) which was confirmed by MRI. All potential procoagulant factors analyzed were normal. A continuous infusion of intravenous heparin (15 U/kg/h) was administered for six days followed by subcutaneous low molecular weight heparin (LMWH (80 mg/12 hours). A decrease in the middle hepatic vein thrombus size as well as a hematoma of the surgical wound were found by doppler ultrasound performed on day 9. HVT had disappeared twenty days after surgery by doppler exam, and heparin was stopped on the 40th postoperative day. No other complication has occurred after five months of follow up.

**Conclusion:** HVT is a rare complication in LDLT. All these patients should be treated with LMWH prophylaxis. It’s important to perform routine abdominal doppler ultrasound at post-op days 1, 2 and 7 to be able to detect early HVT.

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**PO-645 EVALUATION AND PROTECTION OF RENAL FUNCTION IN PATIENTS AFTER LIVER TRANSPLANTATION**

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**Background:** With the increasing success of liver transplantation, more patients are developing late complications such as renal dysfunction. It becomes more important to identify patients with higher risk for this complication.

**Methods:** In 64 patients at various intervals from liver transplantation renal parameter were evaluated over a time of 18 month. As marker for renal function we investigated serum creatinine, urea, renal creatinine clearance and cystatin C. Furthermore urinary sediment was examined by urinary test, automated urinary sediment analyzer and urine microscopy.

**Results:** In patients with renal deterioration we decided to decrease immunosuppressive
LONG TERM RESULTS OF LIVER TRANSPLANTATION (OLT) FOR HCC AT A SINGLE INSTITUTION

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Aim of this study is to analyze the long-term result of OLT for HCC at a single Institution. 38 patients fulfilling the Milan criteria underwent OLT for HCC between 1996 and 2004. TACE or RF/PEI were done in all cases. Clinical TNM was T1 in 20%, T2 in 78%. There were 6 (14%) incidental HCC. Number and diameter of HCC nodules were respectively 1.8±0.9, 2.8±1.3 cm at CT and 2±1.1, 3.8±2.7 cm at pathology (p=0.17 and p=0.03). At histology 5 patients (11%) were T0. Pre-transplant study had 40% of down-staging and 16% of up-staging. 6% had microvascular invasion. 11% were capsulated. Tumor grading was 1 in 5.5%, 2 in 73%, 3 in 21.5%. Necrosis of HCC nodules was 39%±42%. At histology 26% and 18% of patients were respectively outside the Milan and UCSF criteria. According to the modified pTNM 16% were T1, 45% T2, 29% T3 and 10% T4a. No recurrence of HCC developed within the graft; one patient (T4a+microvascular invasion) developed lung metastasis one month after OLT and died 14 months after OLT. The overall, 1, 3, and 5 years survival rates were 81%, 76% and 70%. The 1, 3 and 5 years survival rates were 86%, 79% and 71% for T1 and T2 and 80%, 73% and 73% for T3 and T4a (p=0.64). The 1, 3 and 5 years recurrence free survival rate was 97%.

Conclusion: our data confirm that LT is an acceptable option for patients with the Milan and UCSF criteria. According to the modified pTNM 16% were T1, is important to achieve acceptable outcomes.

REJECTION AFTER SMALL BOWEL TRANSPLANTATION IN PIGS

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Background: Small Bowel Transplantation (SBT) is associated with high rate of acute cellular rejection (ACR) and a reliable serological marker for its diagnosis is still missing.

Aim: To evaluate the role of Citrulline as serological marker for early detection of ACR after orthotopic SBT in swine model.

Material and method: 20 German landrace pigs were divided in 3 groups: – G1: autologous SBT(n=4) as ischemia/reperfusion injury (IRI) model – G2: autologous SBT without immunosuppression (n=6) – G3: allogenic SBT with immunosuppression (Tacrolimus i.m. + Prednisolon) (n=8).

SBT was performed after standard technique using Thiry-Vella loops for daily biopsy. Observation period was 14 days. Serum Citrulline was peroperatively measured by means of HPLC. SBT-specimens were processed with hematoxill/eosin stained sections.

Results: Median cold ischemic and warm ischemic time was 210 and 26 minutes respectively. G1 and G3 animals survived up to POD 14. Median survival of G2 animals was 7 days. Citrulline level showed a similar course in G1 and G3. 50% reduction of basal values at POD2 (32 nmol/ml) renormalization at POD 4 (68 nmol/ml) and steady state up to POD 14. In G2 we observed a similar course like in G1 and G3 up to POD 4 and, immediately after, a progressive decrease up to day 10 (9 nmol/ml). In G1 IRI lesions were histologically detected. In all G2 animals histological demonstrated ACR occurred after POD 4, exactly corresponding the serological decrease of Citrulline. No histological signs of ACR were detected in G3.

Conclusion: Citrulline revealed to be a reliable marker for IRI and for early ACR after orthotopic SBT in swine model.
Recycling System (MARS) improvement of HE as well as decreased levels of neurotoxic substances like bilirubin, ammonia, and urea are reported. The aim: of this study was to evaluate the changes in blood concentrations of amino acids during MARS therapy in severe liver failure before liver transplantation (LTx).

Patients: This study includes 27 consecutive patients with MARS therapy in ICU with severe liver failure. Mainly these patients were listed for LTx if no contraindication existed.

Results: The mean number of treatments was 3.8 (±1.8). The grade of HE decreased during MARS treatments (2.15±1.51 to 1.36±1.66) (p<0.01). All amino acids decreased during MARS. The Fischer’s ratio was pathologically low at the beginning but it improved during MARS therapy (p<0.05). The elevated levels of tyrosine and histidine normalized. During MARS treatment there was a significant decrease in bilirubin, ammonia and urea, 40%, 39% and 79% respectively.

Conclusion: MARS treatment had a favourable effect both on HE and the neuroactive amino acid levels.

PO-651 SMALL-FOR-SIZE GRAFT INJURY IN ADULT-TO-ADULT LIVE DONOR LIVER TRANSPLANTATION
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Purpose: This prospective study was designed to evaluate the possible mechanism of small-for-size graft injury.

Methods: Seventy-one consecutive cases of adult-to-adult right lobe live donor liver transplantation (LDLT) were recruited in this study. Three groups were included: 1) GW/ESLM = 0.4, n=14; 2) GW/ESLM > 0.4, and ≤ 0.6, n=30; 3) GW/ESLM > 0.6, n=22; peak bilirubin/ESLM > 0.6 (p<0.01). The incidence of complications and AST/ALT ratio were analyzed at 24h and 72h after reperfusion. Plasma levels of IL-2, IL-10 and VEGF were detected by ELISA.

Results: The number of C4d+ and C6b+ cells were decreased at 24 and 72h after reperfusion in all the three groups. The number of CD40+ cells were gradually increased with time. A significant elevation of plasma PCC was observed in group 1 at 6hr after reperfusion, and it was also significantly higher than groups 2 and 3 at 6, 12, 24 and 72 hr after reperfusion. Plasma level of IL-10 was significantly increased at 6hr after reperfusion in all the three groups. On the contrast, IL-2 was undetectable in all the three groups during the observation period. The plasma level of FABP demonstrated a similar pattern with IL-10. In groups 1 and 2, the plasma levels of VEGF presented with a gradually increasing pattern with time.

Conclusions: Generation of reactive oxygen species and release of FABP might reflect ischemia/reperfusion injury, especially in the small-for-size graft. A transient increase of plasma IL-10 might reveal the host response to ischemia/reperfusion injury. VEGF production might be related to the regeneration process of partial liver grafts.

PO-652 OPTIMAL PORTAL VENOUS CIRCULATION FOR LIVER GRAFT FUNCTION AFTER LIVING-DONOR LIVER TRANSPLANTATION
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Purpose: We investigated optimal portal venous circulation for liver graft function after living-donor liver transplantation (LDLT) in adult recipients.

Methods: Between June 2003 and November 2004, 28 adult patients underwent LDLT in our institution. We modulated portal venous pressure (PVP) under 20 mmHg in these 28 cases by performing a splenectomy (n=4). The portal venous flow (PVF) and PVP were measured at the end of operation. Complication was calculated by dividing PVF by PVP.

Results: PVF and compliance showed a significant inverse correlation with peak bilirubin levels after LDLT (r=-0.63, P<0.01), and with international normalized ratio at 1 week after LDLT (r=-0.56, P=0.01). Hepatic functional reserves evaluated by Technetium-99m-diethylenetriaminepenta-acetic acid-galactosyl-human serum albumin (99mTc-GSA) liver scintigraphy at one month after LDLT showed significant correlations with PVF and compliance (r=0.64, P=0.05). Compliance also showed an inverse correlation with ascitic fluid volume on the 7th postoperative day (r=0.41, P=0.05).

Conclusions: It is suggested that both PVF and compliance are reliable indicators for postoperative liver graft function.

PO-653 LIVER TRANSPLANTATION FOR HEPATOCELULAR CARCINOMA WITH THE EXPANDED CRITERIA
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Purpose: The most widely accepted criteria to manage patients with HCC and cirrhosis for liver transplantation are the Milan criteria. In our center, if there is no evidence of extra-hepatic dissemination then the patient is considered as a candidate for a liver transplantation.

Methods: Between January 2003 and March 2005, fifteen patients with HCC, aged between 1 to 66 years underwent liver transplantation in our unit. Two of the tumors were diagnosed incidentally in the hepatectomy specimens. These were solitary occult carcinomas, one in an adult recipient with cryptogenic cirrhosis and the other was in a pediatric 1 year old recipient with PFIC-2 disease. Five of the remaining tumors were beyond the Milan criteria. For pre-operatively diagnosed HCC, the donors were 3 siblings, 3 spouses, 2 mothers, 1 father, 1 daughter and 3 cadaveric livers, and for the incidental tumors, one donor was the mother and the other was a cadaveric liver. All patients received tacrolimus monotherapy and low dose corticosteroid with early withdrawal as immunosuppression.

Results: In 2-22 months follow up period (mean 7.8 months), all patients are doing well with excellent graft function and without tumor recurrence. The patients with advanced disease had neoadjuvant chemoradiotherapy with farmarubicin, cysplatina, mitomycin-C and polivinyl alcohol. No patient had received adjuvant chemotherapy.

Conclusion: We believe that the selection criteria of the HCC patients should be expanded and living donor option should be discussed with the family members of the patient.

PO-654 THE BACK-TABLE GUIDE WIRE REPLACEMENT AND STENTING BILE DUCT IN LIVER TRANSPLANTATION
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Purpose: The incidence of biliary tract complications ranging from %15 to %64 after living donor liver transplantation. Initially hepaticojejunosotomy (HJ) was performed but nowadays duct-to-duct (DD) anastomoses are favored but to ease of plasma IL-10 are still a challenge.

Methods: From April 2001 to April 2005 we performed 77 liver transplants. Eighteen of these patients received cadaveric grafts. 35 received right lobes and 24 received left lateral segments from living donors. 11 patients had HJ and 66 patients had duct to duct (DD) anastomosis. Mean follow-up period was 16±13 months. In 8 cases stenosis and in 16 cases leak was determined. For the last 16 cases at the back-table, we placed a guide wire from the hepatic duct and T French drainage catheters were placed in retrograde fashion over the guide wire and pushed until it reached to the choledocus of the recipient.

Results: According to our results, complication rates were not statistically significantly different in DD and HJ groups (p=0.5). In the last 16 cases only one patient had a minor bile leak and the leak healed within a short time after the catheter was opened to maintain external bile drain. In the former cases, three patients treated with percutaneous drainage of the bilioma and all others needed percutaneous transhepatic biliary drainage. Complication rates were statistically significantly low in our technique (p<0.03).

Conclusion: Biliary stents prevent biliary complications and also by maintaining an access route for percutaneous interventions they simplify to treat biliary complications. Retr (n=2) stent placement at the back-table is an alternative and safe method of biliary drainage in liver transplantation.
A REGULATORY CYTOKINE PROFILE CHARACTERIZES TOLERANCE AFTER LIVER TRANSPLANTATION

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Background: Tolerance following allogeneic liver transplantation (LT) is characterized by elevated interleukin-4 (IL-4) and IL-10 in animal models. We compared the levels of T helper cytokines in patients maintained on low and high levels of tacrolimus after LT.

Patients and methods: The serum levels of INF-gamma, TNF-alpha, IL-4, IL-10, IL-2 and TGF-beta were measured (ELISA) in 29 patients (11M:18F, median age 60y [28-79]) with tacrolimus levels <5 microg/L for 12 months and no episodes of acute cellular rejection (group A), and in 21 patients (9M:12F, median age 40y [21-65]) requiring higher tacrolimus levels (>10 microg/L) and more episodes of acute cellular rejection (n=6), chronic rejection (n=15) and recurrent auto-immune hepatitis (n=1) (group B). Indications for LT were chronic end-stage liver disease (n=25, n=9), acute liver failure (n=3, n=3) and re-LT (n=1, n=9) in group A and B respectively. Thirty three healthy adults, (7M, 6F, median age 35y [28-46]) were tested as controls (group C).

Results: Median cytokine levels (pg/ml) in group A, B, and C were: INF-gamma: 1127 (range 0-9545), 922 (0-7416), 780 (0-1098), IL-2: 3 (0-1724), 0 (0-1036), 0 (0-72), TNF-alpha: 18 (0-2283), 0 (0-2224), 0 (0-30), IL-4: 482 (4672), 376 (0-1330), 296 (0-467), IL-10: 58 (0-2849), 47 (0-1254), 21 (0-241), TGF-beta1: 32 (6-73), 37 (4-201), 32 (4-125), respectively.

Patients in group A showed higher levels of IL-4 (p=0.05) and IL-10 (p=0.07) compared to group B (Wilcoxon test). The levels of the other cytokines were similar in the two groups of patients.

Conclusion: Our data showed that elevated IL-4 and IL-10 levels characterize rejection-free liver transplant recipients maintained on low levels of tacrolimus and may be associated with graft tolerance.

HHV-6 DNA IN PERIPHERAL BLOOD MONONUCLEAR CELLS AFTER LIVER TRANSPLANTATION

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Human herpesvirus 6 (HHV-6) infection has been reported after liver transplantation. HHV-6 may cause fever and other clinical symptoms, such as graft dysfunction and auto-immune hepatitis. In this study, the detection of HHV-6 DNA in peripheral blood mononuclear cells (PBMC) was compared with HHV-6 antigenemia in the monitoring of liver transplant patients.

Methods: Consecutive 18 adult liver transplant recipients were frequently monitored for HHV-6. HHV-6 infections were diagnosed by HHV-6 antigenemia test, which detects the viral antigens in PBMC, but is rather qualitative than quantitative. From the same PBMC specimens HHV-6 DNA was demonstrated by in situ hybridization using a biotinylated probe and quantified as DNA positive cells/10000 PBMC. Altogether 130 blood specimens were analyzed.

Results: During the first 3 months (mean 12 days, range 7-19 days) after transplantation, 12/18 patients developed HHV-6 antigenemia. Concurrent HHV-6 DNA was detected in 11/12 patients. The mean peak value of HHV-6 DNA was 110 positive cells/10000 PBMC. Altogether 130 blood specimens were analyzed.

Conclusion: Demonstration of HHV-6 DNA correlated well with HHV-6 antigenemia, and may be used as a semiquantitative test to detect the virus in transplant patients.

OUR EXPERIENCE IN LIVER TRANSPLANTATION IN PATIENTS GREATER THAN 65 YEARS OF AGE

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Objectives: To analyse our early and long-term results of liver transplantation (LT) in patients greater than 65 years of age.

Material and Methods: Between 1988 and 2003, 520 patients underwent LT in our centre. Main indication for LT were post-necrotic cirrhosis in 56%, followed by HCC over cirrhosis in 26%. Half of the patients were HCV +. Overall, all 72 patients were > 65 years of age. Actuarial survival, causes of mortality, post-operative complications, and long-term morbidity in the patients surviving for more than 1 year, were compared between both groups, under and over 65 years of age.

Results: The older group had more Child A, HCV (+) and HCC patients, p<0.05. Donor and surgery characteristics were similar, except for lower multi-transfusion in the older group (p<0.05). Actuarial survival at 1-5-10 years was 77%-60%-48% (~ 65 years) vs 71%-47%-40% (~ 65 years), p<ns. Causes of mortality in patients ~ 65 years were recurrent of underlying disease, medical causes and de novo tumours. In the older age-group, there were lower infections (p=ns) and rejections (p<0.01). Over the 10 years follow-up, there was a higher incidence of rejection (57% vs 24%), DM (27% vs 19%), dyslipidaemia (20% vs 11%), cardiovascular complications (20% vs 15%), and de novo tumour (17% vs 11%).

Conclusion: Results in patients ~ 65 years are comparable to patients < 65 years. If older candidates for LT are carefully selected, CNI immunosuppression should be avoided in older candidates, because its effects could worsen the pre-existing common pathology of elderly patients.

FACTORS CONTRIBUTING TO ALTERED AEROBIC CAPACITY IN LIVER TRANSPLANT CANDIDATES

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Aerobic capacity is usually estimated with oxygen consumption at peak exercise (VO2max). It alteration is underestimated in cirrhotic patients and contributors are largely unknown.

Purpose: To study factors contributing to impaired VO2max in liver transplant candidates.

Patients/Method: Between January 2002 and June 2004, cirrhotic patients evaluated for liver transplantation were referred for cardiopulmonary exercise testing on a cycle ergometer. Patients were classified according to the Child-Pugh score. Predictive variables previously identified or susceptible to alter aerobic capacity (demographic and anthropometric data, past medical history, medication and relevant laboratory tests) were all recorded. Univariate analysis used k2, Kruskal-Wallis and Bonferroni test. Multiple logistic regression was used to identify variables independently associated with altered VO2max.

Results: One hundred fifty one candidates underwent a determination of their VO2max. Cirrhosis was alcoholic in 70% of cases and HCV-related in 15% of cases. Exercise testing was maximal and interpretable in 85% of cases. Eighty nine % of candidates had an impaired aerobic capacity defined by VO2max <54% of predicted VO2max with 80% of severe alteration (VO2max<20 ml/kin). Using univariate analysis, contributors to impaired VO2max were Child-Pugh score (Child C vs Child A/B, 53.4% vs 69%, CI 95%: 15.1-37.3), anaemia (51% vs 67.1%), alcoholic origin (53.4% vs 69%), tabagism (55.5% vs 67.5%) and ascites (52.8% vs 65%). Multivariated analysis identify Child-Pugh score (<10,31; CI 95%: 16-39,3), anaemia (CI 95%: 15-11,3-27) and tabagism (<8,8; CI 95%: -14,3-13,2) as significant predictive factors.

Conclusion: Aerobic capacity was profoundly altered in liver transplant candidates. Independent predictors of it alteration were Child-Pugh score, anaemia and tabagism.

TISSUE-DERIVED CELLS CONTRIBUTE TO ENDOTHELIAL REGENERATION DURING ISCHEMIA-INDUCED NOSVASOULARIZATION

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Recent studies demonstrate that bone marrow (BM)-derived progenitor cells (CPC) contribute to endothelial regeneration. Recent, however, suggests that non-BM-derived cells may be even more important in transplant arteriosclerosis. To thoroughly investigated the contribution and source of non-BM-derived cells, we generated parabiotic pairs by conjoining Tie2-LacZ+ transgenic mice and wild type animals. Without tissue ischemia, incorporation of LacZ+ CPCs into vascular structures was very low (0.1±0.3±13%). However, after ligation of the femoral artery as a model of tissue ischemia, spraying of parabiotic animals with a reverse BM transplantation (wild type BM transplanted into tie2-LacZ mice). Intriguingly, a remarkable percentage of incorporated CPCs (77.6±16.8%) was found in femoral arteries. The BM-derived endothelial cells, however, did not contribute to the pre-existing common pathology of elderly patients. Therefore, we transplanted male liver or small intestine, respectively, into female rats. After induction of limb ischemia, we observed robust incorporation of organ-derived CPCs (liver: 2.9±3.5%, intestine: 1.1±2.2%). Finally, the administration of inductive of putative CPC from the liver (CD45+/CD31+) cells significantly en-
hanced recovery of limb perfusion (no cells: 24±14% of normal blood flow; CPC infusion: 67±21%; P<0.01).

**Conclusion:** Here we directly demonstrate that non-BM-derived CPC contribute to vascular regeneration. Liver and intestine represent putative sources for these tissue-residing progenitor cells.

**PO-660 BILIARY COMPLICATIONS AND THEIR MANAGEMENT IN LIVING DONOR LIVER TRANSPLANTATION**

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Biliary complication is not an uncommon problem after liver transplantation especially in living donor liver transplantation. We experienced 11 biliary complications out of 67 (16.4%) living donor liver transplant patients at our center from 1999 to 2004. There are 8 patients with biliary strictures followed by 2 patients with biloma and 1 patient with bile leakage. For 8 patients with biliary stricture, we first tried external biliary drainage or endoscopic sphincteroto-my with or without biliary stent insertion. Biliary strictures were resolved in 5 patients by these relatively less invasive measures, but 3 patients underwent Roux-en-Y hepaticojejunostomy for relapsing cholangitis secondary to persistent biliary strictures. For 2 patients with biloma, biloma was drained via percutaneous measure with success. For 1 patient with bile leakage due to size mismatch between donor’s and recipient’s bile ducts, duct-to-duct bili-ary drainage was converted to Roux-en-Y hepaticojejunostomy. There was no patient death or graft loss from biliary complications in our series for 6 to 24 months follow-up after their operations.

**PO-661 ANTIVIRAL TREATMENT IN HCV RECURRENT AFTER LIVER TRANSPLANTATION IN HCV-HIV COINFECTED PATIENTS**

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We report our experience in 6 HIV-HCV coinfected patients transplanted in our center.

**Patients:** Between Sept-02-Dec-04, 6 HIV patients were transplanted due to HCV-cirrhosis. Mean age was 44.1 years. Mean MELD was 22.6. All patients were under HAART. Immunosuppression was FK and steroids (2 p.); FK, steroids and MMF (2 p.) and FK and MMF (2 p.).

**Results:** One patient died at postoperative period by multiorgan failure. Five patients presented HCV recurrence after a mean interval of 114 days (r:21-218 days). Mean ALT levels were 507 IU/L (r:110-639 IU/L); mean bilirubin levels were 8.4 mg/dL (r:0.4-24 mg/dL) and mean HCV viral load was 9.2x10^6 IU/ml (r:6.6x10^6–1.3x10^8 IU/ml). In 3 cases, recurrence was cholestatic. Peginterferon and ribavirin was started for refractory acute exfoliative rejection. Two were removed for refractory acute exfoliative rejection (po 15 and 42), and three responded to anti-rejection therapy. Retrospectively, onset of rejection was associated with a parallel increase of sIL-2R (>100% vs baseline) and WIT 28 %.

**Conclusion:** Long-term high dose passive HBIG immunoprophylaxis are effective measure to reduce HBV recurrence after OLT in HBSAg positive patients without replication before transplant.

**PO-663 LBP AND SOLUBLE IL-2R INDICATE ACUTE REJECTION AFTER CLINICAL INTESTINAL TRANSPLANTATION**

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**Introduction:** Acute rejection after intestinal transplantation (ITx) appears focal and specific diagnostic parameters are not established. **Methods:** ITx was performed in 6 short bowel syndrome patients (41 (39-58) y), UW was used for graft preservation. CIT was 30.5±48 min and WIT 28±5 min. Immunosuppression consisted of ATG-bolus followed by anti-L2mAb, tacrolimus (15-20 µg/l), rapamycin (4-8 µg/l), and prednisolone. Graft biopsies were taken endoscopically. Immune monitoring contained interleukin 6 (IL-6), procollatin (PCT), lipopolysaccharide binding protein (LB/P), soluble L2 receptor (sL2-2R), and tumor necrosis factor (TNF) alpha blood concentrations.

**Results:** After a median follow-up of 247 (245-580) days, 5 grafts had suspicion of acute rejection, two were removed for refractory acute exfoliative rejection (po 15 and 42), and three responded to anti-rejection therapy. Retrospectively, onset of rejection was associated with a parallel increase of sL2R (>710 UI/L) and LBP (<15 mg/l), and often preceeded histological changes. Both parameters, sL2R and LBP, declined during successful anti-rejection therapy.

**Conclusion:** Rate of rejection after ITx is high. All parameters including histology failed to predict early onset of severe and exfoliative rejection. Online determination of sL2R and LBP will improve intestinal graft monitoring.

**PO-664 HIGH FREQUENCY OF GASTRODUODENAL CMV-INFECTION IN LIVER TRANSPLANTATION PATIENTS**

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**Purpose:** The frequency and importance of gastroduodenal cytomegalovirus (CMV) infection was studied in liver transplantation patients and controls. **Patients and methods:** Gastroduodenal biopsies were taken from 83 liver transplantation patients with upper gastrointestinal symptoms or suspicion of biliary complication, 131 patients with end-stage liver disease and 26 acute liver failure evaluated for liver transplantation and 43 otherwise healthy pa-tients with dyspeptic symptoms. CMV was demonstrated in frozen sections by immunoperoxidase staining using a monoclonal antibody against CMV specific antigens (pp65).

**Results:** Transplantation patients had more severe duodenal CMV infection than others (mean 1.5 (0-20) vs. 0.6 (0-8) CMV positive cells/visual field, p<0.01). Their most common symptoms were nausea and upper gastrointestinal fullness and most common endoscopic findings were erosions. Despite CMV-inclusions, histological findings associated with CMV infection were non-specific and minor. Helicobacter pylori was found only in 6% of all patients and did not associate with CMV findings.

**Conclusion:** Symptomatic gastroduodenal CMV infection was common in liver transplantation patients, but one third of symptomatic patients with end-stage liver disease and one fourth of healthy controls with dyspeptic symptoms also had positive CMV finding in the gastroduodenal mucosa.
REGULATION OF INTRACELLULAR "DEFENSE PROTEIN" IN KUPFFER CELLS STIMULATED WITH IFNγ AND RAT LIVER TREATED WITH CCL4

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Background: Kupffer cells play an important role in innate immune defense. IFNγ is considered to be crucial in macrophage activation. Aim: To identify genes involved in Kupffer cells activation by IFNγ and evaluate their expression in CCl4 treated rats, to study the mechanism of IFNγ in macrophage defense during inflammation.

Methods: isolated Rat Kupffer cells were stimulated with IFNγ for 8 hours. Differential Display Polymerase Chain Reaction was performed between stimulated and unstimulated cells. Identified genes were investigated by Real Time Methods: isolated Rat Kupffer cells were stimulated with IFNγ.

Conclusion: This study shows relevant novel genes that are playing role in the hepatic inflammatory process. The analysis of their profile of expression could be useful to understand the molecular mechanism of Kupffer cells activation in this specific pathway.

SEPTIC BILIARY COMPLICATIONS IN EARLY PERIOD AFTER LIVER TRANSPLANTATION

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Different types of infections are common problems after organ transplantation. The aim of this study was to assess the incidence of septic biliary complications in early posttransplant period.

Patients and Methods: We analyzed retrospectively 100 consecutive liver transplantation performed between 30.06.2000 to 27.112004. 83 elective and 17 urgent transplantsations were performed. Choledocho-choledochostomy was performed over the straight –Levin type- drain. 255 bile microbiological cultures were performed.

Results: 71 patients had at least one positive bile culture. 21 had symptomatic cholangitis and received antibiotic treatment. 2 of them had 2 episodes of cholangitis.50 patients had positive cultures without any symptoms.146 samples of 255 were positive. Positive results of bile cultures were most frequent in first 2 weeks after transplantation. Positive bile cultures and cholangitis episodes did not have any influence on the liver function. One patient had extrahaepatic bile duct necrosis which required reconstruction of biliary anastomosis.

Conclusions: Despite high number of bile colonization, only 21% of patients had bacterial cholangitis. This high number of bacterial colonization is probably due to biliary drainage and immunosuppression.

MITOCHONDRIAL FUNCTION EVALUATION BY KETOISOCAPROIC ACID BREATH TEST IN PATIENTS WITH HCV INFECTION UNDERGOING ALBUMIN DIALYSIS

Maria Assunta Zocco, Cristina Di Campi, Michele Santoro, Marcello Cardelli, Lorenzo Zleri Dal Verno, Roberto Flore, Anna Chiara Piscaglia, Marialuisa Novi, Giorgia Di Gioacchino, Paolo Pola, Giovanni Gasbarrini, Antonio Gasbarrini. Internal Medicine, Catholic University of Rome, Rome, Italy.

Background and aim: Oxidative injury occurs as direct reults of HCV core protein expression and in vivo and may involve a direct effect of core protein on mitochondria. Kетоisocapric acid (KICA) breath test is a simple, reliable and non invasive test to evaluate hepatic mitochondrial function. Albumin dialysis (MARS) is effective as bridge treatment in patients with acute failure on chronic liver disease.

The aim of our study was to evaluate the improvement of mitochondrial func-

tion measured by KICA in patients undergoing MARS for acute on chronic HCV liver failure.

Materials and methods: Five patients with HCV chronic infection undergoing MARS treatment for acute decompensation have been enrolled. Before and after each MARS treatment patients have been submitted to blood testing for the main hemachemical parameters. The mitochondrial function has been assessed both by KICA breath test and arterial ketone index (AKBR).

Results: MARS treatment was effective in decreasing the serum level of total bilirubin, bilary acids, urea and ammonium. Moreover, the MARS treatment determined and increase in AKBR and in the cumulative percentage of 13CO2 recovered in exhaled air 2 hours after KICA ingestion.

Conclusion: Liver mitochondrial function seems to be beneficially affected by MARS treatment.

Liver mitochondrial function seems to be beneficially affected by MARS treatment.

GENE EXPRESSION PATTERN FOLLOWING LIVER INJURY INDUCED BY ALALLYL-ALCOHOL IN A MURINE MODEL

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Background and Aims: Allyl-alcohol (AA) is known to cause periporal liver necrosis. Restitution of liver necrosis involves proliferation and differentiation of putative liver stem cells (oval cells). We aimed to evaluate the gene expression pattern related to liver regeneration after AA injury.

Methods: Mice were injected intraperitoneally (ip) with AA (40 mg/kg) and killed 4 days after. As controls, we used mice sacrificed 4 days after normal saline ip injection. Livers were tested by microarray analysis. Gene showing significantly different expression were selected and confirmed by RT-PCR. Liv-

ers were also analysed by histology.

Results: As concerning microarray analysis, nearly 10680 out of the 22690 genes represented in the array were expressed in the liver. Among these, AA upregulated nearly 62 genes by over-twofold and downregulated approxi-
mately 205 genes by 50% or more. Upregulated genes belong to a broad range of functional pathways and include cell cycle regulators, genes related to pro-
liferation, oval cell activation, acute-phase-response and inflammatory/immune response, as well as transcription factors. Among downregulated genes we found a great number of metabolic transcripts, like urate-oxodase. RT-PCR con-

firmed array results for selected genes.

Conclusions: AA suppressed the expression of metabolic genes, whereas it seems to induce hepatic proliferation from oval cells. These results support the participation of a stem cell system in liver repair after toxic damage.

COMPARATIVE ANALYSIS BETWEEN MELD SCORE VS. UNOS STATUS FOR PREDICTING POST-TRANSPLANT MORTALITY IN LIVER RECIPIENTS

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Introduction: The Model for End-Stage Liver Disease (MELD) score has re-

placed the conventional UNOS status scores 3/2/0/2 to assess risk for mortality in patients awaiting liver transplantation (LT). However, further studies should be performed to evaluate the predictive value of the MELD score for post-

transplant mortality.

Patients and Methods: A group of adult patients that underwent a LT proce-
dure in our Department during 01/01/2000-30/06/2004 period (n=140, M 100/F 40; age: 52.79±8.93) was enrolled as follows: i) classification in UNOS status 2A (n=13, 9.28%), 2B (n=123, 87.85%), or 3 (n=4, 2.85%); ii) no retransplant-

a
d; iii) full dataset about cadaveric donors (M 92/F 48; age: 49.17±19.25). For each patient was collected the last MELD calculated before LT. The patients were stratified for MELD score as follows: MELD 0-10, n=12; 11-18, n=61; 19-

24, n=33; >25, n=34. Statistical analysis was performed by using Cohen’s k for inter-rate agreement and c-statistic for Receiver Operating Characteristic (ROC) curves.

Results: A poor inter-rate agreement was found by Cohen’s k=(0.048) in UNOS 2B patients for MELD score (MELD 0-10, n=10; 11-18, n=55; 19-24, n=30; >25, n=28). No significance occurred between MELD and UNOS ROC curves for patients mortality at 1 month (P=0.996), 3 months (P=0.714), 6 months (P=0.986), and 1 year (P=0.967).

Conclusions: In this study, no statistical differences was found between MELD score and conventional UNOS statuses in order to sensibility for post-

transplant mortality in liver recipients.

Liver and Intestine; Poster Presentations
Wilson's disease is autosomal recessive inherited. ATP7B is the disease caus- ing gene, which encodes a copper transporting enzyme, the so-called ATPase 7B. Defects within ATP7B result in copper accumulation within hepatocytes, which in turn lead to necrosis. Via necrosis peptides enter into the circulation and subsequently copper accumulation within other cells and or- gans occur. The phenotypic pattern of Wilson's disease is variable in respect to age of onset and symptom presentation. Neurological, psychiatric, and hepa- tological symptoms have to be primarily differentiated. Acute liver failure occurs especially in younger females. We analyzed 652 affected patients genetically and revealed 92 different mutations. Phenotypic implications of the distinct muta- tional pattern and the role of mutational testing in the liver transplant setting will be presented. In addition, a newly designed register for affected patients within Europe, the so-called EuroWilson project, will be introduced.

**Conclusion:**
Transoesophageal echocardiography cardiac output monitoring could decrease of PV (vs 25% for well tolerated HVE patients).

The aim of this prospective study was to evaluate the changes of hemody- namic parameters, with transoesophageal Echocardiography-Doppler, during a five minute hepatic vascular exclusion test (HVE) in patients undergoing liver transplanta- tion.

**Method:** A five minute HVE test was realised at the end of the liver dissec- tion, to evaluate the patient's hemodynamic tolerance and to choose the best procedure for the anhepatic phase: HVE or lateral vena cava clamping (piggy back). We studied 20 adult patients. The cardiac output (CO) was obtained continuously, with its associated hemodynamic values: Left ventricle ejection time (LVETc) as an indicator of volume status, acceleration of blood ejected from the left ventricle (ACC) and peak velocity (PV) as contractility indexes. All the patients received 500ml of 4% Albumin during the HVE test.

**Results:** During the test, we observed a 47% decrease of CO (7.01±2.71/min to 3.46±1.41/min). We found a mean decrease of 27% for LVETc: 343±136ms to 255±45ms; a drop of 33% in accelerometry: 25.4±14 to 20.8±9 and a mean decrease of 27.8% in the PV values 80.8±24cm/sec to 62.4±31cm/sec. When taking mean arterial pressure ~660mmHg as a ma- jor criteria for poor tolerance to HVE, we observed a 35% decrease of LVETc in poor tolerated HVE patients (vs 23% for well tolerated HVE patients) and a 35% decrease of PV (vs 25% for well tolerated HVE patients).

**Conclusion:** Transoesophageal echocardiography cardiac output monitoring could be of help for HVE hemodynamic tolerance evaluation in liver transplantation.

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**PO-674**

**A SECURE PREOPERATIVE PORTAL DECOMPRESSION TECHNIQUE, PROXIMAL SPLENIC ARTERY EMBOLIZATION, IMPROVES SURVIVAL OF ADULT LIVING DONOR LIVER TRANSPLANTATION FOR VIRAL/ALCOHOLIC HEPATITIS**

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To obtain preoperative portal decompression assiectedly, we established prox- imal splenic artery embolization (PSE) technique in adult LDLT.

**Method:** Thirty-four adult LDLT recipients with viral and alcoholic hepatic fail- ure were divided into two groups (Group 1: n=12) or without (Group 2: n=20) PSE. Splenic artery was embolized proximal to splenic hilum 12-18 hrs before surgery.

**Results:** There was no development of abscess in Group 1. Significant short-
Liver and Intestine

Poster Presentations

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PO-675 RECOVERY OF HYPERSENSPLASMEN AFTER LIVER TRANSPLANTATION

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Background: Hyperplenism is common in liver cirrhosis, which is the most common indication for liver transplantation (LT). Splenectomy during LT is suggested for patients with moderate thrombocytopenia to enhance intraoperative hemostasis. Whether the hypersplenism would recover after LT to the same extent either with or without splenectomy has not been well studied.

Aims: To study the changes of hemogram in LT patients at the National Taiwan University Hospital, and to see whether the extent of recovery from hyperplenism is the same in patients with or without splenectomy.

Patients and Methods: 141 successful LT patients were divided into 3 groups: Group 1 (n=46) with low platelet (Pit) count but no splenectomy; Group 2 (n=63) with normal Pit count and no splenectomy; Group 3 (n=32) with low Pit and received splenectomy. The average Pit count, WBC count, Hct and Hb levels were followed from pretransplant to 2 years after LT.

Results: The hemogram stabilized 1 month after liver transplant. Group 3 had the lowest Pit count, WBC count, Hct and Hb level before LT, but the highest levels of all the 4 parameters after LT. Group 1 had the same preoperative levels as Group 3, but had the lowest Pit and WBC count after LT. Group 2 had the highest preoperative levels of all 4 parameters, but with lowest levels of Hct and Hb after LT.

Conclusion: Although all the 3 groups recovered from hypersplenism after LT, but the extents were not the same. Not regarding the surgical complica- tion of splenectomy in LT patients, splenectomy had favorable effect on the hemograms.

PO-676 LIVER TRANSPLANTATION WITHOUT THE USE OF FRESH FROZEN PLASMA: 210 PROSPECTIVE CASES

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Aim of the study: to assume that bleeding is not correlated with pre- transplantation levels of Factor V and that Fresh Frozen Plasma (FFP) is not required to prevent or to treat fibrinolysis and bleeding during LT.

Methods: 210 LT prospectively performed (1996-2003) without the use of FFP. Filling standardized by diluted serum Albumin (DSA) with packed red blood cells (PRC), Aprotinin (Ap), Platelet concentrates (PC) and Fibrinogen administered at the end of anhepatic and post-reperfusion phases. Coagulation factors, Haematocrit, Platelets count, Albumin level, Euglobulin lysis time monitored before LT, 30mn before and 10 mn after unclamping, at the end of the procedure and at day 1, 2 and 7 post LT. Blood loss quantified during and after LT.

Results: operative time 420 mn, hepatic phase 90 mn, cold ischaemic time 585 mn, PRC n=8, DAS n=6 liters, PC n=2, Ap =10 U, Blood loss 3500 mL ± 2700mL (median values); 51 patients (24%) had vena cava clamping. Reinter- vention for haemorrhage was done in 10 patients (4.7%). Pearson correlation test showed no linear regression between blood coagulation factors levels and per or post-operative bleeding. Male gender, and vena cava clamping were signifi- cantly associated with bleeding. At postoperative day 2 Factor V was 80%, Factor VII 56%, Fibrinogen 2.7 g and Platelets count 48 000 (mean values). Bleeding in LT is not correlated with coagulation Factors levels. LT without FFP is feasible with usual rates of bleeding and no excess of morbidity.

PO-677 LONG-TERM EFFECT OF CONVERSION OF CALCINEURIN INHIBITORS (CNIs) TO MYCOFENOLATE MOFETIL (MMF) ON RENAL FUNCTION AFTER LIVER TRANSPLANTATION

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Background: CNI are frequently associated with chronic renal failure in liver transplantation. Withdrawal of CNI and MMF introduction might improve their renal function.

Methods: We have studied Creatinine Clearance (CCL) of 48 liver trans- planted patients treated with CNI with chronic renal failure. MMF (1.5-2g/d) was introduced to reduce or interrupt CNI.

Results: Patients have been transplanted for 7.8 years ± 4.4. The mean CCL was 42.9 ± 14ml/min when MMF was introduced compared to 60.3±19.6, 52.9 ± 14.9, 51.1 ± 15.2 three, five and one years respectively before MMF in- troduction (p<0.0001). Their rate of CCI decline for the 2 last years before MMF was -5.6 ± 5 ml/min. After MMF introduction, CCI increased significantly one, two and three years later (48.8 ± 17, 49.9 ± 18, 58.4 ± 20 ml/min respec- tively). The mean increase of CCI per year on the 2 last years was +4.3 ± 4.2 ml/min and was significantly different from the pre-MMF period (p<0.0001).

Conclusion: Six patients (12%) had no improvement of their renal function at one year but their rate of CCI declined was lower. The improvement of CCL was similar for patients treated with FK506 (n=14) or Neoral (n=34). None of the patients developed graft rejection. MMF has been interrupted in one case for severe side effect.

Conclusion: The reduction or interruption of CNI and the introduction of MMF is safe and is associated with an improvement of the renal function in these patients.

PO-678 ASSESSMENT OF LIVER GRAFT RECOVERY BY MONITORING THE FREE RADICALS IN THE PERIOPERATIVE SESSION

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Studies in both human and animal models have shown increased free radical (ROI) production after reperfusion of liver grafts. Some degree of dysfunction almost inevitable occurs after liver transplantation. The severity of dysfunction correlates with the degree of early hepatic injury. The aim of our study was to assess the relationship between ROI production and graft function.

Method: Graft-, renal function and ROI production of 50 liver transplant pa- tients were monitored at pre-, intra- and 24 days postoperatively. Luminol- dependent chemiluminescence (ROI) was used to measure the serum total ROI content as chemiluminescence intensity (CI in RLU%).

Results: The average CI of recipients was seven times higher (0.77±0.45% vs. 0.05%) compared to healthy controls (less than 0.1%). ROI activity increased significantly following reperfusion (1.1±0.6%) and slightly decreased (0.67±0.4%) by the fifth postoperative day. Significantly smaller CI (0.23±0.19%) was detected in uncomplicated patients two weeks after transplantation. In case of any complication CI remained elevated (0.97±0.3%) from CI higher than 0.77% had severe Child-Pugh score, longer dependency of respirator and more frequently need for renal support.

Conclusion: ROI production is predictor of reperfusion injury. It has a peak- production during the first reperfusion that also lasts for 5 days after liver trans- plantation. The magnitude of the rise is inversely proportional with the graft function and the renal function as well.

PO-679 EVALUATION OF COMPLIANCE IN PATIENTS ON THE WAITING LIST FOR LIVER TRANSPLANTATION

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Liver transplantation (LT) for alcoholic liver disease (ALD) is often controver- sial because of the risk of relapse into alcohol consumption and poor compli- ance to medical prescriptions following LT. The aim of the study was to identify, in patients on the waiting list for LT, risk factors of non compliance. 51 patients (39 with ALD and 12 with nonALD) on the waiting list for LT underwent a ques- tionnaire on habits and adherence to medical prescriptions.

40 patients, 11 female, mean age 48 years, answered the questionnaire. 79.4% of patients were married and 41% were working, 15.3% were smoking >15 cigarettes/day; 12.8% of ALD and 5.2% of nonALD patients were still drinking alcohol despite different medical prescriptions. Among the 51 patients, 61% were taking 3-7 drugs/day, 18% >7 drugs/day and 21% >3 drugs/day, and 88% suffered >1 liver cirrhosis side effects. 17/39 (43.5%) of ALD patients
and 9/12 (75%) of nonALD patients were not taking drugs due to forgetfulness (difference not statistically significant). Poor compliance is reported in an high percentage of patients on the waiting list for LT independently from the etiology of liver disease. Risk factors of poor compliance should be identified before LT, in order to predict non adherence to immunosuppression therapy after LT.

PO-680 PREDICTIVE FACTORS FOR TREATING CYTOMEGALOVIRUS (CMV) VIREMIA IN CMV-POSITIVE ORTHOTOPIC LIVER-TRANSPLANT (OLT) PATIENTS

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The aims of this retrospective study were to determine the predictive factors that were associated with the treatment of a first posttransplant CMV reacti- vation in 45 consecutive seropositive OLT patients. Immunosuppression was based on tacrolimus/steroids. CMV DNAemia quantitated with real-time PCR method was assessed every week for the first month, and then at every 2 weeks. When positive (n=26, i.e. 58%), the decision to treat (IV ganciclovir at 10 mg/kg/d for 14 days) (group I, n=11), or not (group II, n=15) was based on clinical and/or biological grounds. The median time to the first CMV DNAemia was 72 days in group I and 50 days in group II. At the time of the first CMV DNAemia, a viral load lower than 3 log10 copies/ml was significantly more frequent in group I than in group II (median values: 3.55 vs. 2.84; p=0.01). The alkaline phosphatase levels were also lower in group I, i.e. 142 vs 571 IU/L (p=0.001). The alanine/ALT, aspartate/AST, aminotransferase, bilirubin, and g-glutamyl transpeptidase (GGT) levels tended to be higher in group I than in group II. Hemoglobin levels were lower in group I than in group II patients (11 vs 12 g/dl; p=0.04). Other factors were similar in both groups. In multivariate analysis, the only independent predictive factor associated with the treatment of the 1st CMV DNAemia was alkaline phosphatase levels. Finally, the risk of having a 2nd CMV DNAemia was not dependent on the treatment of the 1st episode. The major predictive factors associated with the treatment of CMV reactivation after OLT are the level of DNAemia and the increases in the liver-function tests.

PO-681 ANATOMICAL INJURIES TO POSTMORTEM DONOR LIVERS: INCIDENCE AND IMPACT ON OUTCOME AFTER ADULT LIVER TRANSPLANTATION

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In this study, 826 recipients (83%) were younger than 60 years of age and 165 patients older than 60. We are reporting the outcomes of elderly patients undergoing LT in our institution. The aim of this study was to determine the predictive factors of CMV infection in 65 de novo OLT patients at 3 months posttransplantation. We included all consecutive patients grafted in 2003–2004. We recorded donor(D) and recipi- ent(R) data. Immunosuppression relied on tacrolimus, steroids, in addition to mycophenolate mofetil (n = 54), and/or induction therapy with anti-CD25 monoclonal antibodies (n = 43). CMV prophylaxis was only given to those at high risk of infection, i.e., the D+ R– patients. CMV infection was monitored on the basis of ultrasensitive PCR which detects as low as 50 copies/ml, i.e., 2.69 log10. The median time to CMV infection was 1 month. In unvaried analysis, the significant predictive factors for CMV infection were CMV status, i.e., D+ (vs D–) (p = 0.009), R+ (vs R–) (p = 0.03), D+/R+ (vs other patients) (p = 0.01), any com- bination except D–/R– (vs D+/R+) (p = 0.002), the original liver disease, i.e., HCV infection or alcohol-related cirrhosis (vs others) (p = 0.03), donor’s age (≤ 45 years; p = 0.01), lymphocyte count at M2, i.e., less than 1300/mm3 (p = 0.02), low hemoglobin levels at 1 and 3 months, and low platelet white-blood-cell, and lymphocyte counts at day 7. In multivariate analysis, the independent pre- dictive factors for CMV infection were recipient CMV serostatus, i.e., R+ (vs R–); OR 10.2 (2.2–58.5) (p = 0.01), donor’s age (≤ 45 years); OR = 11.42 (2.2–58.5) (p = 0.003), and lymphocyte count at M2 (≤ 1300/mm3); OR = 7.33 (5.54–35.6) (p = 0.01). In conclusion, this study shows that the major factors associated with CMV infection are recipient’s CMV status, donor’s age and lymphocyte count.

PO-682 PREDICTIVE FACTORS OF CYTOMEGALOVIRUS (CMV) INFECTION AFTER ORTHOTOPIC LIVER TRANSPLANTATION (OLT) USING ULTRASENSITIVE PCR ASSAY

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The aim of this study was to determine the predictive factors of CMV infection in 65 de novo OLT patients at 3 months posttransplantation. We included all consecutive patients grafted in 2003–2004. We recorded donor(D) and recipi- ent(R) data. Immunosuppression relied on tacrolimus, steroids, in addition to mycophenolate mofetil (n = 54), and/or induction therapy with anti-CD25 monoclonal antibodies (n = 43). CMV prophylaxis was only given to those at high risk of infection, i.e., the D+ R– patients. CMV infection was monitored on the basis of ultrasensitive PCR which detects as low as 50 copies/ml, i.e., 2.69 log10. The median time to CMV infection was 1 month. In unvaried analysis, the significant predictive factors for CMV infection were CMV status, i.e., D+ (vs D–) (p = 0.009), R+ (vs R–) (p = 0.03), D+/R+ (vs other patients) (p = 0.01), any com- bination except D–/R– (vs D+/R+) (p = 0.002), the original liver disease, i.e., HCV infection or alcohol-related cirrhosis (vs others) (p = 0.03), donor’s age (≤ 45 years; p = 0.01), lymphocyte count at M2, i.e., less than 1300/mm3 (p = 0.02), low hemoglobin levels at 1 and 3 months, and low platelet white-blood-cell, and lymphocyte counts at day 7. In multivariate analysis, the independent pre- dictive factors for CMV infection were recipient CMV serostatus, i.e., R+ (vs R–); OR 10.2 (2.2–58.5) (p = 0.01), donor’s age (≤ 45 years); OR = 11.42 (2.2–58.5) (p = 0.003), and lymphocyte count at M2 (≤ 1300/mm3); OR = 7.33 (5.54–35.6) (p = 0.01). In conclusion, this study shows that the major factors associated with CMV infection are recipient’s CMV status, donor’s age and lymphocyte count.

PO-683 LIVER TRANSPLANTATION IN ELDERLY: PREOPERATIVE HYPONATREMIA PREDICTS PATIENTS SURVIVAL

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Background: In the past two decades liver transplantation (LT) has been the most important development in the management of end-stage liver disease. However, the supply of donor livers is insufficient to meet the current need for liver transplantation. This led to re-evaluation of selection and listing criteria for liver transplantation, including transplantation of patients older than 60. We are reporting the outcomes of elderly patients undergoing LT in our institution.

Methods: Data were extracted from UK transplant database on 991 consecu- tive liver transplantations performed in our institution between 1994 and 2004. In this study, 826 recipients (83%) were younger than 60 years of age and 165 (17%) were 60 years or older. The following information was collected: age (both of recipient and donor), sex, etiology of liver disease, pretransplant lev- els of prothrombin time, albumin, serum creatinine, and cold ischemia time. Survival statistics were calculated at 30 days and 5 years.

Results: Overall 5-year survival was significantly lower in those older than 64 (61.6%) compared to patients younger than 60 (76.2%), p < 0.05. And there was no significant difference in survival between recipients who received graft survival was shown with advancing age (≤ 64 year versus <60) p < 0.05. Regression analy- sis showed that for patients older than 64, only MELD score ≥24 and preop- erative hyponatremia were independent risk factors, with hazard ratios of 5.6 and 2.6, respectively.

Conclusion: These findings strongly support the conclusion that, elderly pa- tients should offered transplantation earlier in the spectrum of end-stage liver disease, before developing hyponatremia or MELD score ≥24.

PO-684 DENovo POST-renal TRANSPLANT inflAMMATORY BOWel disease SUCCESSFulLy TREATED WHILE ON MYCOPHENolate MOFETiL

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Background: Prevalence of inflammatory bowel disease (IBD) post transplant is affected by the immune tolerance and modality of immunosuppression used. Mycophenolate mofetil (MMF) may have a promoting effect in developing post transplant IBD. Case summary: A 39 years old Omani gentleman had chronic renal failure due to advanced nephrosclerosis. He was on hemodialysis for 9 months till he received live unrelated renal transplant. He was on prednisolone, MMF and tacrolimus which is changed to sirolimus when he developed diabetes met- illus 2 months posttransplant. Five months posttransplant, he developed re- current attacks of bloody diarrhea and abdominal cramps. He was treated under anal fistulae not responding to treatment. Colonscopy showed multiple ery-
LIVER TRANSPLANTATION FOR WILSON DISEASE – INDICATIONS AND OUTCOMES

Krzysztof Zieniewicz 1, Abdulsalam Alsharabi 1, Waldemar Patkowski 1, Pawel Nyckowskyj 1, Bogdan Michalowicz 1, Rafal Paluszkiewicz 1, Tadeusz Wroblewski 1, Ireneusz Grzelak 1, Agata Paczkowska 1, Leszek Pazcek 1, Marek Krawczyk 1. 1Dept. of General, Transplant & Liver Surgery, Medical University of Warsaw, Poland; 2Dept. of Immunology & Internal Medicine, Medical University of Warsaw, Poland.

Liver transplantation (LTx) is the only causal therapy for the patients with Wilson disease and in fulminant course – is a life saving procedure.

Aim of the study: to review the indications and the results of LTx in this group of patients.

Materials & methods: In the period 1994-March 2005, 352 patients underwent LTx, among them - 20 pts (5.7%) for Wilson disease; 5 men, 15 women, mean age 30.5 (20-46 years). 10 patients (1 man and 9 women) were transplanted in emergency settings for fulminant hepatic failure with coma (UNOS 1 and 2A) and renal insufficiency requiring hemodialysis or more recently – albumin dialysis with the use of Prometheus device (2 pts), 11 patients (55%) were transplanted with classical technique with veno-venous bypass, while 9 patients (45%) - piggy back technique.

Results: Overall mortality was 30% (6 patients). All but one, were young women (mean age 27 years) operated on in emergency settings for FHF. Death occurred on 1st-3rd postoperative day. Mortality rate was as high as 70%. Mean survival period was 34 months (range 1-98 months). 1 patient underwent reLTx 3 months after LTx for biliary complications. 13 patients (65%) are alive in good general condition and 1 - with late portal vein thrombosis.

Conclusion: Liver transplantation is a good therapeutic option for the patients with Wilson disease, however in emergency LTx for fulminant liver failure the results are still poor.

Hepatitis B, Tumor Treatment and Immunosuppression Influence Recurrence of Hepatocellular Carcinoma After Liver Transplantation

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Hepatocellular carcinoma (HCC) represents a considerable therapeutic challenge. Trans-arterial chemoembolization (TACE) and percutaneous ethanol injection is orthotopic liver transplantation (OLT). Aim of this study was to identify factors associated with HCC recurrence.

Eighty-five patients with HCC transplanted between 1975-2004 at Hannover Medical School were analyzed retrospectively. Follow-up ranged from 13 to 349 months (mean 88 months). In 6/85 (9.4%) HCC was established post OLT. Etiologies of chronic liver disease included HCV (39%) and HBV (24%) infection, and alcoholic cirrhosis (15%). Cirrhosis was absent in 6/85 (7%). Recurrent HCC occurred in 18.8% after a mean of 3.3 years following OLT. HCC stages at OLT were T1 (18%), T2 (37%), T3 (13%) and T4 (15%). Recurrence was associated with T4 (31% vs 7%, p=0.018, OR 5.82) and with patients receiving tacrolimus (62.5% vs 37.5%, p=0.018, OR 5.82) but not with T1-3, with HBV (60% vs 40%, p=0.02, OR 3.85), the PEI vs TACE group had 28%/0% Child C, 39%/67% Child B, and 32%/35% Child A. Recurrence-free survival was achieved in 80% of patients undergoing OLT. Tumor stage, TACE before OLT, HBV infection and immunosuppression with tacrolimus and steroids were identified as risk factors for HCC recurrence. Pre- and post-operative management of HCC therefore influences the outcome in OLT in HCC.

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Liver Transplantation (LT) for Hepatocellular Carcinoma (HCC)

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Purpose: To compare two techniques of TACE (selective versus unselective) before LT for HCC on patient survival.

Patients/Methods: A case-control study included 30 patients who received selective TACE (STACE group) and 30 independently selected patients who received unselective TACE (UTACE group). Patients and controls were matched for clinical characteristics, period of LT, time spent on the waiting list and preoperative staging. STACE consisted in a selective injection of a mixture of Lipiodol and doxorubicin before mechanical obstruction into the tumor vascular bed. Five years post-LT disease-free survival rates were evaluated using Kaplan Meier method and compared using the Log rank test.

Results: Proportions of patients with modified TNM stage I, II, III and IV disease were similar in both groups. The mean waiting time before LT was 114 days in the STACE group and 125 days in the UTACE group (ns). The mean number of procedures was 1.3 (range 1-5). The median alpha-fetoprotein level, morphologic characteristics of the tumors were similar in the two groups. Five-year disease free survival was 75% with STACE and 72.4% without UTACE (ns). Survival rates did not differ significantly between the two groups, with respect to the time on the waiting list, the tumor diameter, or the type of technique. The overall 5-year probability of HCC recurrence was 13.3% in STACE group and 6.7% in UTACE (ns).

Conclusion: With a mean waiting period of 4 months pre-LT, 5-years disease-free survival and HCC recurrence are not different using STACE or UTACE technique.

Treatment of Recurrent Hepatitis C in Liver Transplant Recipients with PEGylated Interferon-Alpha and Ribavirin: A Retrospective Report

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Purpose: The clinical management of liver transplant (LT) patients with HCV recurrence is controversial, due to early reports of inefficacy of antiviral treatment with recombinant interferon. Availability of pegylated forms of interferon alfa-2b, and aggressive management of complications of ribavirin therapy has led experienced center to utilize this antiviral treatment in LT patients with recurrent HCV. We retrospectively reviewed 4 of our experience on LT patients who received combination pegylated alfa-2b interferon (1.5 mcg/kg/wk) and
impact of Cyclosporine vs Tacrolimus in Evaluation of Psychological Aspects in a Tolerance State of Successful Living Donor Long Term Prophylaxis of Hepatitis B

Miquel Monras, Antoni Rimola, Jose Maria Miro, Neus Freixa, Jordi Blanch, Giorgio E. Gerunda. General Surgery and Transplantation, Liver and Multivisceral Transplant Center, University of Modena and Reggio Emilia, Modena, Italy.

Liver cirrhosis secondary to Hepatitis C virus (HCV)-infection is the leading indication for liver transplantation (LT), however HCV recurrence post LT is nearly universal and can affect patient/graft long term survival. Concerns have been raised about a negative prognostic role of main immunosuppressors, ciclosporine and tacrolimus, on severity and frequency of HCV recurrence. We retrospectively reviewed our experience in LT, with the aim of unveiling virological and histological differences between HCV patients treated with ciclosporine or Tacrolimus before starting antiviral therapy. Serum HCV-RNA levels at month 2, 6 and 12 showed no significant differences in the two groups, and so did Ishak’s grade and stage of recurrent hepatititis 1 year survival rate were also similar, although there was a positive trend in favour of ciclosporine-treated patients. In conclusion, in our experience choice between ciclosporine or Tacrolimus did not impact on patient’s survival after HCV recurrence, nor frequency of virological recurrence or histological severity. Other factors, like pre-LT viremia, HCV genotype and cumulative doses and levels of immunosuppression must be kept into account in longer studies to deepen analysis on HCV recurrence post-LT.

PO-691 EVALUATION OF PSYCHOLOGICAL ASPECTS IN HIV-INFECTED PATIENTS CANDIDATES FOR LIVER TRANSPLANTATION

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Introduction: Liver transplantation (LT) is increasingly indicated in HIV-infected patients. The evaluation of these patients as LT candidates requires specific assessment of several psychological aspects, which may represent additional and unexpected difficulties.

Aim: To assess psychological aspects in HIV-infected patients under evaluation as LT candidates.

Patients: We evaluated 19 HIV-infected patients (17 males; mean age: 41 years) from the psychological point of view during their general evaluation as LT candidates. HIV infection was acquired through iv drug addiction in 13 patients, sexual contact in 2, and unknown route in 4.

Results: The attitude in front of the psychological evaluation was sincere in only 2 patients, passive in 11 and defensive-negative in 6. Thirteen patients had past history of alcohol abuse, although only 7 were conscious of it. In other 4 patients, alcohol abuse was unclear because of their little cooperation. Other drugs consumed by the patients were heroin (n=13), cannabis (n=16), cocaine (n=10) and benzodiazepines (n=19; abuse in 9). There was social-familiar disarrangement in 11 patients, and history of psychopathology in 15, probable personality disorders in 12, neuropsychological disorders in 7 and imprisonment in 2. Three patients were rejected for LT due to psychological reasons.

Conclusions: High prevalence of multiple drug abuse, psychopathology and social-familiar disarrangement can be often observed in HIV-infected patients who are candidates for LT. The little awareness of drug problems and the frequent attitude of patients require an exhaustive psychological evaluation due to the possibility of occultation of information essential for their assessment as LT candidates.

PO-692 CONVERSION FROM TACROLIMUS TO CYCLOSPORINE IN PATIENTS WITH DIABETES MELLITUS AFTER LIVER TRANSPLANTATION

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Introduction: The results of liver transplantation (LT) dramatically improved, when the calcineurin inhibitors became available. However, the toxicity of these drugs is frequent. The aim of this study was to evaluate the feasibility and results of the conversion from tacrolimus to cyclosporine in LT patients presenting with diabetes mellitus (DM).

Patients and methods: Since January 2001, were included the LT patients, presenting with DM after at least 6 months of treatment with tacrolimus. Monthly clinical and biological follow-up included fasting glucose, cholesterol (LDL- and HDL-cholesterol), triglycerids, creatinine, bilirubin, AST, ALT, g-GT, INR and HbA1c.

Results: Twenty five patients were included after a median delay of 54 months after LT (7 women and 18 men, median age 51 years (range 30-69)). Seven patients had past history of DM before LT. At the time of inclusion, there were 11 patients with insulin dependant diabetes mellitus (IDDM) and 14 patients with NiIDDM and the glycemic control was poor (HbA1c > 6.5%) in 13/25 patients (52%). After a median follow up of 13 months after conversion, there were 4 patients with (IDDM) 17 patients with NiIDDM and 4 patients without DM, and the glycemic control was poor in 3/25 patients (12%). No acute rejection or hypertenpidermia occurred. Three patients returned to tacrolimus because of arterial hypertension (n=2) or digestive side-effects (n=1).

Conclusion: Our results suggest that conversion from cyclosporine to tacrolimus in stable LT patients with DM is well tolerated and beneficial. These results have to be confirmed from a larger study.

PO-693 LONG TERM PROPHYLAXIS OF HEPATITIS B RECURRENT AFTER LIVER TRANSPLANTATION WITH LAMIVUDINE AND HEPATITIS B IMMUNOGLOBULIN

Giancarlo Ferretti1, Manuela Meri2, Andrea Onetti Muda3, Stefano Ferretti4, Gilardo Novelli4, Massimo Rossi4, Pasquale Berloco4, 1 Mal.Infettive, Az. Pol. Umb., Rome, Italy; 2 Gastroenterologia, Univ./la Sapienza, Rome, Italy; 3 Anatomia Patologica, Univ. la Sapienza, Rome, Italy; 4 Centro Trapianti di Organo, Univ. la Sapienza, Roma, Italy.

Lamivudine and HBIG prophylaxis for HBV recurrence has strongly reduced the rate of reinfeciton and improved survival. a. Aim of this study was to value if HBIG i.m. used in the follow up had the same efficacy of HBIG IV to protect against HBV reinfection.

Materials: we evaluated 28 patients transplanted for acute or chronic HBV related liver disease (23 M. 5 F, mean age 49±9, mean follow up 18±14). 12 patients started Lamivudine before and sixteen at the time of liver transplantation. HBG were administered intravenously during the first week (500/1000 IU) and intramuscularly thereafter (1200 IU every 4 weeks) to maintain a HBsAb title > 100 IU/L. HBsAg and anti-HBs were controlled regularly and HBV-DNA at least at monthly intervals. Reinfection was diagnosed by HBsAg HBV-DNA positivity. Gravida patients were follow (up 18 months).

Results: all but one patients resulted HBV DNA negative after 527 days of follow up, the only HBV DNA positive patient had a histology compatible with HBV recurrence after 280 days of follow up. Liver biopsy revealed no signs of HBV related hepatitis and negativity of immunohistochemical tests for HBV.

Survival at three years was 83%.

Conclusion: In our study combined use of HBIG i.m. and Lamivudine proved to be highly effective and safe in preventing the recurrence of HBV after liver transplantation with no side effect, good compliance and low cost.

PO-694 A TOLERANCE STATE OF SUCCESSFUL LIVING DONOR LIVER TRANSPLANTATION AFTER BONE MARROW TRANSPLANTATION

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Purpose: The majority of organ transplantation recipients need life-long immunosuppressive treatment to maintain graft function. Therefore, achieving immunological tolerance remains a major goal in organ transplant to maintain stable engraftment of grafted organs. Recent progress in HSCT has provided new methods (non-myeloablative SCT: NST) for reliable engraftment with sublethal conditioning regimens. NST has been successfully applied with minimal toxicity in the treatment of malignant disease and in the achievement of mixed chimerism. This NST approach might be successfully transplanted into the organ transplantation to achieve immunological tolerance.

Methods/Results: We performed NST followed by liver transplantation using an HLA-identical sibling donor in a 54-year-old male patient with both chronic
myelogenous leukemia and liver cirrhosis. We investigated whether NST was possible to induce mixed chimerism and maintain the grafted liver without additional immunosuppressive drugs. Treatment with NST to treat leukemia and to induce immunological tolerance has been well tolerated. 3 months later, following liver transplantation which used minimal immunosuppressive drug for only 3 months after transplantation, has been also tolerated without clinical manifestation of rejection. The patient was monitored for the donor antigen by PCR. At present, the patient has only limited GVHD, which responded to steroid treatment, and is still alive with good graft function by biochemical and histological examination at 3 years of post-NST and post-LT. We also confirmed immunological tolerance by donor skin graft.

Conclusion: It is to assess the rate of biliary complications in 89 consecutive liver transplantation performed in 2004. In the present study MARS-therapy didn’t remove unambiguously cytokines from blood. The mean age was 45.5 years, 23 males/26 females. The aetiology in most cases was either toxic substance (N=26) or unknown (N=19).

Results: One year patient survival was 81.6%. Mean number of treatments was 3. 15 patients were bridged to successful LTx. Native liver recovered in 26 and eight patients were deceased, one with LTx. Within the whole group only IL-10 declined significantly after the first MARS treatment (P=0.01) and also within all treatment intervals. In patients who were deceased or bridged to LTX IL-10 declined and IL-6 increased significantly (P<0.05). In the control group biliary complications occured in only 4 (7.69%) patients (P<0.05). None of them caused organ loss.

Conclusion: Abandoning the drainage of biliary anastomosis has reduced the occurrence of early biliary complications following the orthotopic liver transplantation.

EARLY BILARY COMPLICATIONS IN RELATION OF THE TECHNIQUE OF BILARY ANASTOMOSIS IN ADULT LIVER TRANSPLANT RECIPIENTS

Abdulsalam Alsharabi. Department of General, Transplant and Liver Surgery, Medical University of Warsaw, Warsaw, Poland.

Biliary complications are known as a “Achilles heel” of liver transplantation. In this study we demonstrate that humoral activation, represented by C4D activation, play a role in acute rejection following OLT. Liver samples were subjected to C4D specific immune-histological staining and evaluated by two independent pathologists.

Methods: We performed retrospective analysis of 98 liver biopsies from liver transplanted patients who had either experienced acute rejection, hepatitis-C reinfecion or no pathological alterations serving as controls. Every specimen was taken due to the clinical suspicion of acute rejection after OLT. Tissue samples were subjected to C4D specific immune-histological staining and evaluated by two independent pathologists.

Results: 21 of 36 patients who underwent an acute rejection episode displayed C4D-positive staining in their liver biopsy (58.3%) compared to 4 of 32 patients with hepatitis-C reinfecion were tested positive for C4D (12.5%, p<0.05 compared to rejection group). In the control group 2 of 29 specimen showed C4D positivity (6.9%, p=0.01 compared to rejection group).

Discussion: In this study we demonstrate that humoral activation, represented by C4D activation, play a role in acute rejection following OLT and may be helpful to distinguish between rejection and hepatitis C recurrence in the future.
Prospectively collected data were used. Univariate analysis was performed using chi square, Kaplan-Meier analysis with log rank, and the Mann-Whitney U-test. Variables from univariate analysis with a P-value < 0.1 were entered in a Cox regression for multivariate analysis. P-values < 0.05 were considered statistically significant.

One, three, five, and ten-year patient survival were 75%, 68%, 66%, and 61%, respectively. Eighty patients (39%) died within ten years. Note that 51 of the deceased patients (64%) died during the first year after transplantation, probability of surviving ten years was 81%. After multivariate analysis, per-operative blood loss and use of a VAB appeared significant predictors for both one-year and ten-year patient survival. Patients surviving the first year after liver transplantation have a high probability of surviving ten years as well. The fact that per-operative blood loss and use of a VAB are multivariate predictors for both one-year and ten-year patient survival indicates that surgical technique is important for survival after liver transplantation. One-year actual survival is an excellent predictor for long-term survival after liver transplantation.

### PROGNOSIS AFTER LIVER TRANSPLANTATION PREDICTED BY PREOPERATIVE MELD SCORE

Jae Won Joh1, Jin Wan Park, Kwang-Woong Lee, Sung Joo Kim, Hwan Hyo Lee, Choon Hyuck Kwon, Suk-Koo Lee. Surgery, Samsung Medical Center, Seoul, Korea.

**Purpose:** The model for end-stage liver disease (MELD) is based on 3 serum biochemistry parameters, serum total bilirubin, creatinine, and INR of prothrombin time (PT), and has been an excellent predictor of per-operative and postoperative biliary complications in donor operation.

**Results:**
- Univariate analysis of risk factors for death within 3 months after OLT: serum total bilirubin, creatinine, MELD score, hyponatremia with ascites.
- Multivariate analysis of risk factors for death within 3 months after OLT: serum bilirubin, PT INR, MELD score, serum sodium, ascites, Child-Pugh score, pre-transplant hemodialysis.
- Survival of patients with HCV or HBV monoinfection, hepatitis B and D are known to have a worse prognosis compared to patients with HCV/HBV coinfection.

**Conclusion:**
- We suggest that preoperative MELD score can be a good predictor of short-term prognosis after OLT.

### NEW TNM STAGING AS A PATIENT SELECTION CRITERIA OF LIVER TRANSPLANTATION FOR HEPATOCELLLULAR CARCINOMA

Jae Won Joh1, Hwan Hyo Lee1, Kwang-Woong Lee1, Sung Joo Kim1, Seong Ho Choi1, Jin Seok Heo1, Jin Wan Park1, Choon Hyuck Kwon1, Seung Heui Hong2, Suk-Koo Lee1. Surgery, Samsung Medical Center, Seoul, Korea; 2Transplant Coordinator of Transplant Center, Samsung Medical Center, Seoul, Korea.

**Purpose:** Liver transplantation has been accepted as a therapeutic option for patients with HCC. There are several well known patient selection criteria such as Milan criteria, but there are still debates. We performed this study to evaluate if the new AJCC/UICC TNM staging system can predict recurrence-free survival following liver transplantation for HCC and to assess usefulness of new AJCC TNM staging system as the patient selection guideline of liver transplantation for HCC.

**Methods/Materials:** From September 1996 to December 2003, eighty-seven patients who received liver transplantation for HCC were enrolled in this study and analyzed retrospectively, based on pathological data.

**Results:**
- According to the new pathological TNM staging, 5-year recurrence-free survival rates of pT1, pT2 and pT3 were 95.2%, 83.8% and 43.6%, respectively (p < 0.0001). There were significant differences of recurrence-free survival rates between pT1 and pT2, and between pT2 and pT3 (p < 0.0001).
- Survival of patients with pT1 was significantly better than survival of patients with pT2 and pT3.
- Patients with pT1 had significantly better survival than patients with pT2 and pT3.

**Conclusion:**
- We suggest that new AJCC/UICC TNM staging system can predict recurrence-free survival following liver transplantation for HCC and to assess usefulness of new AJCC TNM staging system as the patient selection guideline of liver transplantation for HCC.

### LIVER TRANSPLANTATION FOR PREOPERATIVE EXAMINATION IN LIVING DONOR

PO-700 LONGER SURVIVAL OF LIVER TRANSPLANT RECIPIENTS IN A SINGLE DUCT GROUP WITH MULTIPLE HEPATITIS VIRUS INFECTIONS

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**Purpose:** We recently identified a beneficial influence of GB virus C coinfection on the course of HIV infection. On the other hand, viral coinfections by hepatitis B and C or by hepatitis B and D are known to have a worse prognosis.

**Methods:**
- A total of 204 patients with hepatitis virus infections who underwent liver transplantation were included in survival analysis. Nine of these patients had HCV/HBV coinfection, 23 patients had HBV/HDV coinfection. Monoinfections after liver transplantation were included in survival analysis.
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**Results:**
- Monoinfections after liver transplantation were included in survival analysis. Nine of these patients had HCV/HBV coinfection, 23 patients had HBV/HDV coinfection. Monoinfections after liver transplantation were included in survival analysis.
- Patients with HBV/HDV coinfection had a significantly better survival than patients with HCV/HBV coinfection.

**Conclusion:**
- The mechanisms of these viral interactions remain to be elucidated.

### PREDICTORS FOR ACTUAL TEN-YEAR PATIENT SURVIVAL AFTER LIVER TRANSPLANTATION

Christian S. van der Hilst1, Alexander J.C. Ultima2, Elisabeth M. TenVerget1, Tjeerd J. Boelstra3, Elizabeth B. Haagsma3, Aad P. van den Berg3, Paul M.J.G. Peeters2, Koert P. de Jong2, Robert J. Porte3, Maarten J.H. Sloot3. 1Medical Technology Assessment, University Medical Center Groningen, Netherlands; 2Gastrohepatoitary and Liver Transplantation; 3Gastroenterology and Hepatology.

**Aim of the study was to assess predictors for actual ten-year patient survival in a single center cohort of 206 adult liver transplant recipients, transplanted between 1979 and 1994. Follow-up was completed until 2004, resulting in at least ten-year follow-up.**

**Methods:**
- We performed this study to evaluate if the new AJCC/UICC TNM staging system can predict recurrence-free survival following liver transplantation for HCC.
- We suggest that new AJCC/UICC TNM staging system can predict recurrence-free survival following liver transplantation for HCC.

**Conclusion:**
- We suggest that new AJCC/UICC TNM staging system can predict recurrence-free survival following liver transplantation for HCC.

### 3D-CT CHOLANGIOGRAPHY PROVIDE A USEFUL IMAGE FOR PREOPERATIVE EXAMINATION IN LIVING DONOR LIVER TRANSPLANTATION

Hiroshi Mitsuta, Toshiyuki Tamoto, Hideki Ohdan, Saburo Fukuda, Yasuhito Fudaba, Kohei Ishiyama, Kentaro Ide, Masayuki Shishida, Hirotsuka Tashiro, Toshimasa Asahara. Department of Frontier Medical Science, Programs for Biomedical Research, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan.

**Purpose:**
- The mechanisms of these viral interactions remain to be elucidated.

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- A total of 204 patients with hepatitis virus infections who underwent liver transplantation were included in survival analysis. Nine of these patients had HCV/HBV coinfection, 23 patients had HBV/HDV coinfection. Monoinfections after liver transplantation were included in survival analysis.

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Hiroshi Mitsuta, Toshiyuki Tamoto, Hideki Ohdan, Saburo Fukuda, Yasuhito Fudaba, Kohei Ishiyama, Kentaro Ide, Masayuki Shishida, Hirotsuka Tashiro, Toshimasa Asahara. Department of Frontier Medical Science, Programs for Biomedical Research, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan.

**Purpose:**
- The mechanisms of these viral interactions remain to be elucidated.
Results: Both groups were similar regarding the sex and the age of the recipients. Child status before LT and preservation solution. During the first year after LT, 12 grafts from group B were lost (37.1%) versus just 11 grafts in group A (11.6%), p = 0.004, RR 3.98, 95CI(1.55-10.191). Acute and chronic rejection and infections were similar in both groups, but biliary and arterial complications were higher in the older donor group. The main cause of graft loss in the older donor group was non-anastomotic biliary stenosis (NABS). Graft survival 12 months after LT was higher in younger donors (88.8% vs 66.67%; p = 0.003).

Conclusion: The use of grafts from donors older ≤60 years is related to a decrease in graft survival in the first year after liver transplantation mainly because of the presence of NABS.

**PO-707**

**TRANSPLANTED BONE MARROW CELLS FUSE WITH RESIDENT HEPATOCYTES UNDER REGENERATIVE CONDITIONS IN INFLAMMATORY LIVER DISEASE**

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Transplanted bone marrow cells generate hepatocytes through cell fusion. However, controversy still exists, whether this phenomenon might be a general response to hepatic injury. We have developed a mouse model of hepatitis in which hepatocytes are killed following T cell activation. Bone marrow from male 178.3 mice (H-2kb background) expressing the H-2kb molecule under its own promoter was transplanted into female B10.BR mice. Hepatitis was induced by repeated injections of Des TCR T cells expressing a transgenic T cell receptor specific for the H-2kb antigen. Donor cell progeny was identified by the H-2kb antigen. Hepatocytes from mice developing hepatitis were purified and cells were sorted for donor H-2kb using FACS. Fluorescence in Situ Hybridization for the X and Y chromosome was carried out to identify fused cells containing the male chromosome.

In animals developing hepatitis, 1 in 106 hepatocytes was of donor origin. FISH analysis demonstrated that sorted H-2kb+ cells were predominantly the result of fusion between donor hematopoietic cells and resident hepatocytes. Despite bone marrow derived cell migration into the liver, the frequency of these fusion events was low.

In conclusion, our results demonstrate that bone marrow cells fuse with resident hepatocytes during liver regeneration. As cell fusion also occurs in other liver regeneration models, our results suggest that fusion might be a physiological response of bone marrow progeny to hepatic injury.

**PO-708**

**MOLECULAR MONITORING OF HCC BEFORE AND AFTER LIVER TRANSPLANTATION**

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Background: Orthotopic liver transplantation (OLT) is the therapy of choice for patients with selected hepatocellular carcinoma (HCC) unsuitable for surgical resection. Recurrence of disease (ROD) and de novo HCC represent the most frequent neoplastic late complication of OLT for HCC. Molecular pathology techniques can help predict ROD and discriminate it from de novo HCC, with important clinical and therapeutic implications. We therefore designed a prospective pilot study of molecular monitoring for all the OLT candidates with HCC presenting in our institution.

Methods: 1) In order to provide a molecular tumor staging we perform a quantification of free plasmatic DNA and circulating tumor cells in the blood of HCC patients before and after OLT by means of Real Time qPCR. 2) Immunohistochemical evaluation of 3 prognostic biomarkers of HCC previously validated covering 16 DNA polymorphic loci.

Conclusions: Our multi-parametric cell molecular analysis on blood and tissues might be highly informative in monitoring OLT patients with HCC. Final results of this pilot, ongoing, study are required to confirm its clinical and therapeutic relevance.

**PO-706**

**THE USE OF OLD DONORS INCREASES THE RISK OF GRAFT LOSS IN THE FIRST YEAR AFTER LIVER TRANSPLANTATION**

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The donor age limit for liver transplantation (LT) has increased over the past years. Although the outcome of liver transplantation does not seem to have been affected by the use of old donors, the real effect remains still to be determined.

**Aim:** To evaluate the outcome of liver transplantation with old donors in the first year after transplantation.

**Methods:** 150 consecutive LT, performed between December 1998 and July 2003, were analyzed. Patients who died with normal liver function before 1year after LT and patients with ABO incompatible donors were excluded (n=20). Most of the analysis was prospective (n=118). LT were divided into two groups depending on donor age: A. ≤60 years old (n=95) and B. >60 years old (n=35). The presence of complications and liver outcome were analyzed.

**Results:** Both groups were similar regarding the sex and the age of the recipients, Child status before LT and preservation solution. During the first year after LT, 12 grafts from group B were lost (37.1%) versus just 11 grafts in group A (11.6%), p = 0.004, RR 3.98, 95CI(1.55-10.191). Acute and chronic rejection and infections were similar in both groups, but biliary and arterial complications were higher in the older donor group. The main cause of graft loss in the older donor group was non-anastomotic biliary stenosis (NABS). Graft survival 12 months after LT was higher in younger donors (88.8% vs 66.67%; p = 0.003).

**Conclusion:** The use of grafts from donors older ≤60 years is related to a decrease in graft survival in the first year after liver transplantation mainly because of the presence of NABS.

**PO-704**

**LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA WITH BILE DUCT THROMBOSI**

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**Purpose:** In a few cases of hepatocellular carcinoma (HCC), the jaundice results from obstructive causes including tumor invasion or thrombosis in the bile duct. The aim of this study is to report on our experience with living donor liver transplantation (LDLT), and to evaluate the role of liver transplantation for HCC patients with BDT.

**Methods**/**Materials:** From September 1996 and August 2004, a total of 140 adult patients underwent liver transplantation for HCC at our center. Four patients (2.9%) who had LDLT performed for HCC with BDT were included in this study.

**Results:** The operation was all men and the mean age was 57.0 years. The initial total bilirubin levels were in the range of 2.0 ~30.7 mg/dL. The sizes of the tumours ranged from 2.0cm to 5.0cm in diameter, and all were single lesions. All the tumors had microvascular tumor emboli. The median follow-up period was 14.3 months (range: 12 to 22 months). Only one case in which the BDT were identified intraoperatively showed the intraportalineal recurrence at 15 months postoperatively, and he died 20 months after LDLT with multiple intrahepatic recurrences. The other 3 patients were alive and showed no evidence of recurrence at the end of the follow-up period.

**Conclusion:** Although further study should be performed, we suggest that liver transplantation is an effective treatment option for HCC with BDT.

**PO-705**

**PROSPECTIVE STUDY ABOUT PREOCUSSION INFECTION IN RECIPIENTS OF A FIRST LIVER TRANSPLANT MADE FROM 1986 TO 2004**

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The infection is the most frequent cause of precocious death in the patients with liver transplant. We have analyzed the infections happened within the first three months of the first liver transplants, grouping the patients into three consecutive periods of time.

During period I (1986-1991) 121 transplants were made, in period II (1992-1996) 149 transplants and in period III (1997-June 2004) 210 transplants.

The survival of patients increased significantly throughout time (64% period I; 82% period II; p<0.011 versus I; and 90% in the III, p=0.025 versus II).

The incidence of global infection (42.9%), bacterial infection (28.6%) and viral (17.1%) in period III was significantly higher than in previous periods (80.6%, 65.3% and 43.8%, respectively in period I and 73.8%, 51.8% and 35.6%, respectively in period II, all p<0.05). The incidence of fungal infection was similar throughout time (23.9%, 12.6% and 7.1%, in I, II and III; NS). The infection was the most frequence cause of death in the three periods (46.4%, 64% and 47.6%, in I, II and III; NS), having remained invariable the mortality by fungal infection (18.5%, 22.1% and 14.2%, in I, II and III; NS).

**Conclusion:** In spite of the diminution of the global incidence of precocious infection, the mortality attributed to infection, remains unalterable throughout the time. It emphasizes the necessity to make studies on factors of risk and antiinfectious prophylaxis, in order to improve the precocious survival of the liver transplant patients.
PO-709  NEWCASTLE ORGAN RETRIEVAL IMAGING SYSTEM (NORIS), ORGAN ASSESSMENT AND PROCUREMENT MOVES INTO THE 21st CENTURY

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Introduction: Assessment of procured livers depends on the retrieving surgeon’s experience. At organ retrieval, judgement on whether or not to accept an organ relies on verbal communication and subjective interpretation of assessment parameters. Using digital technology, images of procured livers can be transmitted to recipient surgeons anywhere using the world wide web (www). The system is named NORIS (Newcastle Organ Retrieval Imaging System), and incorporates the Newcastle Organ Scoring System (NOSSS) to streamline liver assessment.

Methods: NORIS is a secure system delivered over the www using a wireless connection to upload images to a central server and accessed via a secure website. The system has been specifically designed to protect confidentiality and anonymity. NOSSS-Proforma is based on the colour, edges, texture, age and body mass index of donor. A series of images is created and uploaded to NORIS website. The donor surgeon completes a NOSSS-Proforma which gives the procured organ an objective score.

Results: To date, two sets of images of liver from two donors have been successfully transferred from remote retrieval centres to the recipient surgeons. Recipient surgeons were then able to make a reliable assessment based on those images. NOSSS scores remained consistent between donor and recipient surgeons at the time of retrieval and remotely viewed computer screen images. The light and electron studies demonstrated the damage of hepatic sinusoidal construction and consequently the use of donor livers was scored as non-transferable.

Conclusions: The ability of NORIS to allow surgeons to make real time remote assessment of organs is likely to change how donor organs are evaluated and the ability to track initial organ assessment to post-transplant efficacy may provide better insight and a valuable teaching resource.

PO-710  MASSIVE PORTAL FLOW AT REPERFUSION MIGHT INJURE HEPATIC SINUSOIDAL CONSTRUCTION AND MIGHT PROVOKE EXCESSIVE SUPEROXIDE PRODUCTION

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Objective: The aim of this study is to investigate whether the massive portal flow at reperfusion state, which often occurs at small-for-size liver transplantation, might provoke hepatic sinusoidal construction and be the cause of massive superoxide production.

Materials and Methods: The 30 Lewis rat livers were procured and perfused by 20ml of cold (4°C) lactated Ringer solution at normal pressure and each 10 livers were then perfused by 20ml of oxygenated warm (37°C) Krebs-Hansel solution at normal, twice high, and three times high pressure respectively. The light and electron microscopical examination revealed that the superoxide production was increased significantly with the addition of DCFH-DA.

Results: The light and electron studies demonstrated the damage of hepatic sinusoid after reperfusion at three times high pressure was significantly worse than at normal or twice high pressure. The more superoxide production was produced at three times high pressure than at any other pressure.

Conclusion: These results suggest that portal reperfusion at more than twice high pressure might possibly injure hepatic sinusoidal construction and consequently provoke massive superoxide production. This massive flow might be one of the cause of poor prognosis of graft survival at small-for-size liver transplantation.

PO-711  ACUTE RENAL FAILURE FOLLOWING LIVER TRANSPLANTATION IN THE ERA OF IMMUNOSUPPRESSION USING INDUCTION THERAPY

Joelle Guittard1, Olivier Cointault1, Nassim Kamar1, Fabrice Muscari2, Shigeki Hikida1, Mari Ohtani 2, Kazuo Shirouzu3, Teruo Sakamoto1.

Introduction: Acute renal failure (ARF) is a common complication of liver transplantation (LT). ARF is defined as a rise in serum creatinine > 1.5 mg/dL or > 0.5 mg/dL in 24 h in patients with normal renal function before LT. ARF is associated with increased mortality, morbidity, and increased hospitalization costs. The cause of ARF following LT is multifactorial.

Methods: We retrospectively reviewed the medical records of 97 OLT recipients between 2000 and 2003. ARF was defined as a rise in serum creatinine > 1.5 mg/dL or > 0.5 mg/dL in 24 h in patients with normal renal function before LT. ARF was classified as surgical, post-operative, or non-surgical.

Results: Of 97 patients, 20 (20.6%) developed ARF. The surgical ARF group had significantly higher incidence of post-operative ARF compared to the non-surgical ARF group. The incidence of ARF was not different between the two groups of OLT recipients.

Conclusion: A prospective study of 97 orthotopic liver transplantations (OLT) between 2000 and 2003.

PO-712  DNA ANALYSIS IN EVALUATION OF MALIGNANT AND PREMALIGNANT BILIARY STRICTURES IN PRIMARY SCLEROSING CHOLANGITIS

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Background: In patients with primary sclerosing cholangitis (PSC) distinct widening between benign, premalignant and malignant biliary strictures is difficult. The aim of this study was to evaluate DNA analysis in combination with brush cytology as a diagnostic method for detecting malignancy.

Methods: Endoscopic retrograde cholangiography (ERC) with brush samples of biliary strictures (n=33) was performed on 28 patients with PSC (24 sent for evaluation for liver transplantation). Brush samples were taken for cytology and for evaluation of DNA content by flow cytometry.

Results: An aneuploid finding in DNA analysis was found in eight (29%) patients in 24% of the examinations, mean DI 1.2, mean CV 4.6). Cholangiocarcinoma was confirmed in one patient and resection specimens of extrapathetic bile ducts showed dysplasia (two high grade, two mild) in four. Three patients were still under the evaluation. DNA contents was diploid in 20 patients (DI 1.0, mean CV 4.6), five (25%) of whom showed later a malignancy. Two of these patients had peripheral cholangiocarcinoma beyond the reach of brushing and one pancreatic carcinoma. Of all cytologic samples 82% were benign and none strongly malignant.

Conclusion: Determining DNA ploidy added to brush cytology during ERC may serve as a useful tool in identifying those PSC patients who are at higher risk to develop cholangiocarcinoma.

PO-713  HYPOXIA INHIBITS LIVER REGENERATION AFTER PARTIAL HEPATECTOMY IN MICE

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The liver regeneration process include activation of cytokines and other substances of which some are also activated by hypoxia inducible factor-1 (HIF-1). Hypoxia could help liver regeneration by inducing VEGF but it has also been reported to inhibit HGF and c-met in experimental cirrhosis. We wanted to evaluate the role of systemic hypoxia in liver regeneration.

Methods: 16 mice (Balb/c, 24.9g) underwent 70% partial hepatectomy. Eight animals were placed under 6% oxygen concentration (hypoxia) and rest served as controls (normoxia). At 48 hours the hypoxia animals were re-laparotomy, post-op diuresis (> 80 ml/mn), requirement for vasopressive (208 µg/mn), post-op diuresis (< 5 red packed units), post-op diuresis (< 120 m3/h), use of vasopresory drugs, time to asparate aminotransferase (AST) peak (< 12 h), mechanical ventilation duration (< 1 d), ICU stay (< 13 d), and relaparotomy and CNIs transient discontinuation were factors significantly associated with ARF. The multivariate analysis for the outcome of ARF displayed a significant association with time to AST peak (< 12 h), re-laparotomy, post-op diuresis (< 120 m3/h), and a requirement for post-op vasopresory drugs. Independent factors associated with the need for post-OLT hemodialysis were pre-op sCr (> 75 µmol/l), requirement for vasopresory drugs, relaparotomy, and time to ALT peak (< 18 h).

Conclusions: ARF is quite common after OLT. Its independent factors are mainly related to perioperative events.

Conclusions: Hypoxia did specifically impair liver regeneration. Similar mRNA levels may indicate, that it was not the process itself but the speed of it, which was different in hypoxia vs. normoxia. This model offers a new method to study hypoxia and liver regeneration.
INTERRUPTION OF TNF-α SIGNALING AND KUPFFER CELLS DYSFUNCTION IMPROVES SURVIVAL IN THE ARTERIALIZED SMALL-FOR-SIZE LIVER TRANSPLANTATION IN THE MOUSE

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Materials and Methods: 97 liver transplant recipients were examined retrospectively. All examinations were performed by 4 or 16 detector CT scanner. 150 mL of nonionic contrast material was injected to each patient with a rate of 2.5 mL/sec for abdominal MDCT and 5 mL/sec for MDCTA. 3D-MDCTA reconstructions were performed by using maximum intensity projection (MIP) technique in both coronal and axial planes.

Results: In 16 patients, 10 portal venous and 6 hepatic venous complications were detected including 4 portal vein aneurysms, 5 portal vein stenosis, 1 portal vein thrombosis, 4 hepatic vein stenosis, and 2 hepatic vein thrombosis. Of these 16 patients 7 patients (4 portal vein stenosis, 3 hepatic vein stenosis) were diagnosed by MDCTA examination while the diagnoses were made by abdominal MDCT examination in the rest of patients. Diagnoses were confirmed by DSA in 3 patients, and percutaneous transluminal angioplasty (PTA) procedure was done for two portal and one hepatic venous stenosis. Conclusion: With development of MDCT technology, MDCTA of graft liver is now a practical non-invasive method of detecting vascular complications after liver transplantation. Excellent spatial resolution, fast scan times, noninvasiveness are some of the advantages of this technique. We believe MDCT should be the first step radiologic examination in both diagnosis and follow-up of venous complications after OLT.

IMPACT OF OBESITY ON THE OUTCOMES FOLLOWING LIVER TRANSPLANTATION

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AIMS: Obesity is a growing health problem in the western world and is a major risk factor for post-operative morbidity and mortality. The aim of this study was to determine patient survival in severely obese patients (BMI 35 kg/m2) after liver transplantation (LT). Methods: In total 682 LT patients were retrospectively reviewed over a 10 year period in terms of their morbidity and mortality. Patients were stratified according to their body mass index (BMI) kg/m2 into 4 different groups.

Results: Overall 359 were female and 333 male, median age 44yrs. Most patients (69%) had a BMI between 20-30 kg/m2, 19% BMI 30 20 kg/m2, 5.5% 30.1-35 kg/m2 and 3.2% with BMI 35 kg/m2. Severely obese patients had a significant risk of intraoperative death (9% versus 1%, p<0.05) compared to non-obese patients. Thirty day mortality for those with BMI <20 kg/m2 was 13%, BMI 20-30 kg/m2 10%, BMI 30.1-35 kg/m2 8% and 23% for severely obese. 2 year survival for severely obese patients was significantly lower than those with BMI 20-30 kg/m2, 61.9% versus 80% respectively (p=0.04). The mean ITU stay for severely obese patients was 5 days and for those with BMI 20-30, 20-30 and 30.1-35 kg/m2 up to 4 days (p=0.05). Conclusion: LT in patients with severe obesity have a significantly adverse outcome compared to non-obese patients.

SMALL BOWEL TRANSPLANTATION IN PATIENT WITH ANTI PHOSPHOLIPID ANTIBODY SYNDROME: CASE REPORT

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The main indications for Small Bowel Transplantation (SBT) in isolation are short gut syndrome, dysmotility syndrome and enterocyte dysfunction. We report an isolated SBT in a patient with short gut syndrome secondary to antiphospholipid antibody syndrome who died due to acute myocardial infarction on the fourth postoperative day. MLB, a 34-year-old woman, who underwent a cesaria-section because of fetal death, suffered extensive intestinal necrosis from the third portion of the duodenum to the transverse colon. Diagnosis of antiphospholipid antibody syndrome was based on anticardiolipin-antibody positivity, fetal death and mesenteric thrombosis. She evolved with several episodes of blood stream infections (gram negative microorganisms and a yeast-like fungus), two episodes of endocarditis (fungal and bacterial) and loss of two venous accesses. Pre-operative evaluation was normal except for grade IV macro-vascular stenosis by liver biopsy. On the eighth hour after the operation she was exubated and well. Zoom video-endoscopy showed patchy villous enlargement with moderate erythema. On the fourth postoperative day she presented progressivly dysphagia followed by cardio-respiratory arrest. Necropsy indicated acute myocardial infarction as the cause of death. In conclusion, we documented a finding that calls the attention to reactivation of Antiphospholipid Antibody Syndrome as a potential limitation for the success of small bowel transplantation.

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PO-714

PORTAL VEIN STENOSIS AS A LATE VASCULAR COMPLICATION AFTER LIVER TRANSPLANTATION, REPORT OF TWO CASES

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Purpose: Portal vein stenosis is relatively rare vascular complication affects 1-2% of transplant recipients. Differences in diameter of donor and recipient portal veins may increase portal vein related complications which explain higher complication rates after pediatric liver transplantations. Here, we reported two cases of portal vein stenosis in living related liver transplantation as late vascular complication.

Methods: Case 1: 1.5 year old male had left lobe living related liver transplantation due to Alagille Syndrome on March 2004. During routine post-transplant 11th months follow-up, enlarged spleen was detected. Anemia and thrombocytopenia was found. Computerized tomography angiography (CTA) determined that the stenosis ‘s more than 80% at the anastomosis. Percutaneous transluminal angioplasty (PTA) was done confirmed by DSA in 3 patients, and percutaneous transluminal angioplasty (PTA) procedure was done for two portal and one hepatic venous stenosis.

Conclusion: Portal vein stenosis is relatively rare vascular complication affects 1-2% of transplant recipients. Differences in diameter of donor and recipient portal veins may increase portal vein related complications which explain higher complication rates after pediatric liver transplantations. Here, we reported two cases of portal vein stenosis in living related liver transplantation as late vascular complication.

PO-715

MULTIDETECTOR CT IN THE EVALUATION OF VENOUS COMPLICATIONS IN PATIENTS UNDERGOING ORTHOTOPIC LIVER TRANSPLANTATION

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To investigate the role of three-dimensional multidetector CT (MDCT) and CT angiography (MDCTA) in the evaluation of venous complications in liver transplantation recipients who have undergone orthotopic liver transplantation (OLT).

Materials and Methods: 11th months follow-up, enlarged spleen was detected. Anemia and thrombocytopenia due to Alagille Syndrome on March 2004. During routine post-transplant methods: Complication rates after pediatric liver transplantations. Here, we reported two cases of portal vein stenosis in living related liver transplantation as late vascular complication. Portal vein angioplasty represents alternative, safety to reconstitutive surgery in treatment for symptomatic and asymptomatic portal vein stenosis.
**ABSTRACT WITHDRAWN**

**PROMOTIONS IN LIVER TRANSPLANTATION IN SHIRAZ**

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**Introduction:** Intestinal anastomotic leak (n=16), stricture (n=12), sludge (n=3), intrahepatic biloma (n=3) occurred in 31 grafts (26.9%). In 29 of 31 grafts, we performed several interventional radiological techniques (percutaneous transhepatic biliary drainage, drainage of intra-extra-hepatic bile collections, basket extraction of biliary sludge, removal of HAT, cold ischemia and operative times, the use of blood and plasma and the impact of surgery on survival post liver transplantation.

**Results:** Initial technical success was achieved in all patients. In 4 patients, stent thrombosis was observed during follow-up. No interventions were necessary for two patients because they were asymptomatic. Surgical intervention was performed for other two. Ten micron of the hepatic artery were seen during PTA and thrombosis. One of the ruptures was treated with graft covered stent. However, second patient was operated because graft covered stent didn’t seal. Hepatic artery stents of other 10 patients were remained patent. The follow-up was change between 1 month to 3 years.

**Conclusion:** Early and late postoperative stent placement to the hepatic artery technically feasible. This technique needs more development but shows great promise for the future.

**PO-722 INNATE IMMUNITY REACTION IN HEPATOCYTE TRANSPLANTATION AS A CAUSE OF GRAFT DESTRUCTION**

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**Introduction:** Transplanted (tx) hepatocytes (HC) need proper niche at the site of implantation. They need supply of nutrients, prevention from attack of scavenging cells, contact with stromal cells and supply of growth factors. Few syngeneic or allogeneic HC transplanted in suspension into tissues survived first hours after grafting. Destruction of locally implanted HC resembles scavenging phase of wound healing. HC are lysed by granulocytes and macrophages.

**Aim:** To protect tx HC by elimination of recipient scavenger and NK cells, stimulation of HC function by partial hepatectomy and bile duct ligation.

**Methods:** Recipients of HC were irradiated 8 Gy, anti-asialo GM1 antiserum on day 2, were reconstituted with 10^7 syngeneic BMC on day 3 and grafted with 10^7 of syngeneic HC into spleen. Forty percent hepatectomy was repeated after 2 and 4 months. Six months after tx specimens were evaluated. To identify collagen at site of implanted HC, the trichrome staining method was used.

**Results:** Successful 6-month survival HC was obtained. Glycogen-rich but albumin lacking hepatocytes were seen. HC formed regular trabeculae and bile canaliculi. Many HC have lost shape, became disfigured squeezed between fibroblasts. Trichrome revealed collagen deposits. No mononuclear infiltrates close to HC.

**Conclusions:** Attenuation of the innate response by elimination of scavenging and NK cells from spleen and stimulation of hepatocyte proliferation by hepatectomy and bile duct ligation resulted in protection of tx HC and formation of trabeculae and bile ducts. Fibroblast and collagen accumulated along HC but not in other parts of spleen. Presumably stellate cells transplanted with HC are responsible for fibrous tissue.
**EVALUATION OF THE INCIDENCE OF POST LIVER TRANSPLANT DIABETES MELLITUS AND ITS RISK FACTORS IN SHIRAZ TRANSPLANT CENTER**

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**Purpose:** Post transplant diabetes mellitus (PTDM) is a common complication after orthotopic liver transplantation (OLT). The influence of preexisting diabetes mellitus on outcome after OLT has not been well defined. In this study, we wanted to evaluate the prevalence and the risk factors of post transplant diabetes mellitus among liver transplanted patients.

**Methods:** In this study, we evaluated 80 liver transplanted patients in Shiraz Organ Transplant Center and divided them into 3 groups, group A with pre and post transplant DM, group B without pre and with post transplant DM and group C with pre and post transplant DM. The prevalence of diabetes mellitus was diagnosed with fasting blood sugar of more than 126 mg/dl in serum. Age, sex, blood group, source of organ and lab data were evaluated in all patients.

**Results:** Group A consisted of 14 (17.5%) cases, group B with 4 (5%) cases and group C with 62 (77.5%) cases. In group A, B and C respectively, mean age was 38.9±11.6, 25.5±13 and 32.2±12.6, the M/F ratio was 0.75, 3 and 2.26, the prevalent blood group was O, B, and O, source of organ was cadaveric. Viral and autoimmune hepatitis in group A and cryptogenic cirrhosis in group B and C were the most prevalent underlying diseases.

**Conclusion:** In conclusion, the prevalence of pre transplant diabetes mellitus and post transplant diabetes mellitus was 17.5% and 18.25%. The prevalence of patients with de novo diabetes mellitus was 5%. Among the evaluated risk factors the sex of group B and post transplant blood sugar were statistically significant.

**LIVING DONOR LIVER TRANSPLANTATION (LDLT) VS. MALIGNANT/BENIGN LIVER DISEASE (LD): A COMPARISON IN MORBIDITY AFTER RIGHT HEPATECTOMY**

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**Introduction:** The main priority in LDLT program is the donor’s safety. Nevertheless, the right hepatectomy is a procedure which comes along with certain associated morbidity as well as mortality.

**Aim:** To compare the morbidity-mortality associated with right hepatectomies in LDLT program with those performed for liver disease.

**Materials and Methods:** Prospective data from 41 donors in the LDLT program since March 2000 to September 2004 were compared with retrospective data taken from 41 patients in which a right hepatectomy was carried out for LD from February 1995 to October 2004. Demographic data, intraoperative variables, and postoperative liver function tests were assessed. The morbidity was analyzed according to the overall complications associated with the surgery as well as non-surgical complications.

**Results:** 17/30 were men and 24/11 were women in the LD/LDLT group respectively. Mean age was older in the LD group. There were no differences related to the need of blood transfusion, and hospital stay. Intraoperative blood loss was greater in the LD group (p < 0.05). The peak of transaminases was greater in the LDLT in spite of phosphatase alkaline and GGT which reached a superior level in LD group (p < 0.05). Platelet count and coagulation time raised up more quickly in LDLT patients. The incidence of overall complications, together with those related to surgery was less in the LDLT group (p < 0.05).

**Conclusion:** The incidence of postoperative complications after liver resection in the donor is similar to that observed after an elective major liver surgery.

**PORTAL BLOOD FLOW DIVERSION PRESERVE THE INTEGRITY OF NON-PARENCHYMAL CELL LINES AND DO NOT IMPAIR REGENERATION OF SMALL GRAFTS IN ADULT LIVING DONOR LIVER TRANSPLANTATION**

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**Introduction:** Excessive portal perfusion is one of the main factors leading to the small-for-size syndrome (SFSS). In this study we assess regeneration rates and structural integrity of small grafts with hemi-portocaval shunt (HPCS).

**Methods:** From June 2002 to November 2004, 10 out of 65 recipients underwent LDLT with small grafts and HPCs. The mean GRBW was of 0.7±0.1 (range 0.56-0.8). Mean recipient age was of 55±15 y. Donor graft CT volumetry was done before LDLT and at 1 and 6 m after. Serial biopsies were taken between 1 and 4 weeks post LDLT. Results were compared to a series of 5 small grafts transplanted without portal flow diversion. Semiquantitative analysis was done for HE, reticulin (RET), CD68 and smooth muscle actin (SMA) stainings and compared to biopsies taken from 5 other small grafts transplanted without HPCS.

**Results:** One- and six month post-transplantation graft volume/standard liver volume ratio of 80% and 101% in shunted grafts and 72% and 79.5% in non-shunted grafts (p < ns). Severe centrilobular cholestasis, sinusoidal disruption, Kupffer cells activation and transformation of Ito cells into myofibroblasts were observed in non-shunted grafts as compared to small grafts with HPCs showing moderate structural aggression. No SFSS occurred in shunted group of adult liver recipients.
**PO-730** SINGLE CENTRE EXPERIENCE IN ADULT-TO-ADULT LIVING DONOR LIVER TRANSPLANTATION: THE LEARNING CURVE EFFECT

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**Aim:** to evaluate the results of adult-to-adult living donor liver transplantation (AALDLT) after initial experience.

**Patients and methods:** From December 1998 to December 2004, 48 AALDLT were performed in 27 men and 21 women with a median age of 52.5 years (18-66). Main liver diseases were alcohol-induced (n=21) and viral-related (n=17). In 71% of the cases, patients were classified Child C and 39.6% had hepatocellular carcinoma. In 46 cases, the donor right liver without the middle hepatic vein was taken, whereas it was the full left lobe in 2 cases. The median graft-to-recipient weight ratio was 1.24 (0.74-1.99). The results of 2 periods from 1998 to 2001 (group 1, n=21) and from 2002 to 2004 (group 2, n=27) were compared.

**Results:** Overall 1, 2 and 3 year patient survivals were 93.7%, 89.6% and 85.4% respectively. Bilary complications, vascular complications (partial or complete thrombosis of the hepatic artery stenosis) and acute rejection episodes occurred in 18.7%, 10.4% and 16% of the cases respectively. One patient had retransplantation 1.5 year after LT for chronic graft dysfunction without vascular obstruction. When comparing groups 1 and 2, one and two year patient survivals were 90.5% versus 96.3% and 77.3% versus 96.3% respectively and biliary complications happened in 33.3% versus 7.4% of the cases.

**Conclusions:** AALDLT is very effective in adult recipients. Results dramatically improved after the first 20 cases.

**PO-731** BACTEREMIA IN EARLY PERIOD AFTER LIVER TRANSPLANTATION

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**Purpose:** An analysis of bacterial infections of blood in early posttransplant period.

**Materials and methods:** The study comprised the 83 patients after OLT (piggy back technique), between 2001 and 2004. All the patients were followed prospectively for blood infections from the day of OLT and in the first 4 weeks after operation. The immunsuppression consisted of steroids and tacrolimus. For substitution of FVIII the patient received a loading dose of 100 IE/kg Cogenate®, (Baxter) preoperatively and further boli of 50 IE/kg depending on dosage: 36.000 IE. On POD 3 FVIII activity reached 93% corresponding to normal FV and FVII activity.

**Results:** Blood cultures were examined in 59 recipients (71.1%) before operation and in 76 (91.6%) during 1 month after transplantation. In total 249 samples were investigated, 96 of them were positive. The bacterial strains were cultured from 19 recipients before OLT and from 48 patients after operation. Out of the bacterial strains, the most common were Gram-positive cocci (HLAR strains were detected). The Enterococcus spp. occured in 10 isolates (HLAR strains were cultured). The Enterobacteriaceae family - 16 and 15 isolates of Gram-negative nonfermenting rods were detected, some of Gram-negative rods were ESBL(+).

**Conclusions:** 1. The domination of Gram-positive cocci in blood infection is caused by antymicrobial prophylaxis which reduce Gram-negative bacterial strains 2. The MDR bacterial strains caused severe blood infections in liver transplant recipients.

**PO-732** INFLUENCE OF SELECTED FACTORS ON SURVIVAL AFTER ORTHOTOPIC LIVER TRANSPLANTATION

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**Aim:** to evaluate the results of adult-to-adult living donor liver transplantation (AALDLT) after initial experience.

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**Results:** Overall 1, 2 and 3 year patient survivals were 93.7%, 89.6% and 85.4% respectively. Bilary complications, vascular complications (partial or complete thrombosis of the hepatic artery stenosis) and acute rejection episodes occurred in 18.7%, 10.4% and 16% of the cases respectively. One patient had retransplantation 1.5 year after LT for chronic graft dysfunction without vascular obstruction. When comparing groups 1 and 2, one and two year patient survivals were 90.5% versus 96.3% and 77.3% versus 96.3% respectively and biliary complications happened in 33.3% versus 7.4% of the cases.

**Conclusions:** AALDLT is very effective in adult recipients. Results dramatically improved after the first 20 cases.

**PO-733** SUCCESSFUL LIVER TRANSPLANTATION IN A PATIENT WITH SEVERE HAEMOPHILIA A AND ANTI-THROMBOCYTE ANTIBODIES

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**Introduction:** HCV-related liver cirrhosis is a major problem in patients with haemophilia A. Liver transplantation can cure haemophilia but maybe challenging especially if combined with further coagulative disorders. We report on our experience with liver transplantation in a patient with combination of severe haemophilia A and anti-thrombocyte antibodies.

**Case report:** M.S. was a 53-year old man with haemophilia A (FVIII activity <1%) combined with thrombocytopenia and HCV-related liver cirrhosis Child C (MELD: 15)

He received a cadaveric liver graft from an 67-year old man.

The operative procedure remained uneventful with an operation time of 5:05 hours and ischemia time of 12:30 hours.

Immunosuppression consisted of a triple therapy with low dose corticosteroids, MMF and tacrolimus.

For substitution of FVIII the patient received a loading dose of 100 IE/kg Cogenenate®, (Baxter) preoperatively and further boli of 50 IE/kg depending on intraoperative plasma factor clotting measurements for 2 hours (cumulative dosage: 36.000 IE). On POD 3 FVIII activity reached 93% corresponding to normal FV and FVII activity.

The thrombocytopenia reached a minimal count of 3/11 on POD2. Diagnostic tests revealed HLA-antibodies against thrombocytes. After treatment with Pen- taglobin (Biotest) and transfusion of HLA-identical thrombocytes thrombocyte count increased to 40/11.

The postoperative course was prolonged due to the bad condition of the patient. He showed no signs of bleeding postoperatively and no surgical reinter- vention was necessary. There was no sign of graft dysfunction, rejection or infection at any time.

**Conclusion:** Liver transplantation in haemophilia can successfully be performed even if it is complicated by further coagulation disorders.

**PO-734** SEVERE ADENOVIRUS HEPATITIS IN ADULTS AFTER LIVER TRANSPLANTATION

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**Purpose:** Since only a few cases of adenohepatitis (AH) of the liver graft in adults have been described after liver transplantation (LT), we decided to investigate publications regarding this specific disease in LT recipient.

**Methods:** An electronic search of the Medline database (1987-2004) was performed to identify cases of AH after LT. The following search terms were used: “adenovirus”, “adenoviral”, “liver”,” hepatitis” and “transplantation” and various combinations. Initial diagnosis, treatment and outcome were analyzed. In addition one adult case was contributed by the authors.
Results: The search revealed 8 publications. An AH of the graft have been found in 2 adults and 29 children. The diagnosis was achieved in all cases by liver biopsy. In the 2 cases in adults a severe AH with fatal outcome was reported. In our adult patient with acute severe hepatitis 11 days after LT (bilirubin 165 mg/dl, ASAT 1767 UI, ALAT 2236 UI, prothrombin time: 40%), a conservative treatment with reduction of immunosuppression was successfully applied. On the other hand, the outcome of the 29 children with AH after LT varied widely: 11 (36%) were successfully treated with reduction of immunosuppression and in one child ribavirin was also given, 6 (20%) survived through re-transplantation and 13 (44%) died. To our knowledge the presented case is the first adult after LT who survived severe AH of the graft.

Conclusion: Only few data are available for the treatment of AH after LT. After diagnosis, reduction or stop of immunosuppression must be considered. However, since mortality rate is very high, in cases with persistent hepatitis an early re-transplantation should be recommended.

Table 1: Mean antibody titres, Viral load and Injury scores

| Baseline titres | HAI | Fibrosis | Total Injury | Antibody titre |
|----------------|-----|----------|--------------|----------------|
| All patients (n=42) | 5.24±1.93 | 1.19±1.50 | 6.43±3.18 | 31.56±7.96 |
| Patients not treated for HCV (n=13) | 5.17±0.76 | 1.00±1.00 | 6.17±1.61 | 28.34±10.74 |
| Anti-HCV treated patients (n=29) | 5.25±2.07 | 1.22±1.58 | 6.47±3.40 | 32.97±6.13 |
| Responders (n=10) | 4.92±2.42 | 0.92±1.20 | 5.83±3.24 | 34.17±4.51 |
| Not completed treatment (n=9) | 5.20±2.77 | 1.70±2.49 | 6.90±5.18 | 29.66±8.36 |
| Non-responders after 1 year of treatment (n=10) | 5.50±1.52 | 1.33±1.21 | 6.83±2.56 | 34.49±4.21 |

Correlation of viral load and hepatic injury with antibody titre is shown in figure.

Conclusion: HCV antibody titres do not correlate with viral load, hepatic injury or treatment.

PO-735 RELEVANCE OF HEPATITIS C VIRAL (HCV) ANTIBODY TITRE IN LIVER TRANSPLANT (LTX) PATIENTS
Ashok Jain, Marilyn Menegus, Ravi Mohanka, Mark Orloff, Peter Abt, Adel Bozorgzadeh. Surgery, University of Rochester, NY, USA.

Hepatic injury from HCV is due to host immune response.

Aim: Quantitative HCV antibody estimation in post LTx patients, correlation with viral load, hepatic injury and impact of anti-HCV treatment.

Patients and Method: 141 samples, from 42 LTx patients were analyzed for quantitative anti-HCV.

Results: Antibody titres, hepatic injury in all patient subgroups are shown in table.

PO-737 HEPATIC HYPERPLASIA INDUCED BY INCREASED PORTAL INFLOW
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Purpose: Increased portal vein inflow (PVF) in the recipients of a small liver graft is linked to the pathogenesis of post-transplant "small-for-size syndrome" (SFSS).

In this study, effects of high PVF on the liver were investigated using a rat model of portal arterialisation (PVA).

Materials and Methods: In 28 Lewis rats, high PVF was realised by interposing an artificial graft between the portal vesiculae portae and the portal vein. In the control group, only portal clamping was performed. Liver weight/body weight ratio (LW/BW%), hemodynamics, biochemistry, light and electron microscopy were assessed 1 hour postoperatively, and after 1, 2, 7 and 28 days.

Results: Through PVA, PVF was increased average 4.6 times (3.7±2.4 vs. 0.8±0.2 ml/min/g LW, preoperative; p = 0.01) with a reduction of hepatic artery inflow (HAF) (0.1±0.07 vs. 0.3±0.18 ml/min/g LW; p = 0.01), which persisted till the end of study. A transient elevation of serum alanine aminotransferase activity and total bilirubin concentration was more pronounced in the high-PVF group. No parenchymal necrosis or sinusoidal endothelium damage was detected. Only in the high-PVF group, numerous mitoses of hepatocytes were observed on day 2. On day 28, proliferation of interlobular bile ductules was evident (4.7±2.2 vs. 1.6±0.8 per portal space, control; p = 0.001) and LW/BW% was significantly higher than in the controls (4.4±0.5 vs. 3.3±0.2; p = 0.05).

Conclusion: These data demonstrate that increased PVF induces hepatocytes and bile duct hyperplasia, which does not lead to SFSS without reduction of liver mass.
A RETROSPECTIVE ANALYSIS OF FIRST 190 LIVER TRANSPLANTATIONS: A SINGLE-CENTER EXPERIENCE

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Purpose: Liver Transplantation has been done exclusively throughout Iran and some neighboring countries in our center for 11 years. Potential recipients from all over the country or neighboring countries are selected for the waiting list based on the established indications for liver transplantation.

Methods: The first 190 consecutive liver transplantations performed between April 14, 1999 and April 1, 2005, in Shiraz (Southern Iran) organ transplant center.

Results: Among 190 consecutive recipients M/F ratio was 1.8. Mean recipient age was 29.9±14.1 years. Mean cadaver age was 24.2±9.5 years. The operative procedure was performed in a standard manner using duct-to-duct anastomosis in 68% of the cases; piggyback technique was utilized in 90%, veno-venous bypass in the rest. Immunosuppressive regimen included Ciclosporine (Azathioprine for first 10 cases), cyclosporine and methylprednisolone. Major causes of liver failure included cryptogenic (36%), Wilson's disease (16%), and viral hepatitis (14%). Rejection occurred in 27% of cases once and 8% twice. Just one primary non-functioning graft occurred. Most common short-term complications included respiratory (12%), neurologic (10%) and biliary (10%). Long-term complications included rejection (9%), renal failure (6%) and death (16%).

Conclusion: It can be concluded that although young and at the beginning of the way, this only center in the country has done well and can be great source of hope for promotion of science and health.

FIRST 101 ORTHOTOPIC LIVER TRANSPLANTATIONS–SINGLE CENTER EXPERIENCE

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Since our liver transplant (LTx) program was established in July ‘2000, until December ‘2004 101 LTxs were performed in our department. The most common indications were: viral hepatitis (37.6%), AILD (18.8%), AILD (13.8%), acute Wilson’s disease (10.9%). HCC was diagnosed in 5 patients with HCV cirrhosis. In 98 patients the primary LTx was performed (3 re-LTx for late graft failure). Urgent transplantation was required in 18 (17.82%) patients. In 98 patients piggy-back technique was used (97%). The veno-venous by-pass was used once. Donor iliac by-pass graft was used to reconstitute arterial blood supply in 8 cases. Recipient portal thrombectomy was necessary 3 times. In 97 cases biliary anastomosis was performed by end-to-end technique with catheter drainage. All patients received jejunostomy enteral nutrition. Standard immunosuppression was: tacrolimus and steroids.

Results: In 7 cases poor initial function was noted. No case of PNF was ob- served. Acute graft rejection was treated with methylprednisolone 17 recipients (16.8%). Temporary deterioration of renal function was noted in 28 patients (27.72%), 4 of 28 required HD. Patients died in early postoperative period: sepsis (12), CV (4), multi-organ failure (1), irreversible hepatic coma - 1). Further 2 patients died accordingly and 4 and 13 months after transplantation (home acquired fungal sepitis - 1, metastatic HCC - 1). Seven patients required early re-operation: 3 for bleeding (G-1, pleen rupture - 1), diaphragma oozing - 1), one for bowel obstruction, one for CBD necrosis and 3 for biliar (following drain removal). One year graft survival in whole cohort was 91.08% (urgent transplantations - 70%; elective procedures 96%).

Conclusion: Learning curve problem can be omitted by the good international fellowship programs.

SIMULATE VS STEROIDS IN DE NOVO HCV+ LIVER TRANSPLANT PATIENTS: A RANDOMIZED TRIAL

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Liver transplantation in HCV+ recipients is associated with high rate of allograft failure: this negative outcome is probably correlated to HCV recurrence. A steroid-free regimen could potentially reduce the impact of HCV re-infection. The primary objective of this study was to compare the 12-month incidence of graft loss and death in de novo HCV+ liver transplant recipients given basiliximab or steroids.

Methods: Patients were randomized to basiliximab (20 mg iv day 0-4) or steroids (methylprednisolone 500 mg day 0, 125 mg day 1, 40 mg day 2; prednisone 25 mg days 3-30, 15 mg days 31-60, 5mg days 61-90). All of the patients had to take Neoral (C2 levels (ng/ml)): 500-900 day 3-4; 700-900 day 5 (5-month), 6; 500-700 months 7-12) and MMF 2 mg/day (four months). Multiple organ transplant, fulminant liver failure, HbsAg positivity and serum creatinine >160.0 mmol/l were the main exclusion criteria.

Results: 193 patients (73% males; mean age 53 ± 8.1) were enrolled in 11 Italian centers. The mean age of the donor was 51±18.9 years; 55.8% males. The mean cold ischemia time was eight hrs (1±2.6). Results from 6-month analysis on all patients will be available at the meeting.

MELD SCORE IN PATIENTS ACCEPTED FOR LIVER TRANSPLANTATION 1999 AND 2004

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Purpose: MELD (Model for End-Stage Liver Disease) score was developed as a tool in order to give a more objective estimate “of the degree” of sickness in patients with chronic liver disease. The aim of this study was to evaluate MELD scores in patients accepted for liver transplantation (Ltx) at our institution 1999 and 2004 and to analyze MELD score associated with different indications for Ltx.

Methods: MELD scores were calculated retrospectively in all adult patients (>18 years, n=102) accepted for Ltx 1999 and 2004. Auxiliary Ltx; multi visceral transplant and retransplantation within 6 month were excluded. MELD score was not used for organ allocation in any of the patients.

Results:
REPORT OF TWO ADULTS WITH CONGENITAL ABSENCE OF THE PORTAL VEIN AND THERAPEUTIC ORTOTOPIC LIVER TRANSPLANTATION

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There are two different types of Ahernehy Malformation: Type I or Congential Absence of the Portal Vein (CAPV) and type II with an existing shunt between portal vein and inferior vena cava (IVC). This rare congenital extrahepatic portocaval shunt is often associated with hepatic disease and extrahepatic abnormalities.

One 12 YOA male, with coincidental findings of two intrahepatic tumors post chest trauma. The patient developed hepatic encephalopathy 3 years later, with impaired liver function and an adenomatosis. OLT was performed. 3 yr F/U shows stable organ function.

Case II is about a 22 YOA, male, developed severe hepatic encephalopathy, liver biopsy findings showed hepatocellular Carcinoma. OLT was performed. At 1 year F/U, liver function is stable, with one steroid sensitive rejection episode.

Operations were uneventful in both cases. OLT was performed in standard technique. Diagnosis of CAPV was confirmed. There were no signs of portal hypertension, neither did we experience any cardiovascular side effects during reperfusion. Splanchnic congestion was not observed during implantation. Outcome and prognosis depend on overall findings and associated congenital defects. Concluding, CAPV is a rare congenital malformation that is frequently associated with liver tumors and/or cardiovascular abnormalities. We did not experience any of the reported complications. Alternative treatment methods are available to delay an operation, but OLT is the definitive treatment option.

CHANGEOFBLOODFLOWOFTRANSPLANTEDLIVERFROMOPERATIONTOTHEREPERFUSIONDAY

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Short-term changes in splanchnic hemodynamics after liver transplantation is still under debate. In the present report, we analyzed Doppler flow parameters of the transplanted liver from intraoperative period to first postoperative day. 20 recipients (nine female, seventeen male) were included in the study. 20 recipients received living related partial liver transplants and six recipients received cadaveric liver. Values of peak systolic velocities, portal vein and hepatic vein flow velocities and resistive indices from hepatic artery, flow volume of hepatic artery and portal vein measured intraoperatively were compared with values obtained first postoperative day. Student t-test was used for statistical analysis. There were no statistically significant difference between velocities of hepatic arteries, portal vein and hepatic veins. Hepatic resistive indices decreased on the first postoperative day (0.79±0.08 vs 0.71±0.01, p=0.01). Comparing flow volume of portal vein (PBV), the 14 patients intraoperative with early postoperative period, PBV was increased (1.06±0.85 vs 2.34±1.35, p=0.006). Flow volume of hepatic artery in 16 patients was similar (0.12±0.10 vs 0.16±0.18, p=0.48).

In conclusion, hepatic resistive indices tended to decrease while flow volume of portal vein increased in the first postoperative day compared to intraoperative values in the transplanted livers. This implies inoperative high resistance of liver parenchyma and low portal flow should not mislead the surgeon to consider early vascular complications, these findings will return to normal levels in 12-24 hours after the surgery.

A COMPARISONOFMODELSFORASSESSINGDONORLIVERSTEATOSIS:ASSSESSMENTBYMACROSCOPICAPPEARANCE,HISTOLOGICALANDCOMPUTER-IMAGE ANALYSIS

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Aims: Macrovesicular steatosis in the donor liver can result in graft dysfunction. Assessment of steatosis in the UK is based on macroscopic appearances reported by retrieving surgeons. This study was designed to validate, using computer image-analysis, a simple histological grading system for use in the assessment of steatosis.

Methods: Cadaveric livers retrieved between January 2001 and March 2002 were included (N=44). Trainee and consultant surgeons scored livers macroscopically for steatosis [score 0-5] pre- and post-perfusion. Biopsies taken prior to perfusion were stained with haematoxylin and eosin and graded histologically: by histopathologist [grade 0-5] and by computer image-analysis system [Lucia2] to quantify percentage fat by area [%fat], and percentage fat by number [%fat] of involved hepatocytes [%index]. The identification and reproducibility of the histological grades amongst transplant surgeons was also assessed using pictoral representations.

Analysis was undertaken blind to other assigned scores. Spearman rank correlation (S) and Pearson correlation (P) coefficients were calculated.

Results: The positive predictive value of macroscopic assessment versus histological diagnosis of steatosis was very poor [0.275].

Positive correlation [0.043] between histopathologist and image-analysis [0.761 (P)] and between image-analysis scores of [%fat] and [%index] [0.941 (P)].

Histology grades 0-5 corresponded to computer quantification of 2.4-10.18,26 and 0.17 when values were obtained for absolute [%fat].

Using these grades, pictoral assessment by transplant surgeons correlated positively with assessment by histopathologist [0.573 (S) (P<0.05)].

Conclusion: Macroscopic appearances are inaccurate in predicting donor liver steatosis. A simple, reproducible, histological system, that has been validated by computer image-analysis, can be applied to improve pre-transplant assessment.

A NEW SURGICAL MODEL OF HEPATECTOMY IN PIGS

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Introduction: Animal models are suitable to simulate acute liver failure. The established surgical methods for hepatectomy in pigs using en-bloc resection of the vena cava require a temporary extracorporeal bypass and total clamping of the inferior vena cava. These steps lead to severe depression of splanchnic congestion and activation of the coagulation system. Therefore postoperative survival and overall survival is impaired.

Methods: En-bloc hepatectomy including retrohepatic vena cava was performed in twenty female pigs (30-41kg). Using end-to-side anastomosis between the vena cava below the right renal vein, the portal vein above the confluence, and the infraduric venar cava with a three-way vascular prosthesis, blood flow maintained constantly stable during hepatectomy by performing only partial clamping of the vessels. After completion and release of the bypass a gentle hepatectomy with minimal blood loss was performed.

Results: Using this new surgical technique makes it possible to avoid a total clamping of the mayor vena cava. Therefore minimal intraperitoneal vascular hemodynamic stability can be reached. During operation measured hemodynamic parameters like heart rate, mean arterial pressure, central venous pressure, SO2 oximetry stayed extremely stable. Postoperative survival time was 100% after 12 hours, 95% after 24 hours. Maximum survival was 88.5 hours; mean survival was 50 hours. All animals died because of multiple organ failure, particularly lungs and kidneys were affected.

Conclusion: This new surgical technique permits a total hepatectomy with minimal blood loss and stable circulation without using an extracorporeal bypass. Relevant venous obstruction is also avoided. The liable organism of pigs is less stressed, which could be shown in better postoperative outcome and overall survival time.

POST LIVER TRANSPLANT CONTROL OF PRE-EXISTING CARDIO-VASCULAR RISK FACTORS: A COMPARISON BETWEEN PATIENTS RECEIVING CYCLOSPORINE MICROEMULSION OR TACROLIMUS

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New onset diabetes mellitus, hypertension and hyperlipidemia post transplant have been studied but the impact of transplant and immunosuppression on these conditions when pre-existing is not well characterized.

Methods: We therefore analysed the need for treatment of diabetes, hypertension or hyperlipidemia at one year post liver transplant in patients who presented with type 2 diabetes mellitus, hypertension or hyperlipidemia at the time of transplant and were on a combination of glucocorticoids and tacrolimus (CsA-ME) or CsA-ME or CsA-ME with either insulin or antihypertensives or statins.

Conclusions: While immunosuppression will continue to play a role in the control of diabetes mellitus, hypertension and hyperlipidemia post transplant, these data suggest the use of cyclosporine microemulsion may be associated with less frequent treatment of diabetes mellitus, hypertension and hyperlipidemia post transplant.

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**Results:** In both arms, out of the patients with pre-transplant diabetes, 4% had type 1 diabetes and overall 40% were treated at baseline (insulin 37%, oral treatment 3%). At 1 year, significantly more patients receiving tac received acute rejection compared to those receiving CsA (p=0.02). Conclusion: Excellent Results of adult RSLT are achieved when donor and recipient selection are appropriate regardless the preservation or not of the MHV.

**PO-748 RIGHT SPLIT LIVER TRANSPLANTATION (RSLT) FOR ADULTS WITH OR WITHOUT MIDDLE HEPATIC VEIN (MHV)**

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**Aims:** To evaluate results of RSLT for adults according to the type of venous drainage. Patients and Methods: From February 1998 to Jan-2004, 26 patients received 27 cadaveric RSLT. G1=13 received segment-IV-VIII with RHV. G2=13 received segment-IV-VIII with RHV+MHV. All livers were split ex-situ. Donors were 21 males and 6 females with a mean age of 26.4±6.7 years. Bilio-vascular distributions were assessed by careful dissection and back-table arteriography and cholangiography. Section of the liver was performed with harmonic scalpel, hemostasis and biliostasis was completed with running sutures on cut surfaces.

**Results:** Between the 2 groups, there were no significant differences in terms of patients demographics, liver diseases and donor data. Graft-to-recipient-weight-ratio (%) were G1=1.2±1.3, G2=1.6±3.3, CTT (hr:min) G1=10.5±2.49, G2=10.47±3.3. Piggyback was done in G1=11 with 5 associated inferior-RHV anastomosis. Recipient IVC resection was done in G1=2, G2=13. No operative mortality occurred, but 1 post-operatively in each group. There were 2 PV, 1 HA, 1 RHV anastomotic stenosis in G1, successfully treated by radiological intervention. Biliary leak occurred in D-D anastomosis without T-tube (G1=11, G2=21), 1 had late stenosis of right-hepatic duct. Post-transplant renal failure occurred in G1=3, G2=9 requiring VVHf in G1=2, G2=3. The only post-operative statistically significant differences between both group was recorded for bilirubin (p=0.0035). 13-year survival were 92% for both groups. Graft survival were G1=92%, G2=86%. None of the variables were identified as independent explanatory factor for graft or patient survival including the type of venous-outflow.

**Conclusion:** Excellent Results of adult RSLT are achieved when donor and recipient selection are appropriate regardless the preservation or not of the MHV.

**PO-749 LIVING-RELATED LIVER TRANSPLANTATION FOR CHILDREN WITHFULMINANT LIVER FAILURE**

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**Purpose:** Supportive treatment,artificial liver support systems have limited therapeutic value in patients with fulminant liver failure(LFL).Living related liver transplantation(LRLT) is salvage therapy for the LFL.

**Methods:** We investigated children with LFL who underwent LRTL between 2002-5.

**Results:** Six(4 M) children diagnosed with LFL with a median age of 11 years(18 m-17 y) underwent LRTL. Etiological distribution was hepatitis A=2, hepatitis B=1, hepatitis C=1, cirrhosis due to Schistosomiasis=1, Wilson’s disease=1, Miliary tuberculosis=1. Median interval from onset of jaundice to encephalopathy was 14 days(5-60). Encephalopathy grades at presentation were grade IV(2/pts), grade III(2/pts), grade II(2 pts). Patients stayed in pediatric ICU for 1 to 20 days(mean 3.5). Plasmapheresis was performed 1-8 sessions per case(mean 4) for all pts with grade III,IV encephalopathy until the living-donor work-up was completed. On admission serum total bilirubin,NH3 levels were 8.6-70 mg/dl(mean 28),22-250 micromol/L(median 62),respectively.InN Lar levels were 2.9-9. The day of LRLT serum total bilirubin and NH3 levels were 8.5-56 mg/dl(mean 25) and 60-160 micromol/L(median 94),INR was 1.6-8(mean 2.1). PELD scores on admission and day of LRTL were 22-53(median 40) and 4-52(median 21) respectively.4 fathers, a mother,an uncle were the donors. All hepatocarcinoma specimens demonstrated massive necrosis 2 patients(33%) died after 2,2.5 months of LRTL with ARDS,sepsis,4 patients were alive(10days-3y) without any problem.

**Conclusion:** Patients should be monitored closely. If individual’s clinical picture continues to worsen rapidly despite aggressive supportive treatment and if there is suitable living donor,transplantation should be performed as soon as possible. Prompt action is essential and it just takes 4-6 hours to biopsy the donor organ and make all necessary preparations under emergency conditions.

**PO-750 DOPPLER ULTRASONOGRAPHY FINDINGS DURING ACUTE REJECTION IN TRANSPLANTED LIVER**

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**The aim of this study was to assess the value of Doppler ultrasound (DUS) in liver transplant recipients with acute rejection episodes.** 21 patients having acute rejection were included in this study. 17 recipients received living related liver transplants and 4 recipients had cadaveric liver. Thirty-four acute rejection episodes in 21 patients were observed 6 to 3600 days (mean 288 days) after transplantation. DUS was ordered because of the abnormal liver function tests. Another DUS findings of the patients while they have normal liver function were also reviewed for comparison. Biopsy specimens were assigned scores according to Banff method, and rejection activity index (RAI) was calculated. Doppler US parameters were analyzed as absolute values and as mean values changes with respect to values obtained examination before or after rejection was suspected. Paired t-test was used for statistical analysis. Hepatic vein flow velocity was decreased during rejection episodes compare to in patients with normal liver functions (32.5±13.68 vs 40.48±18.89, p=0.036). The other flow parameters were not significantly different in patients with rejection episodes and without clinically relevant rejection. In conclusion, hepatic vein flow velocity decrease during acute rejection episodes. This information is useful in the identification of patients with acute rejection by Doppler US. A marked decrease in hepatic vein flow velocity during follow-up may point an acute rejection episode.

**PO-751 RECURRENCE OF HEPATITIS C VIRUS IS MORE SEVERE IN LIVER TRANSPLANT RECIPIENTS INFECTED THAN IN HCV MONO-INFECTED PATIENTS**

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We compare in a single center, the survival and the severity after LT of HCV recurrence in HIV co-infected and HCV mono-infected consecutive patients. 99 patients (76 M) receiving a first liver graft for HCV liver disease (37 HCC) between 1998 and 2004 were included. Among them, 23 were HIV positive, had HAART-controlled HIV and more than 150 CD4 cells/mm3. Post LT liver biopsies were available in all patients with more than 6-months of survival and during the second year in 55 patients. Co-infected were younger than mono-infected patients (41±8 vs 55±8; p=0.001) and received more dominos (10/23 (43%) vs 17/76 (22%); p=0.01) or livers from living donors (5/23 (21%) vs 11/76 (14%); p=0.02). LT in HIV-HCV co-infected patients is a legitimate indication. However, recurrence of hepatitis C is more severe. Avoidance of drug toxicity, prolonged anti-HCV therapies are mandatory to improve long-term results.
INFLUENCE OF ARTERIALIZATION OF PORTAL BLOOD ON THE REGENERATION OF LIVER AFTER AN ACUTE DAMAGE WITH CARBON TETRACHLORIDE

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The aim of the study is to analyze the influence of portal blood arterialization on the regeneration of liver after an acute damage with carbon tetrachloride.

Materials and methods: 35 pigs (of 25-32 kilos in weight) were divided into 4 groups: 3 studied groups (of 10 animals each) and a control group (5 animals).

The examined animals were administered intraarterial injections of carbon tetrachloride in corn oil solution in doses of 477 mg/kg of body weight to induce an acute hepatic failure. The animals underwent a surgical treatment on the third day after intoxication. In two groups of animals splenic vein was anastomosed with aorta: in group I without splenectomy while in group II with splenectomy. Group III was subjected to splenectomy. The control group I underwent laparotomy only. Surviving animals were reoperated on the tenth day after intoxication. Histopathologic evaluation was based on specimens stained with hematoxylin and eosin, and on the immunohistochemical analysis of regenerative hepatocytes by applying monoclonal serum for CK19[19;CK19];CD56[RTU-CD56-1B6], and CD117[NCL-CD117] (Novocastra). Antigens were assayed using three-level ABC method.

Results: In the first, second, and third group survived 7, 8, and 2 animals, respectively. Parenchyma regeneration was noted mainly in the central zone of hepatic lobules, where small stem cells were observed, which focally possessed expression for CD 56 and CD117 antigens, having no receptor for CK19.

Conclusions: Arterialization of portal blood after an acute liver damage with carbon tetrachloride induces the regeneration of parenchyma through coloization of damaged central zones of hepatic lobules by stem cells of hepatoblast phenotype.

ONE THOUSAND LIVER TRANSPLANTS IN TURIN: REPORT OF A SINGLE-CENTER EXPERIENCE IN ITALY

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Purpose: To report the largest single-center experience of liver transplantation in Italy gathered over a 12-year period. Indications, techniques and results of the procedure were reviewed in order to highlight the major improvements in peri- and postoperative care that have occurred over time.

Methods: From 1990 to 2002, 1000 consecutive liver transplants were performed in 910 patients, mainly cirrhotics. Surgical technique was based on the preservation of the inferior vena cava of the recipient without veno-venous bypass use. Median follow-up of the patients was 41 months (range 1-155).

Results: Overall patient survival rates at 1, 5, and 10 years after LT were 87%, 78% and 72%, respectively. Operating time, warm ischemia time and length of hospital stay significantly decreased over the years, while operating room extravasation became a routine event. Management of retransplantations, marginal grafts, and of HCV-positive, HBV-positive and hepatocellular carcinoma recipients were optimized.

Conclusion: Increasing experience in liver transplantation surgery and postoperative care allowed standardization of the procedure with consistently good results. Avoidance of veno-venous bypass use and routine operating room extravasation paralleled to the expansion of the transplant activity. Organ shortage still mandates use of marginal grafts and implementation of advanced transplant programs like split liver and living donor.

ADVERSE CLINICAL AND ECONOMIC OUTCOMES ASSOCIATED WITH SURGICAL SITE INFECTION AFTER LIVER TRANSPLANTATION

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Purpose: Surgical site infections (SSI) in non-transplant populations are associated with significant morbidity, mortality and increased cost of care. Success of measures to prevent and treat SSI has been assessed by measurement of the frequency of SSI and of the impact of SSI on outcomes. Despite the recognition of the relative importance of SSI after liver transplantation (LT), the frequency of SSI after LT and the adverse outcomes associated with SSI after LT have not been assessed using standardized surveillance methods.

Methods: SSI after first LT in the years 2003 and 2004 were identified using the definitions and methodology of the Center for Disease Control's National Nosocomial Infections Surveillance System. Cox proportional hazards models with time-varying covariates were used to estimate the risk of mortality and graft loss after onset of SSI through March 2005. Costs for medical care from day 0 to day 60 after LT were collected and assessed.

Results: 62 (16%) of 378 patients developed SSI after first LT. Relative risks of death and graft loss after development of SSI were 2.83 (95% CI: 1.22-6.76) and 3.81 (95% CI: 2.04-7.12) respectively. Median cost of care after LT for those who survived this interval without retransplantation was higher for patients who developed SSI ($173,303 vs $140,692, p=0.039).

Conclusion: SSI increased the risk of death, the risk of graft loss, and the cost of care after LT. Standardization of surveillance of SSI at centers of LT would assist assessment of measures taken to prevent SSI and to mitigate their adverse impact upon clinical and economic outcomes.

SAFETY OF DONOR RIGHT HEPATECTOMY FOR ADULT-TO-ADULT LIVING DONOR LIVER TRANSPLANTATION

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(Purpose) The purpose of this study is to evaluate the safety of donor right heptectomy, comparing with that of donor left heptectomy.

(Patients and Methods) Fifty-four donors who underwent donor heptectomy for adult-to-adult LT at our hospital by a single team were included in the study. There were 32 men and 22 women, with the median age of 30 years (range, 18 to 61 years). The donors were divided into two groups according to the type of harvested graft: left lobe (Segment 2+3+4) (group L; n = 11), right lobe (Segment 5+6+7+8) without middle hepatic vein (Group R; n = 43).

(Results) Median remnant liver volumes were 62.6% (49.6-75.7%) in L group and 41.8% (28.9-51.9%) in R group. The median operation time and blood loss were 469 min and 310 ml in group L, 440 min and 330 ml in group R, respectively. No donors received homologous blood transfusion. Three of the 54 donors (5.6%) had 4 postoperative complications including bile leakage with necessity of endoscopic therapy, postoperative bleeding following the formation of hematomata with necessity of reoperation, and peptic ulcer, pleural effusion in one each donor. There was no donor death. Although all these complications occurred in R group, there was no significant difference in the morbidity between the two groups (0% vs. 7%). Median postoperative hospital stays were 16 days in L group and 15 days in R group. (Conclusions) Regardless of the extent of donor heptectomy, the procedures can be performed safely with minimal morbidity.

SAVING FATTY LIVERS FOR TRANSPLANTATION: A NOVEL MODEL FOR CREATING AND REVERSING NON-ALCOHOLIC FATTY LIVER DISEASE USING AN ISOLATED PERFUSION CIRCUIT

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The use of livers for transplantation is limited by the shortage of organs. Attempts to overcome this problem include the use of marginal organs. Fatty livers have been associated with alcohol. Recently non-alcoholic fatty liver is acquiring epidemic proportions. Its association with obesity, diabetes and hyperlipidaemia has generated great interest. There has been an interest in developing a fatty liver model in large animals. To date, this has only been achieved in rodents and small animals. Combining some events which lead to developing steatosis in the non-alcoholic fatty liver syndrome we have validated a porcine model of steatosis.

Material and Methods: A permanent diabetic state was achieved in White Landrace pigs weighing 30-40 kg by administration of streptozotocin. For a period of three weeks the animals were fed with a high fat diet. Liver biopsies were taken prior to administration of streptozotocin and weekly thereafter for three weeks. Specimens were stained with haematoxylin-eosin for assessment of morphology and Oil-Red O, which stains lipids.

Results: A diabetic state was achieved within 24 hours of streptozotocin administration for a period of three weeks the animals were fed with a high fat diet.

Liver biopsies were taken prior to administration of streptozotocin and weekly thereafter for three weeks. Specimens were stained with haematoxylin-eosin for assessment of morphology and Oil-Red O, which stains lipids.

Conclusion: A porcine model of liver steatosis can be achieved by inducing diabetes in a porcine model. This model by measuring weight loss during the first 60 days after LT for those who survived this interval without retransplantation was higher for patients who developed SSI ($173,303 vs $140,692, p=0.039).

Conclusion: SSI increased the risk of death, the risk of graft loss, and the cost of care after LT. Standardization of surveillance of SSI at centers of LT would assist assessment of measures taken to prevent SSI and to mitigate their adverse impact upon clinical and economic outcomes.
LIVING DONOR LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA PATIENTS

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**Aim:** To evaluate the outcome of living-donor liver transplantation (LDLT) for hepatocellular carcinoma (HCC) patients.

**Methods:** Until the end of March in 2005, 59 adult patients underwent LDLT at our institution. Of them, 21 received the procedure for HCC (mean age 54 years, male/female 16/3, hepatitis B/hepatitis C 8/13, Child-Pugh A/B/C 2/6/13, preoperative TNM stage I/II/III 4/7/82, including incidental HCCs in 3). Mean MELD score before LDLT was 14.9 (range: 3.1 - 35.2). Seven of 21 HCC patients underwent LDLT for recurrent HCCs after partial hepatectomies. Patients who and did not meet Milan criteria were 13 and 8, respectively.

Transplanted grafts were a right lobe (Segment 5+6+7+8) in 20 and left lobe (Segment 2+3+4) in 1.

**Results:** HCC recurrences occurred in 2 patients (portal venous dissemination in one, bone metastasis in one) within one year after LDLT. The causes of death included sepsis in two, chronic rejection, and progressive cancer recurrence in one each. Three-year survival and disease-free survival are 78.8% and 72.2%, respectively. When the Milan criteria applied, both 2-year survival and disease-free survival in patients who met Milan criteria were 82.5%, whereas, in those who did not meet were 71.4% and 53.6%, respectively.

**Conclusion:** LDLT is an ultimate treatment for HCC and can be accepted with acceptable survival in HCC patients who met Milan criteria. Moreover, our result indicated that LDLT might be able to rescue the selected patients with advanced HCC.

OUTFLOW RECONSTRUCTION IN LIVING DONOR LIVER TRANSPLANTATION

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**Purpose:** Hepatic venous reconstruction is the key procedure in living donor liver transplantation (LDLT). We describe our experience and analyze the results of outflow reconstruction in LDLT.

**Patients and Methods:** 195 patients underwent LDLT from June 1994-2004. There were 115 pediatric and 80 adult recipients. 1 patient received dual graft and was excluded. In 112 left lobe LDLT, 105 underwent venoplasty of right, middle and left hepatic veins; and 7 underwent venoplasty of middle and left hepatic veins only. In right lobe LDLT, middle hepatic vein (MHV) was routinely harvested with graft when donor-recipient body weight ratio is ≤ 50%. Right and left lobe graft-recipient standard liver volume ratio (RLRSLV) ≤ 50% is widely presumed: However, it has not been proven as yet. We prospectively analyzed glucose metabolism in recipients of living-donor liver transplants (LD-LTX) and compared our findings to those in healthy donors.

**Result:** 28 patients received right lobe grafts with reconstruction of MHV tributaries by interposition grafts. Patency rate of venous interposition grafts was 75%. 8 cases of RLRSLV ≤ 50% received right lobe grafts without MHV, 1 developed small-for-size syndrome, 6 developed hepatic vein stenoses (1-right lobe, 5-left lobe) and were managed by interventional radiological procedures (2-stenting, 4-balloon dilations).

**Conclusion:** Single, large outflow reconstruction without graft malposition is ideal in left lobe LDLT by recipient triple venoplasty and graft venoplasty. In right lobe LDLT, MHV reconstruction is recommended in recipients with RLRSLV ≤ 50%, and whose donor remnant liver is estimated to be ≥ 35%.

PO-759 CLINICAL IMPACT OF HEMODYNAMIC CHANGES FOLLOWING LIVING DONOR LIVER TRANSPLANTATION

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**Introduction:** Living donor liver transplantation (LDLT) in adults results in unique hemodynamic patterns characterized by portal venous hyperperfusion due to reduced total vascular sectional area of the segmental graft when compared to that of the removed recipient’s organ. So far unknown is whether this finding influences clinical outcome of the recipient. The present study shows hemodynamic data collected by means of doppler ultrasound in comparison to complications following adult LDLT.

**Methods:** 18 recipients of segmental liver grafts underwent three subsequent ultrasound examinations each within the first 72 hours after transplantation. Sonografic measurements were exerted using a HDI 5000 system (Advanced Technologies Laboratories, United States). All grafts were right liver lobes, consisting in segments V, VI, VII and VIII. All of them had one right hepatic artery and one right portal venous branch. The donor livers had been examined pre-operatively focussing the branches of portal vein and hepatic artery supplying the right lobe.

**Results:** Living donor liver grafts profoundly change their main hemodynamic patterns postoperatively within the first 72 hours following the transplantation. Each graft showed a significant portal hyperperfusion when compared to pretransplant findings (mean 1309 vs. 477 mL/min, p<0.001). One patient developed hepatic artery thrombosis leading to successful urgent retransplantation, and one suffered from severe and eventually lethal upper gastrointestinal bleeding concomitant with ascitis and renal insufficiency. Both did not show overwhelming portal hyperperfusion in the initial postoperative score when compared to pretransplant findings (mean 672 vs. 423 mL/min).

**Conclusion:** Portal hyperperfusion does not inevitably lead to clinical complications resembling those in case of portal hypertension. Other factors contribute to hemodynamic patterns which eventually lead to graft loss or lethal complications.

PO-761 GLUCOSE METABOLISM IN LIVING-DONOR LIVER TRANSPLANTATION (LD-LTX): MAJOR INFLUENCE OF LIVER FUNCTION ITSELF BUT NOT OF IMMUNOSUPPRESSION

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**Introduction:** Immune surveillance of glucose metabolism is widely presumed. However, it has not been proven as yet. We prospectively analyzed glucose metabolism in recipients of living-donor liver transplants (LD-LTX) and compared our findings to those in healthy donors.

**Methods:** Recipients and donors without overt diabetes mellitus were investigated longitudinally before and on day 10, month 6 and month 12 after LDLTX. Insulin sensitivity (SI) was assessed by analysis of a frequently sampled intravenous glucose tolerance test with 300 mg/kg BW glucose 50%. β-cell responsiveness (first and second phase of β-cell secretion, Phi 1 and Phi 2) was determined by a c-peptide modeling analysis (SAAM II software). Initial immunosuppression in all recipients consisted of tacrolimus and prednisolone with basiliximab induction.

**Result:** Blood glucose at 260 min was significantly reduced (Δ-47%, p<0.01). One patient developed insulin resistance by day 10 (SI 2.65 ± 0.41 10^-4 µU/milliliter vs. 4.90 ± 0.50 10^-4 µU/milliliter in control, n=18, p<0.01) which was normalized again by month 6 and 12. In contrast to healthy donors, recipients were insulin resistant pretransplantation (mean 0.36 10^-4 ± 0.28 µU/milliliter vs. 0.41 10^-4 ± 0.01 µU/milliliter, n=18, p<0.01). After transplantation glucose tolerance normalized completely equally to donors during a 1 year follow up. SI showed a clear interaction with parameters of liver function and injury.

**Discussion:** Liver transplantation of the right lobe normalizes impaired glucose metabolism in cirrhosis independent from the original disease. Immuno-
suppression did not influence glucose tolerance. Liver function itself has a major influence on glucose tolerance which is more pronounced than known until now.

**POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE (PTLD) IN OLT PATIENTS IN UNIVERSITY HOSPITAL “MERKUR” ZAGREB**

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 PTLD is associated with EBV and CMV infection in SOT (solid organ transplantation)

In University Hospital " Merkur" Zagreb 108 liver transplants have been performed. Two patients developed PTLD. The first was 54 years old men transplanted for HCV RNA cirrhosis Child C. 4 months after OLT he was CMV DNA positive and received ganciclovir 2x5mg/kg twice daily 14 days i.v. and 3x1 gr peroral for daily 3 months. EBV DNA was negative. NHL- B cell lymphoma in abdominal lymph nodes was diagnosed and he received rituximab, but died within 2 months because of NHL progression. The other pt 56 old men was transplanted for alcoholic cirrhosis. 6 months after OLT CMC DNA was positive and the same schedule of ganciclovir was applied. EBV DNA was negative. NHL- B cell lymphoma in liver graft and abdominal lymph nodes was diagnosed. He underwent rituximab and CHOP chemotherapy and is still alive.

Conclusion:The risk of PTLD during the first year post-transplant in EBV positive but CMV positive patients is higher even the therapy with ganciclovir was provided.

**THE IMPACT OF PREOPERATIVE TCRγδ T CELL SUBSETS ON REJECTION AFTER LIVING-DONOR LIVER TRANSPLANTATION (LDLT) FOR HCV PATIENTS**

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Cellular immunity plays an important role in the persistent HCV infection and liver injuries. The etiology of HCV was strongly associated with early acute rejection(EAR).

Results: HCV patients with low percentage and absolute number of Vγδ T cells were more prone to EAR. We hypothesized that preoperative alterations in PBMC may predict EAR in HCV recipients.

Method: 18 HCV (f/m=6/11, 53.8±4.5y) and 17 non-HCV (f/m=8/9, 41.5±11.8y) LDLT recipients were enrolled. PBMC populations were analyzed preoperatively using flow cytometer. EAR was defined as rejection within 3 months post-LDLT.

Results: HCV patients with low percentage and absolute number of Vγδ T cells were more prone to EAR. We hypothesized that preoperative alterations in PBMC may predict EAR in HCV recipients.

Method: 18 HCV (f/m=6/11, 53.8±4.5y) and 17 non-HCV (f/m=8/9, 41.5±11.8y) LDLT recipients were enrolled. PBMC populations were analyzed preoperatively using flow cytometer. EAR was defined as rejection within 3 months post-LDLT.

Conclusions: Preoperative alterations in PBMC may predict EAR in HCV recipients.

**RELATIONSHIP BETWEEN CYP2E1 GENE POLYMORPHISM AND ALCOHOLIC LIVER DISEASES**

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Genetic variations of ethanol-metabolizing enzymes can affect alcohol drinking behavior. The aim of this study was to investigate genetic polymorphism of CYP2E1 in alcoholic liver diseases and evaluation of association between this polymorphism and alcoholism. 59 patients were admitted to this study: 57 with alcoholic liver cirrhosis and 54 nondrinkers as a control group. Genotypes of CYP2E1 were identified by PCR and RELP methods using PstI and Rsal as the restriction endonucleases. Genomic DNA was extracted from peripheral leukocytes. We investigated the frequency of c1 and c2 allele occurring in these two groups. In all nondrinkers only the c1allele was observed. All patients of control group were homozygotic c1/c1 frequency of c2 allele in alcoholic liver cirrhosis group was 3.5%, and was higher than in the control group. In any patients were found homozygotic c2/c2, four of them were heterozygotic c1/c2. These results suggest that the allele c2 frequency is very low in Polish population may be a risk factor for the developing alcoholic liver diseases.
forming Growth Factor alpha (TGF-α) and of Vascular Endothelial Growth Fac-
tor (VEGF) were well described in the context of hypertrophy and regeneration after
liver resection, but not yet known in the transplantation situation.
In 63 consecutive liver recipients (graft survival > 2 weeks) the factors HGF, TGF-α, and VEGF were determined. An ELISA in the serum and correlated to graft survival (Kaplan-Meier). The medium concentrations of HGF were constant in total during the observa-
tion period (day 1: 259 pg/ml, day 7: 234 pg/ml, day 14: 2490 pg/ml). An individual increase to levels above 4000 pg/ml in the middle of the observation period correlated to a significantly decreased one-year graft survival (54% vs.
85%). Similar was the course of TGF-α. An increase from the median concentra-
tion of 39 pg/ml to levels above 80 pg/ml was observed in the context of
decreased primary function. Regarding VEGF an almost linear increase of the median concentration from 60 pg/ml via 177 pg/ml to 424 pg/ml (day 1, 7, 14) was observed. Here it
became obvious, that an extensive increase of the VEGF concentration corre-
lated to a good transplant function. Under the premise that the systemically determined concentrations were in
relevant correlation to the secretion and the local concentration in the liver, it
can be concluded that vascular regeneration induced by VEGF substantially
contributes to graft survival, whereas an temporal increase of HGF and TGF-α
rather has to be interpreted as an indicator of an injured graft with a decreased
functional prognosis.

**PO-767 ALCOLOH DEHYDROGENASE 3 GENE POLYMORPHISM
AND ALCOHOLIC LIVER DISEASES**

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Alcohol abuse is being regarded as the main cause of liver cirrhosis. The aim of this study was to investigate genetic polymorphism of alcohol dehy-
drogenase 3 (ADH3) in alcoholic liver diseases and evaluation of association
between this polymorphism and alcoholism.

59 patients were admitted to this study: 57 with alcoholic liver cirrhosis and 54
nondrinkers as a control group. Genotypes of ADH3 were identified by PCR
and RFLP methods using StuI and as restriction endonucleases. Genomic
DNA was extracted from peripheral leukocytes. We investigate the frequency of
ADH3*1 and ADH3*2 allele occurring in these two groups.

Frequency of ADH3*1 allele in alcoholic liver cirrhosis group was 62.3%,
and was significantly higher than in the control group (χ²=10.31, p < 0.001 (***)).
ADH3*1/ADH3*1 genotype was observed in 45.6% and was significantly higher
than in the control group (χ²=16.16, p < 0.001 (**)). ADH3*1/ADH3*2
and ADH3*2/ADH3*2, and 21% in alcoholic liver cirrhosis group (χ²=10.17, p < 0.001 (**)).
These results may suggest that allele ADH3*1 may be a risk factor for the
developing alcoholic liver diseases and allele ADH3*2 can protect against alco-
holism in Polish population.

**PO-768 COMPLICATIONS IN THE RIGHT-LOBE ADULT LIVING
DONOR LIVER TRANSPLANTATION (LDLT)**

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Barcelona, Spain.

**Introduction:** Potential advantages of LDLT have been tempered by the risk
of injury or death of a healthy donor.

**Aim:** To report the morbidity and mortality after right-lobe liver donation during
2 periods of time.

**Patients and methods:** A total of 41 LDLT resections have been performed in our
hospital: 18 on the 1st period (March 2000-December 2001) and 24 on the
2nd period (January 2002-September 2004). One donor operation was aborted due to
a plastic perforitis of the recipient. 30 men and 11 were women. Mean age
was 32 ± 8 years. Mean intraoperative blood loss was 953.42 ± 817.71 cc (1st
period) and 487.92 ± 270.17 cc (2nd period). Mean operative time was 426.67 ±
102.18 minutes (1st period) and 346.14 ± 42 minutes (2nd period). The mean
follow-up of the 41 donors was 24 months.

**Results:** There was no mortality. Two patients of the 1st period required blood
transfusion from the blood bank. During the 1st period major complications in
6 patients included bile leak (4) (two of them required reintervention) and
pneumonia (2). Four patients had minor complications including urinary infec-
tion (2), abdominal wall hernia (1), and wound infection (1). During the 2nd
period major complications in 6 patients included bile leak (4), bilioma (1) and
thrombosis middle hepatic vein (1). One patient had minor complication (urinary in-
fection). Mean hospital stay was 13 ± 9.5 days (1st period) and 10 ± 3.9 days
(2nd period). Five patients required readmission for bile leaks.

**Conclusion:** With the learn curve, the presence of complications has signif-
icantly improved over time, however the morbidity continues being signifi-
cant.

**PO-769 LIVER TRANSPLANTATION AND ASPERGILLUS
FUMIGATUS INFECTION: A FAVOURABLE OUTCOME CASE**

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Aspergillus fumigatus infection has been reported in literature by different se-
ries in 6.5% of all liver transplants. The mortality rate can be as high as 80-
100%, in association to risk factors for mycotic infections. We report a case
of a 54-year-old man that underwent liver transplantation for HCC treated with
TACE, resection and thrombolysis. A great amount of blood transfusions
were necessary and a temporary closure with packing was performed. In the
ever-p.o.period renal and hepatic function were observed, demanding dialetic
and ventilatory support and metabolic detoxification by MARS treatment. The
progressive liver functions failure for drug-resistant acute rejection, lead to re-
transplantation. The post-operative period was characterized by a slow recovery
of renal and lung function and by lung infection with repeated and prolonged
microbiologic isolations of enterococci and aspergillus. The chest x-rays out-
lined invasive pulmonary aspergillosis. After aimed antibiotic therapy with te-
iclopin and amphoarten B lipiddispersomes at maximal doses, in
addition to the reduction of immunosuppressive doses, the complete resolu-
tion of the infection and of all surgical problems was observed.

The therapeutic approach of aspergillus fumigatus infection, in terms of both
prophylaxis and treatment, has changed with the introduction of amphotericin
B mesocloidal/loposomal therapy. An aggressive pharmacological treatment,
even though potentially nephrotoxic, with probable need of dialysis, is justified
by the high mortality rates in case of infection. Accurate abdominal toilette,
limiting blood losses, the contraction of operative times and re-operations are
necessary to reduce the overall infectious risk.

**PO-770 LONG TERM OUTCOME OF SPLIT LIVER
TRANSPLANTATION**

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**Introduction:** It has been described that 15% of donors are eligible for split liver transplantation (SLT) procedures, this could account for 59 additional patients transplanted per 100 donor livers suitable to split.

**Aim:** The aim of the study was to compare SLT and whole liver transplantation (LT) in a single center experience.

**Materials & methods:** we performed 15 SLT, 7% of all liver transplants per-
fomed between 1998 and January 2005. In-situ harvesting produced left grafts
(II-III) for pediatric transplantation at other Italian centers and right grafts (I, IV-
VIII) for adult transplantation at our hospital.

**Results:** SLT and LT groups were comparable for recipient age, sex, main
indication for transplantation, and UNOS status prior to transplantation.

**Table 1**

|               | SLT (15) | LT (208) |
|---------------|---------|----------|
| Generalities  | Mean (SD)| Mean (SD) |
| Donor age     | 34.9 (17.6) | 47.3 (17.2) |
| CIT (min)     | 650 (145) | 554 (170) |
| Complications |          |          |
| PNF (%)       | 7       | 26       |
| HAT (%)       | 7       | 4.7      |
| Bilary (%)    | 21      | 17       |
| CIT: cold ischemia time; PNF: primary non function; HAT:hepatic artery thrombosis

**Longer CIT and inferior donor age in the SLT group were observed. The overall incidence of complications was 35% in the SLT group with no statistical differences with LT. Patient and graft survival were similar between both groups.**

**Table 2**

|               | SLT (15) | LT (208) |
|---------------|---------|----------|
| Patient survival(%) | 1 year | 3 years | 5 years |
| SLT           | 83      | 73       | 73       |
| LT            | 82      | 80       | 75       |
| Graft survival(%) | 1 year | 3 years | 5 years |
| SLT           | 73      | 73       | 73       |
| LT            | 76      | 70       | 66       |
| p              | 0.56    | 0.44     |
Conclusions: SLT technique is technically challenging requiring to LT and requires expertise of the whole transplant team. Nord Italian Transplant allocation of both organs to different transplant teams demonstrates a 100% feasibility. In our experience, though limited, SLT results are comparable to those obtained with LT, expanding the cadaveric donor pool.

PO-771 POLYCYSTIC LIVER DISEASE: DEROOFING, RESECTION OR TRANSPLANTATION?
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Aim: To evaluate the indications and outcomes for conservative treatment, fenestration, liver resection (LR) and liver transplantation (LT) for PLD Patient and Methods: Over a 14-year period, 46 women and 6 men (median age 52 years) were treated. 50% of patients had a history of concomitant poly-cystic kidney disease. Median length of follow up is 28.6 months (range 1-145). Selection for treatment is pragmatic and based on (1) the lobar involvement of the liver (unilobar or bilobar) (2) distribution of cysts (dominant or diffuse) and (3) a normal liver parenchyma within each lobe.

Results: Surgery was performed in 54% of patients and outcome of treatment is excellent.

| Outcomes of Surgical Management of PLD | Fenestration (n=7) | Resection (n=6) | Transplantation (n=15) |
|--------------------------------------|------------------|----------------|-----------------------|
| Length of Stay/days                  | 2 (2-5)          | 6 (6-10)       | 10 (10-71)            |
| Mortality                            | 14%              | 16%            | 46%                   |
| Mortality                            | 0%               | 0%             | 0%                    |
| Symptom-free                         | 72%              | 100%           | 100%                  |
| Recurrence                           | 28%              | 0%             | 0%                    |

PO-772 POST-BIOSPY ARTERIOPORTAL FISTULAS IN LIVER-TRANSPLANT PATIENTS
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Background: Biopsy-related arteriportal fistulas (A-P) are not uncommon (5%), but they are usually asymptomatic and close spontaneously. Portal hypertension, secondary to formation of an intrahepatic A-P fistulas after biopsy, has been exceptionally reported in transplant recipients, despite extensive use of biopsy in the post-transplant period, and requires early diagnosis and treatment.

Materials and Methods: We report about two liver-transplant patients (out of 505) who experienced ascites, gastrointestinal bleeding and congestive splenomegaly after liver biopsy. We first considered these features as a consequence of liver graft dysfunction. Doppler-ultrasonography, showing arterialized hepatofugal portal flow and angio-MR, detecting an anomalous intrahepatic vascular area, raised the suspicion of an A-P fistula. Diagnosis was confirmed by angiography, which showed early portal visualization, and provided identification of the feeding vessels. During angiography selective embolization of the A-P fistula was safely performed. Closure of the A-P fistula was incomplete in one case, and transient (due to subsequent fistula's refedding by collateral) in the other, thus requiring a second successful embolization attempt, followed by clinical improvement. Disappearance of the A-P fistula was confirmed by doppler-US and angio-MR.

PO-773 TOLERGENIC EFFECT OF INTRA-OPERATIVE DONOR-SPECIFIC BLOOD TRANSFUSION IN PEDIATRIC LIVING-RELATED LIVER TRANSPLANTATION
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With the introduction of cyclosporin, donor-specific blood transfusion (DSBT) has become less popular. However, its experimentally proven efficacy, relative safety and technical easiness still make DSBT an attractive tolerogenic strategy. We examined safety and efficacy of DSBT in Living-Related Liver Transplantation (LRLT).

Methods: Eight ABO-identical pediatric LRLT performed between August and December 2004 were prospectively included in the DSBT protocol. Unirradiated whole blood (ten % of the recipient’s total blood) was taken from the donor after harvesting the hepatic graft and transfused in the recipient portal vein after reperfusion. Tacrolimus based immunosuppression was administered. The incidence of rejection (encountered up to 8 weeks post LRLT) was compared with thirteen ABO-identical pediatric LRLT performed in 2004 without DSBT (Non-DSBT group).

Results: In Non-DSBT group, rejection occurred in 62% (8/13). DSBT reduced the incidence of rejection to 25% (2/8) in DSBT group (p=0.01 vs Non-DSBT group). Of them, only 1 patient (13%) required steroid pulse therapy, while it was given 54% (7/13) to treat rejection in Non-DSBT group (p=0.05). GVHD was absent clinically in recipients of unirradiated DSBT. Harvesting blood, in addition to the hepatic graft, caused neither anemia nor hypotension.

Conclusion: In donors, harvesting the blood, in addition to the hepatic graft, causes no morbidity. In recipients, DSBT appears to be safe, causes no GVHD, and no sensitization. Intraoperative DSBT reduced rejection requiring steroid pulse therapy. These promising results encourage us to study further tolerogenic effect of DSBT in a large population of LRLT.

PO-774 LIVER TRANSPLANTATION IN CONGENITAL PEDIATRIC ARTERIO-PORTAL FISTULA
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Intrahepatic arterio-portal fistula (APF) is a rare condition in paediatric population. Aetiology is congenital, traumatic, iatrogenic or related to hepatic artery aneurysm. Portal hypertension caused by fistula determines ascites, bowel congestion, gastrointestinal bleeding, anemia and malabsorption with steatorrhea. Endoscopic recognition is mandatory to assess variceal status. Commonly APF is treated by radiological embolization. If unsatisfactory hepatic resection and/or hepatic artery ligation represented the treatment of choice. For multiple or central hepatic vascular malformation is mandatory liver transplantation.

Two patients affected by centrohepatic APF with recurrent gastrointestinal bleeding were referred to our Institute. Both had received unsatisfactory radiological embolization. The fistula dimension and the intraparenchymal site were in contrast with a resective option and both patients were listed for hepatic transplantation. Both were alive after 14 and 36 months respectively. In conclusion liver transplant is a concrete therapeutic option for patient with APF unre sponsive to radiological embolization. Hepatic resection or hepatic artery ligation surgery options suitable only in selected patients. For central intraparenchymal position resection is not feasible; for complex fistula vascularization artery ligation is not possible. About transplant option, timing is important in order to reduce waiting time and effective resection risk. Technically attention is necessary for portal vein anastomosis because of the small diameter and the thick arterialized wall due to reverse blood flow. The diffusion of split technique in live pediatric transplant increase difficulties because of vascular discrepancy and spatial arrangement of portal branch with increased risk for thrombosis.
HEMODYNAMIC CHANGES IN ADULT LIVING DONOR LIVER TRANSPLANTATION (ALDLT)

Joana Ferrer 1,Jose Fuster1,Guillermo Alvarez 1, Juan Turres2, Constantino Fondevila 1, Ramon Charco 1, Juan Carlos Garcia-Pagan 2, Juan Carlos Garcia-Valdecasas 1, 2, Liver Surgery and Transplant Unit, IMD, Hospital Clinic, Barcelona, Spain; 3, Hepatic Hemodynamic Laboratory, Liver Unit, IMD, Hospital Clinic, Barcelona, Spain.

Introduction: Living grafts are by definition "small for size" grafts when transplanted in cirrhotic patients, which causes increased graft dysfunction and morbidity.

Aims: To study hemodynamics changes in recipients of ALDLT and their correlation with postoperative morbidity.

Materials and methods: Between May 2003-March 2005, 11 adults patients underwent transplantation using right lobe. The men/women ratio was 6:5 and mean age 62.5 ± 17.5. Hepatocellular carcinoma stage liver disease secondary to hepatitis C virus in 1, alcoholism 2, hepatocellular carcinoma 6, non-alcoholic steatohepatitis 1, primary biliary cirrhosis 1. Mean Hepatic Venous Pressure Gradient (HVPG) was 16.4 ± 1414 mmHg. Mean weight of the right liver graft was 742 ± 115 gm. Intraoperative arterial flow measured was (n=1) 877 ± 81 ml/min as well as portal (n=1) 390 ml/min. We have analyzed liver function in the immediate postoperative period and the HVPG in the first 72 hours and 3 months following LDLT as well as associated morbidity to this procedure.

Results: Mean liver function 3 days/3 months following LDLT was: Alanine transaminase: 263 ± 159 μIU/l, aspartate aminotransferase: 170 ± 51 μIU/l, γ-glutamyl transferase: 141 ± 1360 μIU/l, GGT: 36 ± 1360 μIU/l, total bilirubin: 5,1 ± 1360 μIU/l, prothrombin time (%): 59 ± 4. Meand HVPG of the AV at 3 days and 3 months were 8.3 ± 3mmHg and 3.5 ± 1.2mmHg respectively. Five patients developed biliary complications, 3 ascites and 1 patient had postoperative bleeding. The mean peak of transaminases was significantly higher in the HVPG >8mmHg (mean of 11 patients) group at 72 hours. The mean value of HVPG at 3 months was <6mmHg in all patients. No other relevant significance was found related to the other variables.

Conclusion: There are no significant differences related to index of complications and HVPG. The study of HVPG performed at 72 hours postop, showed a correlation between value of transaminases and HVPG >8mmHg. Nevertheless, it is necessary to include more cases to confirm these results.

Hepatic resection and liver transplantation (LT) compete as the therapy of choice for end-stage liver diseases. The shortage of donors and the increased number of patients with end-stage liver diseases implies an accurate management of the waiting list. The present study the whole transplantation process of a single LT center has been evaluated on an intention-to-treat basis, considering the patient from the time of listing to the late follow-up.

Background: Liver transplantation represents the therapy of choice for end-stage liver diseases. The shortage of donors and the increased number of patients with end-stage liver diseases implies an accurate management of the waiting list. In the present study the whole transplantation process of a single LT centre has been evaluated on an intention-to-treat basis, considering the patient from the time of listing to the late follow-up.

Methods: From 1stJanuary 1999 to 1stJune 2004 373 adult patients were considered for LT listing at our center. We were excluded UNOS status 1 and 2 LT. The mean age was 52 ± 13 years, sex distribution was 197 males and 176 females. The mean Model for End-Stage Liver Disease score (MELD score), Child-Pugh classification, UNOS status, etc. The Kaplan-Meier method was used to calculate overall survival function according to intention-to-treat analysis and the follow-up was continued until late follow-up or death.

Conclusion: Median waiting-list time was 20 months (range: 1-27). The following variables at listing significantly influenced the overall survival at uni-
PO-780

TWELVE YEARS EXPERIENCE PREVENTING HEPATITIS-B RECURRENT WITH INTERFERON AND HEPATITIS-B IMMUNOGLOBULIN IN LIVER TRANSPLANT RECIPIENTS

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Purpose: We reviewed our experience using Interferon and Lamivudine to eradicate replicating hepatitis-B virus (HBV) prior to liver transplantation (LTx).

Methods: Pre transplantation: We used Interferon alpha-2B to suppress viral replication in HBeAg+ and/or HBVDNA+ patients. From 1996, Lamivudine was given +/- Interferon. Only HBeAg- and HBVDNA- patients were transplanted.

Post transplantation: Hepatitis-B immunoglobulin (HBIG) (low dose, 2000IU intramuscular) maintained Anti-HBsAb titres. Lamivudine and HBIG were given to patients given Lamivudine pre-LTX. Patients who were spontaneously only HBeAg- received HBIG alone. Patients given Interferon pre-LTX received only HBIG post-LTX. HBeAg+ and/or HBeAg+ defined HBV-recurrence.

Results: Exclusion criteria included death within one month. Fifty-nine liver transplants in 50 HBV+ve patients were analysed. Mean donor age was 40.6 years (11 to 76). Forty-three (86%) patients were male, mean age 55 years (23 to 72). Mean MELD score was 28.25 with 26 (44%) scoring ≥25. Seventeen patients (34%) received Interferon. Seventeen patients (34%) had Lamivudine. All patients received HBIG. Thirteen patients died with mean survival 2.3 years (0.16 to 6.22), none had HBV-recurrence. Six patients (12%), not treated with Interferon, became transiently HBeAg+ (n=4). HBeAg+ (n=1) and HBVDNA+ (n=1). Two Lamivudine patients (4%) had HBV-recurrence with HBeAg+ and HBVDNA persistently detected. Patient survival at 1, 5 and 10 years was 92.6%, 78.6% and 72.4%.

Conclusions: Patients who were spontaneously only HBeAg- pre-LTX, and HBV+ve patients converted to a low replicating state pre-transplant using Interferon, required only HBIG to prevent recurrence. Interferon was superior to Lamivudine. Patients given Interferon pre-LTX and HBIG mono-therapy post-LTX had a 100% freedom from recurrence.

PO-781

GENE EXPRESSION PROFILE OF REGENERATION IN HUMAN LIVING-DONOR LIVER TRANSPLANTATION

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Purpose: Both in injured deceased donor (DD) grafts and in adult-to-adult living donor (LD) grafts, hepatocyte replication is essential for restoration of the liver mass. In this study we assessed the differences between human DD and LD grafts in gene expression profiles in the very early phase of regeneration.

Methods: We compared gene expression profiles in core biopsies taken at the end of cold ischemia/CI and after reperfusion/Rep) to a baseline sample of the same graft.

Results: After reperfusion in DD, 221 genes were up-regulated, mostly related to inflammation (IL-8, IL-1B) and cell-cycle progression (IL-6,IL10,FOS,MYC,221). In LD, 569 genes were differentially expressed at the end of CI. Up-regulated genes were related to RNA and protein synthesis and cell-cycle progression (CAD,POLR1C,EIF2F2,STAT3,p21), indicating induction of regeneration following parenchymal transection. Down-regulated genes involved fatty-acid and ethanol metabolism (PPARα,CEBPα,ADH4). At this stage, there was a marked absence of inflammatory genes. After reperfusion however, inflammation related genes were up-regulated and genes associated with glucose and albumin metabolism were down-regulated.

Conclusion: In DD and LD the expression pattern was similar, but it was greater in magnitude in LD’s. LD grafts also showed marked increase in RNA biosynthesis and structural protein metabolism and down-regulation of oxidative phosphorylation and global lipid metabolism, not seen in DD grafts. This study confirms classical patterns of liver regeneration in human partial liver transplantation. The findings might have important clinical implications, as partial grafts seemed to have a greater affinity towards regeneration in the immediate phase, rather than supporting metabolism in the recipient.

PO-782

HCV LIVER TRANSPLANT RECIPIENTS SHOW HIGHER HLA CLASS I POLYMORPHISM: IMPLICATIONS FOR ANTIVIRAL TREATMENT RESPONSE AND POST-TRANSPLANT OUTCOME?

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Purpose: We reviewed our experience using Interferon and Lamivudine to prevent hepatitis-B virus (HBV) prior to liver transplantation (LTx). We used Interferon alpha-2B to suppress viral replication in HBeAg+ and/or HBVDNA+ patients. From 1996, Lamivudine was given +/- Interferon. Only HBeAg- and HBVDNA- patients were transplanted.

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Results: Exclusion criteria included death within one month. Fifty-nine liver transplants in 50 HBV+ve patients were analysed. Mean donor age was 40.6 years (11 to 76). Forty-three (86%) patients were male, mean age 55 years (23 to 72). Mean MELD score was 28.25 with 26 (44%) scoring ≥25. Seventeen patients (34%) received Interferon. Seventeen patients (34%) had Lamivudine. All patients received HBIG. Thirteen patients died with mean survival 2.3 years (0.16 to 6.22), none had HBV-recurrence. Six patients (12%), not treated with Interferon, became transiently HBeAg+ (n=4). HBeAg+ (n=1) and HBVDNA+ (n=1). Two Lamivudine patients (4%) had HBV-recurrence with HBeAg+ and HBVDNA persistently detected. Patient survival at 1, 5 and 10 years was 92.6%, 78.6% and 72.4%.

Conclusions: Patients who were spontaneously only HBeAg- pre-LTX, and HBV+ve patients converted to a low replicating state pre-transplant using Interferon, required only HBIG to prevent recurrence. Interferon was superior to Lamivudine. Patients given Interferon pre-LTX and HBIG mono-therapy post-LTX had a 100% freedom from recurrence.

PO-783

LONG-TIME INTENSIVE CARE THERAPY IN ANHEPATIC PIGS

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Introduction: Establishment of new intensive care therapy options in anhepatic animal model is required to realize new long-time survival studies of liver failure.

Methods: Hepatocectomy was performed in 16 female pigs (30-41 kg) by reconstucting the vena cava and portal vein through a three-way vascular prosthesis with end to side anastomosis. The following parameters were recorded continuously: electrocardiogram, mean arterial pressure, SO2 oximetry, core body temperature, intracranial pressure, urinary output. Serum electrolytes, acid-base balance, blood gas analysis, and glucose levels were monitored hourly and immediately corrected as required. Pigs received sodium chloride 0.9%, hydroxyethylstarch 6% and fresh-frozen plasma units. All pigs received furosemid to keep on diuresis as long as possible, when renal failure occurred they were treated with CVVH.

Results: After hepatocectomy a continuous worsening of the other organ systems appeared. To maintain adequate mean arterial pressure Noradrenalin was given in heightening dosage up to 30 µg/min. Blood lactate concentration stayed stable during sufficient circulation and raised when decomposition occurred. Pulmonary function impaired progressively and therefore it was necessary to increase PEEP and airway pressure to maintain sufficient ventilation and oxygenation. Though this regime blood concentration of ammonia could be kept constantly low.

Conclusion: We established a new intensive care therapy treatment which can be used for long-time survival studies examining anhepatic situations and also other questions about liver failure.
Liver biopsy specimens performed after the third treatment showed reduced cholestasis in both cases when compared to the pre-treatment biopsy. At the end of the 3 cycles of PAP both cases experienced a bilirubin reduction toward normalization within 30 days after transplantation. Those preliminary data suggest that PAP selective for bilirubin removal could not only reduce bilirubin level but also improve the histological pattern of the graft in terms of reduced cholestatic signs.

**PO-785 CYCLOSPORINE DELAYS THE DEVELOPMENT OF LIVER FIBROSIS IN PATIENTS TRANSPLANTED FOR HCV CIRRHOSIS**

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HCV recurrence shows an accelerated course after liver transplantation. A recent study suggests that use of tacrolimus at 1 year was an independent predictor of accelerated fibrosis progression, but other studies do not support this detrimental effect of tacrolimus. We performed a retrospective study on the development of liver fibrosis after HCV recurrence in liver transplant recipients treated with either cyclosporine or tacrolimus.

**Methods:** At our center 38 patients were transplanted because of HCV-related liver cirrhosis. Sixteen were treated with cyclosporine and 22 received tacrolimus. All received low-dose steroids during the first year of transplantation and showed HCV recurrence within 8 months after transplantation. Liver biopsies were performed when indicated. Liver biopsies were performed in 23 patients with a median time of 15 months (range 3-48 months) after transplantation. A pathologist blinded to the immunosuppressive regimen assessed liver fibrosis according to the Ishak and Metavir score.

**Results:** The 1 and 4 year survival were comparable between the cyclosporine and tacrolimus treated patients. Donor and recipient age was not different in both groups. The mean fibrosis score was lower in the cyclosporine treated patients with a median time of 15 months (range 3-48 months) after transplantation.

**Conclusion:** This retrospective study demonstrated that cyclosporine delays the development of liver fibrosis in liver transplant recipients. A large, randomized clinical trial with a drug-to-drug comparison, however, is needed to further elucidate this potential protective effect of cyclosporine on HCV recurrence.

Liver transplantation (LTx) is used in children with Langerhans cell histiocytosis (LCH). Between 97 and 04, 256 children underwent LTx, 239 in Bergamo and 17 in Palermo; 3 children were affected by LCH, Skin involvement, splenomegaly, and lymph node enlargement were present in all children, diabetes insipidus in 2, bone lesions and lung involvement in 1. All patients developed end-stage liver disease, and received chemotherapy. One child was in remission prior to LTx and 2 had active LCH. Median age at LTx was 65 months; all children received an in situ split liver transplantation. The immunosuppression included tacrolimus and steroids and in 2 cases basiliximab. None of the patients developed acute cellular rejection. At 3 patients had relapse at a median of 12 months. The child with LCH remission at LTx is currently asymptomatic. One patient developed LCH recurrence in the lungs 1 month after LTx, and was treated with chemotherapy. In the third child, 10 months post-LTx, intrahepatic LCH recurrence was diagnosed. LCH activity was initially controlled by chemotherapy, but, as chemotherapy was stopped because of endocarditis, liver function tests worsened and follow-up cholangiography demonstrated an increased size of cholangiopathy. Patient is listed for retransplantation. An higher risk of acute rejection as been reported in LHC patients; our patients had no rejection. Active LCH at LTx are at risk of relapse that can compromise graft function.

**PO-787 PEDIATRIC IN SITU SPLITT LIVER TRANSPLANTATION FOR LANGHERANS CELL HISTIOCYTOSIS – ACUTE REJECTION AND DISEASE RECURRENCE**

Enrique Canepa, Daniel Azoulay, Didier Samuel, Denis Castaing, Olivier Scatton, René Adam, Marylène Plasse, Luc-Antoine Veilhan, Olivier Canepa, Daniel Azoulay, Didier Samuel, Denis Castaing, Henri Bismuth. CHB, Hôpital Paul Brousse, Villejuif, France.

To evaluate LT as a last resort treatment of unresectable HCC developed on normal liver and to compare its outcome to that of LT for HCC in cirrhotic patients.

Among 298 patients consecutively transplanted for HCC in our center, 34 had unresectable HCC developed in normal liver (G1) and 264 had HCC with cirrhosis (G2). LT was performed according to Mazzaferro’s criteria for cirrhosis. Characteristics and outcome of patients and tumors were compared in both groups. The number of nodules and their maximum size were significantly larger in G1 than in G2. After a mean follow up of 53 months, 70% of patients had a tumor recurrence in G1 vs 16% in G2 (p < 0.001). Surgical resection of recurrence was possible in 50% in G1 compared to 10% in G2. Overall survival was similar. In G1, the size and the number of tumors, pre-transplant alfafetoprotein, and a previous chemoembolization with or without tumor downstaging had no impact on overall survival. However, a maximum tumor size greater than 4 cm significantly decreased the disease-free survival (31% vs 9% at 10 years, p=0.04) while surgery of tumor recurrence significantly increased overall 5-year survival compared to non surgical treatment (66% vs 30%, p= 0.04).

From a donor with null genotype developed de novo IH, but of those who received a positive organ, only the recipients with a null genotype could develop de novo IH. All of them had elevated titer of anti-GSTT1 antibodies at the time of diagnosis, which correlated with severe graft damage and a bad outcome if treatment was not implemented.

Liver transplantation performed after the third treatment showed reduced cholestasis in both cases when compared to the pre-treatment biopsy. At the end of the 3 cycles of PAP both cases experienced a bilirubin reduction toward normalization within 30 days after transplantation. Those preliminary data suggest that PAP selective for bilirubin removal could not only reduce bilirubin level but also improve the histological pattern of the graft in terms of reduced cholestatic signs.

**PO-786 GLUTATHIONE S-TRANSFERASE T1 MISMATCH CONSTITUTES A RISK FACTOR FOR DE NOVO IMMUNE HEPATITIS AFTER LIVER TRANSPLANTATION**

Isabel Aguileras 1, Jose Manuel Sousa 2, Francisco Gaviñán 3, Angel Bernardos 2, Ingeborg Wichmann 1, Antonio Nuñez-Roldan 1.

1Immunology, Hospital Universitario Virgen del Rocío, Sevilla, Spain; 2Liver Transplant Unit, Spain; 3Pathology, Spain.

**Purpose:** Our main objective was to determine if any of the 4 possible Glutathione S-transferase T1 (GSTT1) donor-recipient allelic combinations could be used as a predictor of de novo immune hepatitis (IH) after a liver transplant.

**Methods/Materials:** A cohort of 110 consecutive liver transplanted patients with a post transplant period of more than 30 months. PCR was performed to analyse GSTT1 polymorphism in donors and recipients of liver transplants. Antibody detection was done by indirect immunofluorescence and Western blot.

**Results:** Distribution of the 4 different GSTT1 donor/recipient allelic combinations is summarized in Table 1. None of the recipients who received a graft from a donor with null genotype developed de novo IH, but of those who received a positive organ, only the recipients with a null genotype could develop de novo IH. All of them had elevated levels of anti-GSTT1 antibodies at the time of diagnosis, which correlated with severe graft damage and a bad outcome if treatment was not implemented.

**Conclusion:** We present current evidence that a particular GSTT1 mismatch (donor/recipient null) is associated with a statistically significant increased risk of de novo IH in liver transplant patients (p=0.0001). This is a clear example of alloimmune response against a donor specific antigen with production of antibodies.

**PO-787 LIVER TRANSPLANTATION (LT) FOR HEPATOCELLULAR CARCINOMA (HCC) IN PATIENTS WITHOUT CIRRHOSIS: IS IT WORTHWHILE?**

Olivier Scatton, René Adam, Marylène Plasse, Luc-Antoine Veilhan, Enrique Canepa, Daniel Azoulay, Didier Samuel, Denis Castaing, Henri Bismuth. CHB, Hôpital Paul Brousse, Villejuif, France.

To evaluate LT as a last resort treatment of unresectable HCC developed on normal liver and to compare its outcome to that of LT for HCC in cirrhotic patients.

Among 298 patients consecutively transplanted for HCC in our center, 34 had unresectable HCC developed in normal liver (G1) and 264 had HCC with cirrhosis (G2). LT was performed according to Mazzaferro’s criteria for cirrhosis. Characteristics and outcome of patients and tumors were compared in both groups.

The number of nodules and their maximum size were significantly larger in G1 than in G2. After a mean follow up of 53 months, 70% of patients had a tumor recurrence in G1 vs 16% in G2 (p < 0.001). Surgical resection of recurrence was possible in 50% in G1 compared to 10% in G2. Overall survival was similar. In G1, the size and the number of tumors, pre-transplant alfafetoprotein, and a previous chemoembolization with or without tumor downstaging had no impact on overall survival. However, a maximum tumor size greater than 4 cm significantly decreased the disease-free survival (31% vs 9% at 10 years, p=0.04) while surgery of tumor recurrence significantly increased overall 5-year survival compared to non surgical treatment (66% vs 30%, p= 0.04).

Nonresectable larger and increased in number, HCC with normal liver have similar survival after LT, as HCC with cirrhosis. The higher risk of tumor recurrence
is palliated by increased possibilities of surgical resection post-LT. HCC with normal and cirrhotic liver are separate entities with different indications but equal justification to be transplanted.

**PO-789 MEMBRANE-BOUND AND SOLUBLE HLA CLASS I EXPRESSION ON CULTURED HUMAN HEPATOCYTES IN PRESENCE AND ABSENCE OF IFN-γ**

Thomas Schreiter¹, Vera Rebmann¹, Annika Dolar¹, Hauke Lang², Guido Gerken³, Hans-Grosse-Wilde¹. ¹Institute of Immunology, University Hospital Essen, Germany; ²Department of Gastroenterology and Hepatology; ³Department of General Surgery and Transplantation.

The liver is able to support both T-cell responses and T-cell tolerance. For analysis of this dual function the expression of membrane-bound and soluble HLA class I (mHLA-I, sHLA-I) derived from normal hepatocytes was examined. Resected liver tissues from 17 patients were digested by collagenase and the expression of mHLA-I and sHLA-I on the cultured hepatocytes was studied as a function of time (0, 24, 48, 72, 96 h) and of IFN-γ concentration (0, 10, 100, 1000 U/ml). After specific immunoprecipitation and 1D-IEF (mHLA-I) or SDS-PAGE (sHLA-I size variants of 43, 39 and 35 kD) HLA-molecules were detected by Western blot and analyzed by densitometry. mHLA-B antigens were found without and with IFN-γ at 1.5 fold higher expressed than mHLA-A antigens (p<0.0001), which remained stable over time. Under IFN-γ the release of 35 and 43 kD sHLA-I variants increased time-dependent (p<0.0001), but was only for the 43 kD variant dependent on the IFN-γ concentration (p<0.015). The expression of the 39 kD sHLA-I molecule reached a maximum after 48h and was not further increased by IFN-γ. By combination of specific mAbs HCA2 and HC10 the 35 kD and 39 kD sHLA-I variants belonged mainly to sHLA-B/C alleles for both without and with IFN-γ (p<0.001 and p<0.033) and after stimulation with IFN-γ (p<0.011 and p<0.023). The preferential expression of HLA-B/C encoded alleles might have implications for liver allotransplantation and for immunotherapeutic treatment of viral liver diseases and liver malignancies.

**PO-790 LIVING DONOR LIVER TRANSPLANTATION (LDLT) IN EUROPE**

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From October 1991 to June 2004, from 53389 transplants, 1588 LDLT (3%) have been performed in 61 centres. The outcome of LDLT was compared to that of Full Size Cadaveric Liver Transplantation (FSCLT).

LDLT procedure becomes now used mainly in adults. Donation included the right liver in 92% of adult recipients and the left lobe (86%) or the left liver (12%) in children. Donor mortality within 2 months was 0.25%. 4 donors died of pulmonary embolism (1), of sepsis (2) and of cardiac failure (1). Early donor morbidity was 21% of which 6% following a biliary complication, 5% following an infection and 3% in relation with a transient hepatic insufficiency. In adult recipients, indications of LDLT included as many cirrhosis, more cancers and less fulminant hepatitis and retransplantation than FSCLT. 5-year Graft survival was 69%, better in children (77%) than in adults (58% - p<0.001). In children, results were better than the FSCLT performed during the same period (77 vs 72%). In adults, graft survival was lower than in FSCLT performed during the same period.

In conclusion, adult LDLT is currently in progression in Europe. Donors’ mortality is 0.25% and early morbidity is 21%. The indication includes more cancers than the FSCLT. Overall graft survival is better in children and lower in adults compared to FSCLT, non-specifically related to the technique but also to differences in the indication.

**PO-791 END TO SIDE (ES) VENOUS OUTFLOW RECONSTRUCTION (VOTR) IN ADULT PIGGY-BACK LIVER TRANSPLANTATION (PB-LT)**

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The aim of this study is to analyse a single center experience with an ES-VOTR in adult patients. From 1995 to 2002 149 PB-LT were performed in 139 patients using the ES-VOTR. All retransplantations (second and third grafts) performed in this study were PB-LT. In nine (6%) PB-LT a temporary portal caval shunt (TPCS) was used. ES-VOTR was performed as described by Cherqui with slight adaptations: (1) the recipient hepatic veins were closed either with vas-
nor initial immunosuppression played a relevant role. No increase of incidence of ITBL over the last 14 years was documented.

**Conclusion:** Further investigation regarding ITBL will be necessary to establish preventive screening and treatment concepts for patients suffering from ITBL.

**PO-794 EVOLUTION OF LIVER TRANSPLANT AND LIVER-PANCREAS TRANSPLANT PATIENTS UNDER A STANDARDIZED PROGRAM OF POST-OPERATIVE PHYSICAL THERAPY**

Chetna Bhalla. Physiotherapy, University Hospital, Geneva, Geneva, Switzerland.

The post operative rehabilitation programme for liver and kidney-pancreas transplant patients is not well developed in geneva compared to post opera- tive pulmonary transplantation rehabilitation programme.

The objective of this research was to compare the evolution of liver and kidney-pancreas transplantation under a standardized programme of physical therapy. It was also aimed to develop a specific programme of rehabilitation for these two groups of transplanted patients.

The patients were evaluated in the pre-transplantation phase and in the post transplantation phase. The tests used for evaluation were spirometry, 6 Minute- walking test, test of effort, gasometry, questionnaire about the quality of life. In the post transplantation phase the tests were performed each week for 3 weeks after operation and the questionnaire about quality of life filled in be- fore the end of hospital stay. The follow up of all these tests was done in the out patient clinic to observe the evolution and a review of the questionnaire of quality of life was done.

The factors that influenced the evolution of these patients were the status of the transplanted organ (verified by biopsy results), the urea-creatinine values, medicines taken by patients, the immunosuppressors taken by patients, the post operative respiratory problems.

The post-operative rehabilitation was standardized for these two groups of pa- tients. The programme consisted of positive pressure utilisation for respiratory care (CPAP), mobilization, renforcement exercises, cycling with progressive re- sistance, analysis of activities of daily living. All these activities were performed by all these patients in the same chronological order and intensity and period.

**PO-795 RESULTS OF INTESTINAL AND MULTIVISCERAL TRANSPLANTATION IN ADULT PATIENTS: ITALIAN EXPERIENCE**

Antonio D. Pinna, Augusto Lauro, Alessandro Dazzi, Giorgio Ercolani, Matteo Cescon, Marco Vivarelli, Giovanni Varotti, Gianluca Grazi, Massimo Di Simone, Stefano Faenza. UO Chirurgia dei Trapianti di Fegato e Multiorgano, Policlinico S.Orsola-Malpighi University of Bologna, Bologna, Italy.

**Purpose:** We report our 4 year experience in intestinal and multivisceral trans- plant.

**Methods:** We performed 20 intestinal transplants and 7 multivisceral, 3 with liver. Underlying diseases were short bowel syndrome (12), chronic intesti- nal pseudo-obstruction (7), Gardner syndrome (5) and others (3). Indica- tion for the transplantation were loss of venous access, rejection (14), recurrent sepsis (B) and electrolyte-fluid imbalance (5); 12 patients presented liver dysfunction. Im- munosuppression was based on induction agents like Daclizumab (followed by Tacrolimus and steroids) in the first period (from 2000 to 2002), Atemezumab or Thymoglobin with Tacrolimus in a second period after 2002. In case of nphrototoxicity or ongoing rejection we added Sirolimus.

**Results:** Mean follow-up was 718 days. Three years patient actuarial survival rate was 94% for intestinal transplants and 42% for multivisceral (p= 0.003). Death rate was 18.5%, subsequent to graft loss in 3 cases. Three years graft actuarial survival rate was 83% for intestinal patients and 42.8% for multivisceral (p=0.02). Graft loss was mainly due to rejection (60%). Mean rejection rate was 0.82 ACR/pt/year in the first period while it was 1.99 after 2002. Com- plications were mainly represented by bacterial infections (88% of patients), followed by rejections (80%) and relaparotomies (73%). We experienced two episodes of chronic rejections. Three patients with PTLD were treated by Rit- uxmab and surgery, with 2 survivors.

**Discussion and conclusion:** Intestinal transplantation has achieved high rates of patient and graft survival: immunosuppressive management remains the key factor.

**PO-796 THE EFFECT OF RAPAMYCIN ON WOUND AND BILE DUCT HEALING**

Wendy Spearman, Anwar Mall, Delawir Kahn. Surgery, University of Cape Town, Cape Town, Cape, South Africa.

Rapamycin is a potent immunosuppressive agent which inhibits cellular prolif- eration during mitosis. It also has a strong inhibitory effect on fibroblasts and there has been a suggestion that there may be an increased incidence of post transplant wound problems. The aim of this study was to investigate the effect of rapamycin on the healing of the bile duct.

Large while X Landrace pigs (n=12) weighing 22.30kg were subjected to laparotomy and resection of intestine. The bile duct was divided into 2 anastomosed using a continuous 6/0 PDS suture. The animals were ran- domised to receive either rapamycin 2mg orally daily (Group 1) or no treatment (Group 2). After five days the animals were sacrificed. The anastomoses were examined histologically (Haematoxylin-eosin and Chromotrop Aniline Blue) and biochemically (hydroxyproline levels). The breaking strength of bile duct strips were also measured.

All Duct anastomoses were healed and there were no macroscopic differences between the two groups. Serum bilirubin, alkaline phosphatase and AST lev- els were also within normal limits in the two groups. The breaking strength was lower in the rapamycin treated animals (177± -36g versus 296– -72g). Hydroxyproline levels in the bile duct was also lower in the rapamycin treated animals (9.75±5.9 versus 15.1±1 – 4.3ug/ml). Histologically there was no differ- ence in morphology or collagen staining.

These findings show that rapamycin may impair the healing of the bile duct.

**PO-797 LIVER TRANSPLANTATION WITH SYSTEMATIC CAVA PRESERVATION**

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In our institution we initiated the liver transplantation program using routinely the vena cava preservation technique, without the use of the venous bypass pump in any case.

**Patients and Methods:** 103 out of our 104 cases have been performed with retrohepatic vena cava preservation, and 1 case with cava resection. All the cava preservation cases except one were performed with the anastomosis of the graft suprahepatic vena cava to a common conduit created with the three hepatic veins of the recipient. A temporary portocaval shunt was done in 3 cases, one of which was left anhepatic and transplanted in a second stage, as we had to discard the graft and wait for another. A cavaloc Hungarian 2016 transplantation was done in case of massive splanchic thrombosis.

**Results:** There were three intraoperative deaths related to splanchic conges- tion, within a period of nine months. After them, we introduced the temporary portocaval shunt for risk patients, and we have not had this problem again in the last 50 cases.

**Discussion:** Some patients have a param umbilical recanalization as their main internal spontaneous shunt, which is ligated and severed at the beginning of the operation. During the operation a slowly progressive splanchic edema de- velops, which can progress fast during the anhepatic phase, making it impos- sible in extreme cases to perform the portal anastomosis.

**Conclusions:**

- Preservation of the retrohepatic vena cava is always feasible.
- Veno-venous bypass with extracorporeal pump is not necessary.
- Transplant portocaval shunt should be used in patients at risk of splanchic edema.

**PO-798 GRAFT FLUSHING TECHNIQUES AND THE PROCALCITONIN LEVEL CHANGES AFTER LIVER TRANSPLANTATION**

Janos Fazakas, Gabor Ther, Marina Varga, Eniko Sarvary, Jeno Järáy. Department of Transplantation and Surgery, Semmelweis University, Budapest, Hungary.

**Purpose:** Elevated procalcitonin (PCT) serum levels were observed after liver transplantation (OLTx). The aim of this study was to analyse the regional and systemic changes of PCT serum level during and after OLTx according to the hepatic flush technique used before graft reperfusion.

**Methods:** In 41 liver transplanted patients systemic PCT measurements were done during OLTx. The aim of this study was to analyse the regional and systemic changes of PCT serum level during and after OLTx according to the hepatic flush technique used before graft reperfusion.

**Results:** There were no PCT level changes during hepatectomy and in the anhepatic phase. The first elevations of PCT began after graft reperfusion (group B: 1.0±0.32 vs. group A: 0.99±0.2ng/ml). Independently of the liver flushing technique used, higher hepatic vein PCT levels occurred compared to the systemic or portal vein levels (Group B: 1.2±0.43nmol/ml vs. 0.16±0.26ng/ml; 0.23±0.15ng/ml; Group A 1.0±0.39 vs. 0.29±0.13 or 0.30±0.19 ng/ml). The
postoperative PCT levels were significantly higher in Group B than in Group A.

Conclusion: The elevated hepatic vein PCT levels suggest that the first elevation of PCT may originate from the donor liver itself. The postoperative levels were significantly higher in the case own blood hepatic flush technique used.

PO-799 NURSING CARE AND THE PRE AND POST TRANSPLANTATION PHASES
Fabienne Scherrer. Surgery (Transplantation), University Hospital of Geneva, Geneva, Switzerland.

Introduction: The transplantation service of University Hospital Geneva comprises of an eleven bed ward and an out patient department. The type of transplantations which take place here are: Liver, Kidney, Kidney-pancreas, Intestines and also multi-organ transplantations.

The number of patients transplanted in the year 2004 were 79. The activities of the nursing team are concentrated in the pre and postoperative phases where the team works together for the patient care, patient education and psycho-social support. The majority of team members have an experience of 5-10 years in the field of transplantation.

Objective: To identify the needs of patients based on the theory of Virginia Henderson, who is a reference figure here for nursing care in University Hospital Geneva.

To analyse and thereby recognize the specificity in the patient care in transplantation ward.

Methods: The Brainstorm approach was utilized to gather information from the nursing team. The information consisted of “KEY WORDS” which determine the characteristics of nursing care approach towards the patients and the interventions already performed and to be performed.

Perspective: The experience of working for this poster made the nursing team share the value of "Team Spirit", integrate their practical knowledge acquired together and the importance of "Patient Education" in the treatment programme.

We desire that the enormous work done by the nursing team be recognized.

We also realize that there are not many publications in the field of nursing care in transplantation.

PO-800 ASSESSMENT OF EARLY LIVER GRAFT FUNCTION AND LONG TERM RESULTS IN RELATION TO DIFFERENT PRESERVATION FLUIDS
Marcin Kotulski, Krzysztof Zieniewicz, Piotr Hevelke, Bartosz Ciesiak, Piotr Remiszewski, Waldemar Patkowski, Jacek Pawlak, Marek Krawczyk. Department of General, Transplant and Liver Surgery, Medical University of Warsaw, Warsaw, Poland.

Introduction: Among a few solutions used to abdominal organ preservation no one present significant advantage of efficiency. The aim of this study was to assess of early liver graft function and long term results in relation to two of them: UW and Celsior.

Material and Methods: 356 patients underwent orthotopic liver transplantation in our Department until 1.04.2005. From 28.05.2002 to 31.03.2004, in 120 cases, two types of preservation fluids: UW (60 procurements) and Celsior (60 procurements) were used alternatively. Groups of recipients were approximated in many respects: gender - M/F: 31/29 in both groups, age - 38±12 UW, 43±13 Celsior (p>0.05); cold ischaemia time - 8.5±2.7h UW, 9.0±2.2h Celsior (p>0.05); indications to transplantation urgent/elective - 12/48 in both groups; re-transplantations - 2/6 (UW, 5/long term) Celsior (p>0.05).

Results: Serum level of AST, ALAT at day 1/2/3 after transplantation was lower in UW-group (p=0.01/0.03/0.00, p=0.02/0.06/0.01). INR was higher at day 1/2/3 in UW-group (p=0.01/0.06/0.06). At day 5/7/14 difference between both groups decline. There were no differences in bilirubin serum level. Complications: biliary 5(8%)-UW, 7(12%)-Celsior (p>0.05); vascular 11(18%)-UW, 6(10%)-Celsior (p<0.05); 1-year survival time: 93%UW, 77%Celsior (including long term re-transplantations).

Conclusion: Celsior similarly to UW may be safely used in multi-organ harvesting, in order to unification and simplification of procedure and considering the price.

PO-801 IMPACT OF MELD SCORE ON PATIENT OUTCOMES FOLLOWING ADULT LIVING DONOR LIVER TRANSPLANTATION (ALDLT)
Constantino Fondevila, Ramón Charco, José Fuster, Joana Ferrer, Alberto Sánchez-Fueyo, Miguel Navasa, Antonio Rimola, Juan C. García-Valdecasas. Department of Surgery, Liver Transplant Unit, Hospital Clinic, University of Barcelona, Barcelona, Spain.

The aim of this study is to analyze if MELD score may be helpful in the selection of candidates for ALDLT.

Patients and methods: Forty-five cirrhotic patients who underwent ALDLT between March 2000 and March 2005 were included in the study. Twenty-six were male (58%) and 19 female (42%). Mean age was 55±11 years (n=23-68). Thirty patients (65%) had HCV related cirrhosis, 7(15%) alcoholic cirrhosis and 8 (20%) had other hepatic diseases. In 20 cases (43%) the main indication for liver transplantation was the presence of hepatocellular carcinoma. The median follow-up was 27 months (CI 95%: 21-32).

Results: Child-Pugh classification/mean MELD score was: 13 (29%) A9-3 points, 16 (36%) B11-4 points and 16 (36%) C18-4 points. Overall mortality was 20% (9 patients). Five of 32 patients with MELD>18 (16%) and 4 of 8 patients with MELD>18 (50%) died (p=0.02). In this last group two patients died due to septic complications at 2 and 4 months after the transplantation due to HCV recurrence at 34m and due to lung cancer at 23m.

Causes of death during follow-up for patients with MELD >18 were: HCV re- cure (3), secondary biliary cirrhosis (1), pulmonary fibrosis (1). One- and 5-yr actuarial patient survival rates were: 86% and 71%.

Conclusions: Early post-transplantation mortality after ALDLT is low when MELD score is less than 26. Despite the low number of patients, the relative risk for late mortality in our series seems to be affected by MELD score.

PO-802 VALIDATION AND CALIBRATION OF CARDIOVASCULAR RISK SCORES IN A EUROPEAN LIVER TRANSPLANT POPULATION
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Although an increased prevalence of cardiovascular risk factors has been described in liver transplant recipients, an individual risk determination has not yet been established. Here, we evaluate cardiovascular risk scores in an European liver transplant population.

Methods: Out-patient charts of 438 primary liver transplants performed between 9/1988 and 4/1994 were reviewed. Three established cardiovascular risk scores were calculated at 6 months post-transplantation and were correlated with cardiovascular events observed during 10 years of follow-up. ROC-analysis was performed to validate SCORE, PROCAM and Framingham (FRS) scores.

For calibration, the Hosmer-Lemeshow-Test was performed and the risk ratio was calculated.

Results: 303 patients with a median age of 48 years were available for analysis and demonstrated complete follow-up data. 37 patients died before census (8.5%). 26 were re-grafted and 72 were excluded for various reasons. 50 out of 303 patients experienced fatal or non-fatal cardiovascular events (16.5%). Numbers of patients meeting the different inclusion criteria for SCORE, PROCAM and FRS calculation were 126, 67 and 93, respectively.

In ROC-analysis, corresponding area-under-the-curve were calculated with 0.800, 0.778 and 0.707. The FRS demonstrated a low discrimination capability for high risk patients. Goodness-of-fit for SCORE was acceptable (χ²=9.1, p=0.330).

PROCAM demonstrated an improved goodness-of-fit (χ²=6.9, p=0.046) and the risk ratio calculated with 0.887 (95%-CI: 0.241-1.532).

Conclusion: SCORE and PROCAM proved valuable in discriminating our liver transplant recipients for their individual risk of cardiovascular events. The FRS, derived from an US-population, did not generalize well with our transplant population. With its excellent calibration, PROCAM provides a tool to calculate number-of-patients-needed-to-treat (NNT) for intervention trials.

PO-803 TRANSARTERIAL CHEMOEMBOLIZATION (TACE) IN PATIENTS WITH PRIMARY CARCINOMA ASSOCIATED WITH CIRRHOSIS OF THE LIVER. ITS INFLUENCE ON LONG-TERM SURVIVAL FOLLOWING CURATIVE OR PALLIATIVE TREATMENT
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Background: The aim of the present study was to analyse the impact of TACE on the long-term survival of patients with primary liver carcinoma in a cirrhotic liver treated either in palliative or curative intent.

Patients and Methods: Between 1996 and 2004, a total of 93 patients were admitted to the study, in 59 patients TACE was performed as a palliative measure, in 4 patients as preparatory treatment prior to elective liver resection (LR), in 20 patients as a "bridging measure" prior to planned liver transplantation (LTX).

Results: In the patients with a purely palliative indication, a survival rate of 29.5% after 12 months and 17.4% after 24 months was observed. 3/4 of the patients undergoing LR (hemipatectomy) and preparatory TACE are still alive and recurrence-free 3-101 months after surgery. To date, 8/20 of the evaluated and chemoembolized patients scheduled for liver transplantation have been transplanted. In 5 of these patients, the tumour stage at the time of TACE was already outside of the “Milan criteria.”
Lung

**Poster Presentations**

**PO-804**

THE ROLE OF THE COORDINATING NURSE AND SOCIAL WORKER IN TRANSPORTATION OF LIVER TRANSPLANT CANDIDATES TO REMOTE TRANSPLANT CENTERS

Mina Rowe, Yemima Lupo. Liver Unit, Hadassah Medical Center, Jerusalem, Israel.

**Purpose:** As a result of donor shortage in Israel and in order to save life, patients with end-stage disease are occasionally transported to remote liver transplant centers. Thus, the coordinating nurse and the social worker have additional tasks beyond their original job description.

**Methods:** Between 2000-2004 we conducted counseling sessions with candidates for liver transplantation who suffered from fulminant hepatitis or end-stage liver disease. Topics discussed: Making the decision and dealing with fears regarding death and the outcome of surgery; living abroad in a foreign country without kids/family members and finding and financing adequate lodging. The socioeconomic status of most patients (82%) was reasonable, but some patients (18%) had financial difficulties, which required special attention.

**Results:** Forty-five patients were transported to: Germany, Belgium, Italy, USA and China. Nine died prior to operation, eight after transplantation; three recovered spontaneously and the rest were transplanted. All patients were accompanied by a family member, 17 patients were also escorted by a physician. The majority of patients (57%) resumed jobs, but 17% were too old, 12% too young and 14% were only a short period after surgery. From meetings we conducted with patients on their return, it was evident that the guidance and preparation assisted patients to cope with difficulties whilst abroad.

**Conclusion:** Transporting patients for liver transplantation out of Israel proved to be life saving. Pre-travel guidance was of significant importance for patients and their families and enabled them to overcome many of the difficulties encountered during that long process.

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**PO-805**

CMV PROPHYLAXIS IS INEFFECTIVE AGAINST HUMAN HERPESVIRUS-6 IN LUNG TRANSPLANT RECIPIENTS

Juho T. Lehto, Maija Halme, Jorma Sipponen, Irmeli Lautenschlager, Dept of Pulmonary Diseases, Hyvinkää Hospital; Div of Respiratory Diseases; Dept of Thoracic Surgery; Transplant Unit Research Laboratory and Dept of Virology, Helsinki University Central Hospital, Helsinki, Finland.

**Purpose:** We report the incidence of human herpesvirus 6 (HHV-6) and human herpesvirus 7 (HHV-7) in lung transplant recipients receiving prophylaxis against cytomegalovirus (CMV).

**Methods/Materials:** 19 lung transplant recipients were prospectively monitored for the three betaherpesviruses (HHV-6, HHV-7 and CMV) during the pre-operative intake of oral CS (low dose ≤5 mg/d, high dose >5 mg/d), and investigated for surgical ≤2d and non-surgical ≥3d postoperative bleeding requiring rethoracotomy.

**Results:** Mean CS levels in recipients with late postoperative bleeding (n=11, 12.8%) were significantly higher (16.6 ±4.6 mg) compared to 70 patients (81.4%) with no bleeding (6.9 ±8.0 mg, p<0.01), or early bleeding (3.5 ±3.4 mg) in 5 patients (5.8%). Furthermore, perioperative mortality (30d or hospital mortality) was significantly increased in the group with late bleeding (27.3%) compared to the group without (4%), p=0.026) or early bleeding (0%), p=0.3.

**Conclusion:** Patients listed for lung transplantation with high dose preoperative oral CS intake have a significantly increased risk of late postoperative bleeding. The perioperative mortality and the probability of 1-year survival of recipients with late bleeding are severely affected compared to patients with no or early bleeding.

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**PO-806**

PREOPERATIVE ORAL CORTICOSTEROIDS PREDICT THE RISK OF LATE POSTOPERATIVE BLEEDING AND PERIOPERATIVE MORTALITY IN LUNG TRANSPLANTATION

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**Purpose:** Preoperative treatment with oral corticosteroids (CS) is common in patients listed for lung transplantation (LTX). It was the aim of this study to investigate if high dose preoperative corticosteroids are associated with increased incidence of late postoperative bleeding.

**Methods:** 86 (mean age 51.7 ±11.8 years) out of 107 consecutive lung transplant patients between November 1, 1993 and August 31, 2004 were evaluable for pre-operative intake of oral CS (low dose ≤5 mg/d, high dose >5 mg/d), and investigated for surgical ≤2d and non-surgical ≥3d postoperative bleeding requiring rethoracotomy.

**Results:** Mean CS levels in recipients with late postoperative bleeding (n=11, 12.8%) were significantly higher (16.6 ±11.1 mg) compared to 70 patients (81.4%) with no bleeding (6.9 ±8.0 mg, p<0.01), or early bleeding (3.5 ±3.4 mg) in 5 patients (5.8%). Furthermore, perioperative mortality (30d or hospital mortality) was significantly increased in the group with late bleeding (27.3%) compared to the group without (4%), p=0.026) or early bleeding (0%), p=0.3.

**Conclusion:** Patients listed for lung transplantation with high dose preoperative oral CS intake have a significantly increased risk of late postoperative bleeding. The perioperative mortality and the probability of 1-year survival of recipients with late bleeding are severely affected compared to patients with no or early bleeding.

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**PO-807**

NAC REDUCES INFLAMMATORY CELLS IN BRONCHO-ALVEOLAR LAVAGE IN A MURINE LUNG ISCHEMIA-REPERFUSION INJURY MODEL

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**Purpose:** Ischemia-Reperfusion Injury (IRI) remains an important risk factor for the early survival of lung transplant recipients. Neutrophils are crucial in the development of IRI. N-Acetyl Cysteine (NAC) is known to be a potent antioxidant. In this study we investigated the impact of NAC on cellular events in Broncho-Alveolar Lavage (BAL) in a model of in situ ischemia and reperfusion.

**Methods/Females:** Small SWISS mice were divided in 5 groups (n=6/group). After thoracotomy, the hilum of the left lung was clamped to induce warm in situ ischemia for 90 minutes in all groups, except in SHAM and unclogged group (n=6). NAC (50 mg/kg) or saline was instilled endotracheally for 15 minutes before the onset of ischemia. After sacrifice, BAL was obtained by instillation of 4x500 µl saline in the left lung for microscopic analysis of cell count.

**Results:** Mean ±SD are listed in Table.

| Group        | Total (n=6) | NAC+I+R | 80.3 ±6.6 | 15.0 ±4.4 | 4.8 ±3.2 |
|--------------|-------------|---------|-----------|-----------|---------|
| **SHAM**     | 87.2 ±2.7   | 11.9 ±3.1 | 0.4 ±0.2  |           |         |
| **Saline+I** | 77.8 ±4.6   | 21.8 ±4.5 | 0.8 ±0.5  |           |         |
| **NAC+I**    | 84.2 ±3.8   | 15.2 ±3.7 | 0.8 ±0.5  |           |         |
| **NAC+I+R**  | 72.2 ±6.7   | 14.0 ±3.4 | 14.3 ±2.9 |           |         |

**Conclusion:** Administration of NAC attenuated the lymphocytic increase during ischemia and resulted in a decrease in neutrophils after reperfusion. Whether there is a biochemical trigger between lymphocytes and neutrophils needs to be further investigated. Donor pretreatment with NAC could be a promising tool to reduce IRI in lung transplantation.
INCIDENCE OF INFECTION IN SINGLE LUNG TRANSPLANT RECIPIENTS. COMPARISON OF MYCOPHENOLATE MOFETIL AND AZATHIOPRINE

Steve J. Richardson, John R. Cain, James B. Barnard, Mohamad N. Bittar, Nizar Yonan, Cohn Leonard, The Transplant Centre, South Manchester University Hospitals Trust, Wythenshawe, Manchester, United Kingdom. Mycophenolate Mofetil (MMF) is increasingly used as a first or second line immunosuppressant in lung transplant patients in conjunction with Cyclosporine and Prednisolone. Azathioprine (AZA) is the established alternative. The comparative incidence of infective complications between the two drugs is not clearly defined in the literature. In this study we compared the rates of infection in two groups of patients, one treated with AZA, and the other with MMF.

Methods: We assessed 34 consecutive single lung transplant patients who were assessed in a prospective study between 1996 and 2003 were studied. Group 1 received MMF and group 2 received AZA. All positive microbiology and virology reports generated over 1 year following transplantation were collected. We collected data regarding site of infection, infecting organism, and time post transplantation.

Results: Patients were well matched in terms of age and sex between groups. There were more viral respiratory tract infections in the MMF group (Cy-tomegalovirus, PCR positive, log > 4.6) in the first month post-op (p = 0.015) this trend continued throughout the rest of the study period (p = 0.099). There was no statistically significant difference in bacterial infection rates between the two groups, however a trend towards increased bacterial infection in the MMF group was observed.

Conclusion: Use of MMF for immunosuppression following single lung transplantation carries a higher risk of viral infection, particularly in the first month following surgery. All other infection rates may also be increased but further studies with larger sample size are required.

PO-809 PDGF, TGF-β, AND CTGF IN POST-TRANSPLANT OBSTRUCTIVE BRONCHIOLITIS (OB)

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Introduction: PDGF, TGF-β, and CTGF promote fibroblast proliferation and mediate inflammatory responses. The expression of these growth factors and the effect of imatinib, a protein tyrosine kinase inhibitor targeting PDGF receptors was assessed in a porcine model of OB.

Methods: Small bronchi were transplanted subcutaneously into 12 pigs. Study included autografts, nontreated allografts, and allografts treated with imatinib (daily orally 10 mg/kg). The grafts were harvested on days 4, 7, 11, and 14.

Results: By day 7, nontreated allografts showed complete epithelial destruction, which was slightly less extensive in the treated allografts. Obliteraton was slower in the treated group (p = 0.05 on day 11). Imatinib reduced recruitment of CD4+ lymphocytes, of CD8+ lymphocytes, and of macrophages (p < 0.05). Expression of PDGF-A, PDGF receptors, and of TGF-β was elevated in the nontreated allografts in comparison to autografts. PDGF-B expression was mild in all groups. In inflammatory cells in nontreated allografts, moderate positivity for PDGF-A appeared; in treated allografts it was mild (p < 0.05). Fibroblasts and inflammatory cells showed milder positivity for the PDGF receptors in the treated group (p < 0.05). In the endothelium, receptor expression was mild in both groups, except on day 7, when it was moderate in nontreated allografts (p < 0.05). In both allograft groups, TGF-β and CTGF expression ranged from moderate to intense.

Conclusions: These findings confirm the contribution of PDGF and TGF-β to OB. Imatinib, and agent targeting PDGF receptors, modified the expression patterns of PDGF-A and PDGF receptors, and had influence on the number of CD4+ and CD8+ lymphocytes, and of macrophages, and to some extent on obliteration. This indicates the importance for OB development the pathways signaled through PDGF receptors.

PO-810 IMPROVEMENT OF CHRONIC RENAL IMPAIRMENT WITH EVEROLIMUS IN COMBINATION WITH TACROLIMUS AFTER LUNG TRANSPLANTATION

Peter Jaksch1, Susanne Guth1, Bernhard Schlechta 1, Wilfried Wisser 1, Federico Venuta 2, Nizar Yonan, Colm Leonard. The Transplant Centre, South Manchester University Hospitals Trust, Wythenshawe, Manchester, United Kingdom. Everolimus administration allows amelioration of renal function with a relatively low morbidity and is useful for chronic renal impairment after lung transplantation.

Conclusions: Everolimus administration allows amelioration of renal function with a relatively low morbidity and is useful for chronic renal impairment after lung transplantation.
CONVERSION TO SIROLIMUS AND MYCOPHENOLATE 
KIDNEY-PANCREAS TRANSPLANT IMPROVES 
RESTING FORCED OSCILLATION 
TECHNIQUE PREDICTS THE 
NEW PANCREATIC TRANSPLANTATION BENCHWORK 

Akihiko Aoyama, Takuji Fujinaga, Mitsugu Omasa, Nobuharu Hanaoka, Hiroshi Hamakawa, Hiroaki Sakai, Izumi Matsumoto, Fengshi Chen

Conclusions: After BOS is diagnosed, conversion to Sirolimus and MMF can stabilize graft function only in a small part of the converted patients. Whether this conversion can really diminish the progress of BOS has to be investigated in larger, randomized trials. Earlier administration of Sirolimus-based immunosuppression might be a more promising approach.

PO-814 
FORCED OSCILLATION TECHNIQUE PREDICTS THE SEVERITY OF PHYSIOLOGIC DYSFUNCTION IN THE LUNG TRANSPLANT CANDIDATES WITH LYMPHANGIOLEIOMYOMATOSIS: APPLICATION OF IMPULSE OSCILLOMETRY

Hiroshi Hamakawa, Hiraoki Sakai, Izumi Matsumoto, Fengshi Chen, Akihiko Aoyama, Takaji Fujinaga, Mitsuhiro Omasa, Nobuharu Hanaoka, Toru Bando, Tatsuo Fukuse, Hiromi Wada. Department of Thoracic Surgery, Kyoto University, Kyoto, Japan.

Background: Impulse Oscillometry (IOS: Erich JAGER GmbH, Germany), which is recently introduced as a new noninvasive and repeatable method to evaluate pulmonary function, is to be able to differentiate between central and peripheral components of airway condition at different oscillation frequencies. Purpose: To assess the severity of physiologic dysfunction, IOS was used to the lung transplant candidates with pulmonary lymphangioleiomyomatosis (LAM). Materials and Methods: Seven lung transplant candidates with LAM, whose mean age (±SD) was 29.7±4.8 years, range (24 to 39 years), underwent lung function test using Spirometry, lung volumes and IOS in stable condition. Relationships between the traditional lung function parameters (i.e., FVC, FEV1, PEF, RV/TLC and so on) and following parameters of IOS were assessed with Pearson correlation coefficients. As the parameters of IOS, we used Resistance at 5 Hz (R5), Reactance at 5 Hz (X5), Respiratory Frequency (RF) and integrated low-frequency reactance area between 5 Hz to RF (AX) to evaluate the lung mechanical properties. Results: R5 correlated with %FEV1 (r=0.74), FEV1% (r=0.72), PEF (r=0.79) and RV/TLC (r=0.90). RF correlated with PEF (r=0.82), 1/AX had good correlation with FVC (r=0.82), FEV1 (r=0.75) and %FEV1 (r=0.77). Conclusions: Several parameters of IOS had correlations with physiologic measurements of airflow and lung volumes, statistically. Therefore, IOS could be a useful and potential monitoring tool to evaluate disease severity and prognosis of LAM patients.

PO-815 
THE PRESSOR RESPONSE AND AIRWAY EFFECTS OF CRIOCID PRESSURE DURING INDUCTION OF GENERAL ANESTHESIA

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Background: CRIOCID pressure (CP) has been used to protect the patient from regurgitation and gastric insufflation. Because the hemodynamic effects of CP have not been evaluated independently, we designed this prospective study. Method: Eighty ASA I adult patients were prospectively included in the study. Patients were randomly divided into CRIOCID and Placebo groups. In the CRIOCID group, after the induction of anesthesia, bimanual CP was performed, and in the Control group, simple placement of hands without exerting pressure was performed. Peak inspiratory pressure and exhaled tidal volume were recorded before and during the application of CP. Arterial blood pressure and heart rate were recorded before and after application of CP. The data were compared between and within groups by using the mixed-design analysis of variance. Results: Peak inspiratory pressure increased and tidal volume decreased significantly after the application of CP compared with the Control group and baseline values. Arterial blood pressure and heart rate increased significantly after the application of CP compared with the baseline values and with those of the Control group. Conclusion: The result of this study shows that CP can cause a relatively strong pressor response, and so in old patients with borderline heart disease we must decide about using CP only if it is necessary.

PO-816 
KIDNEY-PANCREAS TRANSPLANT IMPROVES RESTING CARDIAC HIGH ENERGY PHOSPHATES METABOLISM IN TYPE 1 DIABETIC (T1DM)-UREMIC PATIENTS: A 31P-MRS STUDY

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Heart failure occurs in 40% of patients with end-stage renal disease and is recognized to be the major determinant of mortality in patients with T1DM and uremia. We assess in humans in a cross-sectional fashion: 1) whether patients with T1DM and uremia are characterized by abnormal resting heart HEPS metabolism notwithstanding a preserved resting ejection fraction and absence of cardiovascular events and 2) the effects of kidney (K-Tx) or combined kidney-pancreas (KP-Tx) transplantation on HEPS metabolism using in vivo heart 31P-MR Spectroscopy. We studied 8 T1DM patients with uremia, 7 K-Tx, 13 KP-Tx and 11 healthy subjects matched for anthropometric features. We used a 1.5T Gyroscan MR System (Philips Medical Systems). A 100-mm-diameter surface coil was used to acquire 31P-spectra and 3D-ISIS was used to select the volume of interest. 31P-spectra were quantified automatically and corrected for partial saturation effects and for ATP contribution from blood. In the 31P-MRS heart spectrum, the phosphocreatine/PCr/ATP ratio is the parameter of major interest of HEPS metabolism. PCr/ATP ratio resulted to be reduced in T1DM with uremia (1.31±0.05; P=0.000) with respect to normals (1.58±0.05). This parameter resulted to be normal in both K-Tx (1.48±0.10; P=0.32 vs normals) and KP-Tx (1.59±0.07; P=0.95 vs normals). In conclusion, diabetic uremia is characterized by early alterations of heart HEPS metabolism which may be reversed by K- or KP-Tx.

PO-817 
NEW PANCREATIC TRANSPLANTATION BENCHWORK TECHNIQUE – REPORT AT SINGLE CENTER

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The aim of this new technique is to decrease operative time, increase safety, and simplify this complex procedure. The pancreas benchwork preparation consists of splenectomy overrunning the duodenal staple lines identification and ligation of periampullary lymphatic tissue and small vessels, and vascu- lar reconstruction using an arterial extension iliac Y graft for the donor. In the classical benchwork, individual vessels are identified and double ligated. This technique is time consuming, requires extensive graft manipulation and has the disadvantage that complete haemostasis is difficult to achieve. We have used the ETS-FLEX (articulating) Endoscopic Linear Vascular Cutter (ELVC) for dividing vessels in the pancreas benchwork. The vascular stapler applies three staple lines proximally and three distally and divides the vessel between them. There are three steps where the ELVC is applied: (a) the splenic flexures, (b) the superior mesenteric and (c) the spleno- pancreatic lymphatic tissue. We have used this technique in 24 pancreatic grafts. The versatility for the benchwork preparation including the Y-graft anastomosis was 46±15 min. Following revascularization, there was excellent reperfusion of all grafts with minimal bleeding. We believe that our modification makes a complex and time-consuming procedure simple and fast, minimizing the chances for postoperative complications and resulting in excellent patient and graft survival.
From Apr 2003 to March 2005 in 17 simultaneous pancreas and kidney transplants sphincterotomy was performed. After revascularisation of the pancreatic transplant, the donor duodenum was open longitudinally and sphincterotomy was performed. Duodenal button was prepared and anastomosed to jejunum. Additionally side-to-side jejunal anastomosis was made. Kidney artery was anastomosed to the external iliac artery. The pancreatic graft was transplanted using standard technique. Immunosuppression consisted of mycophenolate mofetil and steroids. All recipients are alive without renal transplant dysfunction. After sphincterotomy in 16 pancreatic grafts a good outflow of clear pancreatic juice and a lessening of graft tenseness was observed during operation. In two transplants additional sphincterotomy of Santorini duct sphincter was necessary. In one recipient no pancreatic juice secretion was observed after operation. Independence was not obtained therefore this graft was removed. In 13 recipients there was no graft pancreatitis and peripancreatic fluid collection which required any intervention. In 3 recipients who developed graft pancreatitis 2 required graft pancreatectomy. Sphincterotomy facilitates pancreatic juice outflow therefore reduces intraoperative oedema and subsequent inflammation. Further study on factors inducing graft pancreatitis is necessary to eliminate this severe complication.

PO-821 USEFULNESS OF GENTAMYCIN-COOATED SPONGE IN LOCAL INFECTIOUS PROPHYLAXIS AFTER SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATION

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The incidence of infectious complications after simultaneous pancreas and kidney transplantation (spktx) is higher than in other solid organ recipients. The aim of our study was to assess the usefulness and safety of a gentamycin-coated sponge in local prophylaxis of infection after spktx. Between Nov 2003 and March 2005 in 12 spktx recipients, local additional antibiotic prophylaxis was used, by wrapping the pancreatic graft during transplantation with two gentamycin-coated sponges. Intraoperative and postoperative microbiological samples from abdominal cavity drains were analyzed. Prophylactic graft function measured by serum glucose level and insulin requirement were evaluated. Kidney graft function was assessed by creatinine level. All recipients presented with a good kidney graft function in the postoperative period. In 11 patients (91.6%) good pancreatic graft function was established as mean fasting glucose level was 98.7±19.1 mg/dl 10 days posttransplantation with no insulin requirement. Three transplant pancreatectomies were performed between 7th and 60th days because of pancreatic necrosis and deterioration of graft function. During pancreatectomy local signs of infection were found. In another three recipients microbiological cultures from drains were positive however only one required administration of antibiotics. No signs of nefrotoxicity of gentamycin on transplanted kidney and pancreas function were observed in all cases. Local placement of a gentamycin coated sponge seems to be a promising additional prophylaxis, however this method had a little effect on development of infection due to pancreatic graft necrosis.

PO-822 QUALITY OF LIFE (QOL) – ASSESSMENT OF COMPLICATION AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION (SPKTx)

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The aim of this study was to assess the progress of diabetic complication after SPKTx and psycho-social status of these patients. 48 SPKTx were performed in our Department between 1988 and 2004. Mean patient age was 34 years mean length of diabetes treatment was 23 years. Prior to SPKTx all patients were on maintenance haemodialysis. By the end of 2004, 37 patients were alive. 26 had functioning pancreas and kidney grafts. A questionnaire was sent and received from 26 patients with functioning pancreas grafts. 19 of them consented to take part in the study. 21 of 19 patients had lower limb amputations and 7. 3 patients from this group received both grafts. From the group of 19 patients 7 of 19 patients were totally blind. 13 had retinopathy. 19 reported their QOL as improved compared to pre-transplant status. This was mainly attributed to being dialysis- and insulin-free. 14 of 19 reported controlling their glycaemia regularly which was associated with fear of losing the pancreatic graft. 7 of 19 persons returned to work after transplantation.
Patients should be qualified to SPKTx before occurrence of diabetic complications which can make the return to normal life after SPKTx difficult. Patients after SPKTx experience an improvement in the QOL and, in some cases, return to professional life.

The aim of the study was to evaluate various methods of vascular reconstruction in preparation of pancreas for transplantation. Between 1996 and 2004, 43 whole pancreas grafts during multiorgan harvesting, out of which 37 required vascular reconstruction. In all these cases elongation of the portal vein was done using a donor’s external iliac vein. Bifurcation of the donor’s common iliac artery was used for arterial reconstruction in 33 cases. In remaining cases: the splenic artery was anastomosed to the side of the graft superior mesenteric artery in 3 patients and the brachiocphalic trunk bifurcation was utilized in one patient.

In all the cases perfusion of the transplanted pancreas was achieved. In the early postoperative follow-up, 2 venous and 1 arterial thrombosis were noted. Reconstruction of the pancreas’ vessels does not significantly affect effect of the allotransplant in recipients while notably increasing the available donor organ pool.

In the present investigation we reviewed 102 SPK transplantations performed between July 1996 and July 2004 to study the impact of obesity on this complex surgical procedure and on the outcome of the diabetic recipients. All patients received whole pancreas with enteric drainage, 45 with systemic and 57 with portal venous drainage. At transplantation time ninety recipients presented a BMI less than 25.

We did not show any significant differences in long-term patient survival either kidney or graft survival. However, the significant higher rate of thromboses in the group of obese recipients might indicate a more difficult surgical procedure in these patients and invite to select preferentially SPK transplant recipients with a BMI less than 25.

Conclusion: Enteric conversion is a safe procedure, followed by very low morbidity and mortality and does not increase the rate of graft loss.

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OUTCOME OF PANCREAS TRANSPLANTATION IN A NEW PROGRAMME WITH RAPID STEROID TAPER WITHOUT LIPASE EVALUATION OR PANCREATIC BIOPSY

Aishin Tavakoli, Sanjay Mehra, Ravi Paranajasingam, Mark Clancy, Babatunde Campbell, Hany Riad, Neil Parrott, Titus Augustine. Transplant Unit, Central Manchester and Manchester Children’s University Hospitals, Manchester, United Kingdom.

Aim: We evaluate the outcome of pancreas transplantation in a new programme with focus on early steroid minimization without lipase assay or pancreatic biopsy.

Methods: Between June 01 and April 05, 52 pancreas transplants were done, (40) SPK and (12) PAK, in patients (age range 15 to 59) suitably screened. All recipients had Basililakim induction and maintenance immunosuppression with Tacrolimus, Mycophenolate Mofetil and Prednisolone. Steroids were tapered after 4 weeks and between 3-6 months stopped entirely. Rejections were monitored by a combination of kidney biopsy (SPK), serum amylose, CRP and blood sugars. Rejections were treated with steroid pulses.

Summary: 48 patients are alive and well. In the SPK group, there were 3 peri-transplantation infections and one death with functioning grafts at 1 year from a CVA. 4 patients developed pancreas thrombosis with maintained kidney function. Of the PAK group all patients are alive and well with 8 functioning grafts. 3 grafts were lost from thrombosis and 1 from immunosuppression reduction due to PTLD. All patients with functioning grafts are off insulin entirely with normal HbA1c. There have been 10 episodes of acute rejection in 8 patients requiring ATG. The main morbidity in this series has been surgical with interventions for infective complications in 54% of patients.

Conclusion: Experience from this learning curve seems to suggest that excellent outcomes can be obtained from dual immunosuppression with early steroid taper, once the surgical learning curve has been dealt with.

SYSTEMIC AND CENTRAL NERVOUS SYSTEM INFECTION COMPLICATIONS AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION (SPKTx) – A RETROSPECTIVE SINGLE-CENTRE STUDY

Grzegorz Michalak, Artur Kwiatkowski, Jaroslaw Czerwinski, Monika Bieniasz, Michal Wolszada, Rafal Nosek, Andrzej Chmura, Jadwiga Meszaros, Wojciech Lisik, Leszek Adadynski, Piotr Mikołajski, Sławomir Feslowicz, Tomasz Kasprzyk, Magdalena Durlik, Janusz Wałaszeski, Wojciech Rowinski. Department of General and Transplantation Surgery, Warsaw Medical University, Warsaw, Poland.

SPKTx improves long-term survival of insulin-dependent diabetes mellitus patients with diabetic nephropathy. The morbidity and mortality following SPKTx remain high, mainly due to infections. A study was performed to investigate the infection complications following SPKTx. 48 patients underwent SPKTx in our centre. Of that total, 20 patients had a primary (neonatal) (19%) and 28 patients had enteral drainage (ED). Prior to SPKTx all patients were treated by bariatryy. Overall mortality in the investigated group was 23%. Infectious complications were the main cause of death (81%), including systemic infections (45%) and CNS infections (36%). The etiology of CNS infections was fungal in 2 patients. One patient had positive latex reaction with Cryptococcus neoformans antigen from cerebrospinal fluid, in 2 patients the fungal infection was diagnosed on the grounds of clinical symptoms. Relaparotomies were performed in 19 SPKTx patients (39.6%), mostly for urinary fistula. Only one patient was reoperated on because of infectious complications (intra-abdominal abscess). Perioperative complications were observed in 32/37 surviving patients. CMV infection occurred in 25% of patients despite ganciclovir prophylaxis policy. Urinary tract infections were observed in 14 patients, more frequently in the group with UD. Infectious complications are the main cause of morbidity and mortality following SPKTx, especially for UD. The use of enteric drainage combined with administration of a broad-spectrum prophylactic antibiotics, anti-fungal and anti-viral agents is recommended.

DERANGEMENT OF LIVER FUNCTION AFTER PANCREAS TRANSPLANTATION

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Introduction: The early complications of pancreas transplantation, including haemorrhage, graft pancreatitis, anastomatic dehiscence, vascular thrombosis and prolonged intestinal ileus are well documented. However, the systemic effects of pancreas rejection and rapid changes in glucose homeostasis are less well understood. We therefore investigated the effect, if any, of pancreatic transplantation on liver function.

Methods: 45 patients underwent pancreas transplantation at our institution (40 SPK, 3 PAK, 2 pancreas alone) during 2000-2004 using intrabdominal im-plantation, caval venous drainage and enteric exocrine drainage. Serum ala-nine aminotransferase (ALT), alkaline phosphatase (AP) and gamma glutamyl transference (GGT) were recorded pre-operatively and on days 3, 5, 10, 14 and 20 post-operatively.

Results: 37 patients (82%) had functioning grafts at median follow up of 1 year. 25 patients (56%) developed abnormal liver function during the first 20 days after pancreas transplantation. Elevated ALT and AP peaked at day 10 and GGT at day 14. By day 20, ALT and AP had returned to normal in 19 patients whereas GGT remained elevated in 24 of 25 patients for median 3 months (range 1-12 months). There was no correlation between liver function derangement and graft loss, CMV mismatch, drug therapy or early complications.

Discussion: Pancreas transplant is associated with significant liver dysfunction in over 50% of patients and may take up to 12 months to resolve. The mechanism is unclear but reflects the systemic response to pancreatic reperfusion and altered insulin delivery via the systemic circulation.

ABSORPTION PROFILING OF CYCLOSPORINE MICROEMULSION (NEORAL) DURING THE FIRST 3 WEEKS AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

Michael Gock 1, Rainer Wacke 2, Bernd Drewelow 2, Ernst Klar 1, Wolfgang Schareck 1. 1 Department of General, Vascular, Thoracic and Transplantation Surgery, University of Rostock, Germany; 2 Institute of Clinical Pharmacology, University of Rostock, Germany.

Purpose: Immunosuppression with cyclosporine microemulsion (Neoral) in combination with short time cortis and MMF is an established therapy regimen after simultaneous pancreas-kidney transplantation although therapy with tacrolimus is considered to be the gold standard. Standard through level monitoring was shown to be inadequate for precise concentration-controlled therapy after kidney transplantation. Therefore we tested the pharmacokinetic profile of Neoral as a superior approach for guiding clinical immunosuppression after de novo simultaneous pancreas-kidney transplantation.

Methods: A total of 10 pancreas-kidney recipients with type-1 diabetes and end-stage renal disease were included consecutively. All patients received treatment with triple drug immunosuppression consisting of Neoral, MMF, and prednisone. Full (B-point) pharmacokinetic studies (C0,C1,C2,C4,C6,C8,C10,C12) were performed on day 3 and day 16 to examine the pharmacokinetic profile of Neoral. All patients agreed to the informed consent to take the blood sampling repetitively.

Results: One patient had to be converted to intravenous cyclosporine due to insufficient enteric absorption after oral intake. Three patients had to be switched from cyclosporine to tacrolimus due to episodes of acute rejection on day 6, 15 and 16. Mean area under the curve (AUC) over the 12-hr dosage interval (AUC[0-12]) was 513±2258 µg.h/L by day 3 and remained stable by day 16 (515±915µg.h/L). Peak cyclosporine concentration (C2) on day 3 was 639.6±227.3 µg.h/L and remained stable on day 16 (687.5±142.5 µg.h/L).

Conclusion: Absorption of Neoral is highly heterogeneous after pancreas-kidney transplantation. Our preliminary data support that C2 and C4 sampling are more accurate predictors of the AUC than C0.

EXPERIMENTAL SURGERY TO CLINICAL SUCCESS: THREE DECADNES OF PANCREAS TRANSLANTATION AT A EUROPEAN INSTITUTION

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Purpose: Outcome of kidney pancreas transplants (PKT) in diabetics according to surgical techniques (ST) and immunosuppression (IS) that evolved during three decades in a European small volume PKT program.

Methods: All PKT from 1973-2004 were analyzed. According to ST and IS, three treatment eras were defined. Era1: 1973-1980, prednisone/azathioprine, various ST including enteric drainage and segmental transplantation; Era2: 1981-1996, introduction of Cyclosporine A, various ST including bladder drainage and segmental transplantation; Era3: 1997-2004, prednisone/MMF/tacrolimus and anti-IL2R-antibodies, predominantly enteric drainage. Primary endpoint was patient survival at 1 and 5 years. Secondary endpoints included graft survival, causes for patient death and graft loss, incidence of surgical, infectious, neoplastic and cardiovascular complications.

Results: 160 PKT were performed in 152 patients (complete followup in 145). In Era1, 1/7 patients survived the first year and is alive 24y thereafter. 1 and 5y survival rates were 76% and 63% in Era2 (n=110) and 100% after 1 and 5y in Era3 (n=35). Pancreas survival at 1 and 5y improved from 58% and 53% in Era2 to 100% in Era3. Kidney survival improved from 67% and 53% to 100% after 1 and 5y in Era2 and Era3. Patient death (total n=96) was mainly due to cardiovascular (n=31) and infectious (n=12) reasons. Main reasons for
pancreas loss (total n=77) included acute (n=28) and chronic (n=11) rejection and thrombosis (n=22). Kidney loss (total n=60) was mainly due to chronic (n=28) and acute (n=7) rejection.

Conclusion: PTK for treatment of diabetes has evolved into a highly successful therapy. Implementation of ST in combination with current IS makes PTK an excellent therapeutic option, even in a small volume PKT center.

**CORTICOSTEROID WITHDRAWAL IN SIMULTANEOUS Pancreas-KIDNEY (SPK) TRANSPLANTATION: A 3-YEAR REPORT**

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Corticosteroids are an important element of immunosuppressive protocols, but their long-term use has detrimental effects on patients' health, necessitating eventual discontinuation. This 3-year prospective, open-label study evaluated the feasibility of corticosteroid withdrawal in SPK transplant patients randomised to receive tacrolimus (n=103) or ciclosporin microemulsion (ME)-based therapy (n=102). Starting daily doses of tacrolimus (0.2mg/kg) and ciclosporin-ME (7mg/kg) were titrated to give trough levels of 8-15mg/mL and 150-250mg/mL, respectively. Patients also received MMF, iATG and corticosteroids, which were progressively tapered to 5mg on day 43-90 and stopped thereafter. During the 3-year study, fewer patients withdrew from treatment with tacrolimus than with ciclosporin-ME (n=28 vs n=55, respectively). In patients remaining in the study, corticosteroid withdrawal was achieved in 54 patients receiving tacrolimus and in 37 receiving ciclosporin-ME. Overall, there was no increased risk of acute rejection following corticosteroid withdrawal (32%) compared with ciclosporin-ME maintenance (48%). Renal function, assessed by serum creatinine (1.4±0.3 vs 1.5±0.6mg/dL) and creatinine clearance (67±20 vs 65±25mL/min), was similar in the corticosteroid withdrawal group to that in the ciclosporin-ME maintenance group and was also comparable to the tacrolimus/corticosteroid-ME groups. Corticosteroid withdrawal had no adverse effect on pancreatic function determined by fasting levels of blood glucose (88±16 vs 85±10mg/dL) and C-peptide (2.6±1.3 vs 2.7±1.5ng/mL). Total cholesterol was lower (p<0.05) with tacrolimus than with ciclosporin irrespective of corticosteroid use. Longer follow up is needed to confirm these encouraging results and to evaluate the potential positive effects of steroid withdrawal on glucose metabolism and hypertension.

**FIFTEEN YEARS EXPERIENCE OF THE "EN BLOC" TECHNIQUE FOR Pancreas AND KIDNEY TRANSPLANTATION**

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Combined kidney and pancreas transplantation (P-Kd Tx) is usually performed by placing intraperitoneally the kidney graft in one iliac fossa and the pancreas graft in the other iliac fossa. In order to reduce the operative time, the extent of the dissection and to avoid any delay in the revascularization of the grafts, an "en bloc" technique was designed and performed for the first time in 1991. The "en bloc" P-Kd Tx technique has already been presented at the ESOT meeting in 1993.

Briefly, it consists in:

- The vascular pedicles of both grafts are attached to the donor aorta and inferior vena cava, the proximal part of these vessels is closed and the distal part is anastomosed to the iliac vessels of one iliac fossa.
- Since 1991, 26 P-Kd Tx have been performed in 25 patients for type 1 diabetic nephropathy. One and five year graft and patient survivals are depicted in table 1. Mean operative time was 5 hours (4-7 hours) and total ischemia time was the same for both organs. In our population, the longest survivor has now reached more than 11 years with both organs functioning well.

**Table 1**

| One year | Five years |
|----------|------------|
| Patient Survival | 85% | 76% |
| Graft Survival | 77% | 71% |
| Pancreas | 81% | 57% |

"En bloc" kidney and pancreas transplantation constitutes a valuable alternative to the standard bilateral technique of kidney and pancreas transplantation. It offers the advantage of restricting the dissection to one single iliac fossa and to reduce the operative time.

**ANALYSIS OF SHORT TERM Pancreas GRAFT OUTCOME WITH THREE DIFFERENT PROTOCOLS OF SOLUTIONS FOR IN SITU AORTIC FLUSH**

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Different organ preservation solutions have been used and compared for pancreas transplantation. Costs and benefits of each one of them are still to be defined. A retrospective analyses was performed comparing biochemical performance and the survival of 62 pancreatic grafts which were divided according to in situ aortic flush: Group 1(UW-UW)=35, Group 2(UW-EC)=14 and Group 3(3C=UW)=13. During perfusion of group 2 (UW+EC), mesenteric superior and splenic arteries flows were interrupted using vessel loops after one liter of UW, trying to avoid EC infusion into the pancreas. All grafts were stored in UW. Donor criteria were analyzed, including age, BMI, ICU time, cardiorespiratory arrest, vasoactive drugs, cause of death, serum amylases and glucose levels. Mean values of serum glucose, amylase, amylase peak, lipase, lipase peak and urinary amylase of each group were monitored for 10 days as well as survival rates, technical failures and graft outcome. Chi square (Pearson/Fischer) and ANOVA tests were applied to compare all results. Primary descriptive analysis showed better results in group 1, where lower rates of technical failure and insulin dependence occurred. Statistical significant differences were found only in serum lipase means values that were lower in group 2 (p=0.029;95:166-302). Similar graft outcomes were observed after these three protocols of pancreas preservation although a slight tendency of worse outcome was shown when EC was infused after UW regardless vascular flow interruption.

**CORONARY ARTERY DISEASE IN Pancreas-KIDNEY TRANSPLANT RECIPIENTS – A CHALLENGE FOR THE PRETRANSPLANT EVALUATION**

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Simultaneous pancreas/kidney transplantation (SPK) is a life-saving procedure for patients with diabetes mellitus type I and end-stage renal disease. These patients are predisposed for cardiovascular disease and coronary artery disease (CAD) is a major cause of death following SPK. From 12/03 to 4/05 25 patients were evaluated for SPK, 9 received successful transplantation, 12 are listed with the urgency "T" and 4 "NT". The group consisted of 11 women and 14 men with a mean age of 42.8 (± 9.6) years. The mean duration of diabetes was 26.8 (± 8.7) years, mean duration of dialysis was 17.5 (± 20.0) months, 7 patients were listed prior to dialysis. All patients underwent mandatory non-invasive cardiac stress testing, 12/25 (48%) adenosine nuclear scan and 7/25 (28%) dobutamine echocardiogram. 12/25 (48%) patients underwent coronary angiographies (CA). In 5/25 (20%) patients the non-invasive diagnostic showed impaired coronary perfusion without signs of coronary artery stenosis in CA. In 6/25 (24%) cases CA was performed at first, 1 due to older age (65 years) and 3 because of cardiac symptoms. In 7/25 (28%) patients the CAs did not reveal any sign of CAD, 2/25 (8%) patients needed intervention with angioplasty and stent, both had had history of CAD. Following transplantation one patient died due to myocardial infarction. He had a history of angioplasty and stent. For evaluation of coronary artery disease prior to SPK listing we suggest routine non-invasive cardiac stress tests. In case of any suspicious result or previous cardiac events like infarction or cardiac bypass a CA is mandatory.

**Pancreas Transplant for Systemic Allergy to Insulin**

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Introduction: Hypersensitivity reactions to insulin preparations, particularly the allergy to metacresol, are quite rare and pose a difficult dilemma for the management of insulin dependent diabetic patients. Case Report: e report on a 30-year old man with type 1 diabetes mellitus for 14 years who developed generalized allergy to insulin. He presented several bouts of tremor, tachycardia, breathlessness and short syncope. He had no history of atopy. Strong positive reactions to protamine and metacresol were demonstrated by skin-prick testing. Symptoms persisted despite use of antihistamine therapy, Actrapid HM Paraben and Monotard (insulin preparations without metacresol and protamine) and immunosuppression therapy.
(tacrolimus). He underwent a cadaver pancreas transplantation with portal-enteric drainage in June 2003. Following ATG induction, basal immunosuppression was achieved by tacrolimus and rapamycine, without steroids. Exogenous insulin was stopped on day 9 post-transplantation. The patient subsequently reports a complete resolution of his symptoms and excellent glycemic control (HbA1c 6.1%) without rejection. Six months later, skin-prick tests remained positive for proamine alone. Twelve months after transplantation, the patient developed recurrent infections and severe leucopenia that were initially attributed to proamine. Rapamycine was substituted by prednisolone (without benefit on white cell count); this led to acute rejection and increased steroids requirements. Exogenous insulin had to be restarted for five weeks and all allergic reactions occurred. Leucopenia resolved concomitantly to atorvastatin withdrawal and prednisolone dosages were progressively tapered. Currently, 18 months after transplantation, the patient is euglycemic without insulin therapy (HbA1c 6.2%) and he is again completely free of allergic reactions.

**Conclusion:** Pancras transplantation alone is an attractive therapy for systemic allergy to insulin in type 1 diabetic patients.

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**Pediatric Transplantation**

**PO-839**

**GROWTH IN PEDIATRIC LIVER RECIPIENTS BEFORE & AFTER TRANSPLANTATION**

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**Purpose:** Growth retardation occurs commonly in children with chronic liver disease. The aim of the current study was to review the factors influencing growth and final height following liver transplantation.

**Methods:** In this retrospective analysis we evaluated the growth of 42 pediatric liver transplant recipients from 1992 to 2002. Inclusion criteria were age younger than 18 years, follow-up longer than 1 year, transplantation for a non-tumor indication, no retransplantation & Child-Pugh classification of B and C. Linear height and growth velocity SD scores were correlated to age, sex, indication for transplantation and graft type.

**Results:** Growth retardation was common (95%) especially in ages more than 11 years old. Recipients aged younger than 24 months showed growth within the first year to achieve a height distribution equal to that of an age-matched population. Post-transplantation growth did not correlate with height standard score at transplantation. Children older than 2 years at transplantation established new growth curves, but remained growth retarded. Growth retardation in transplant recipients with biliary atresia was less common and also showed increased growth performance after that compared with those who underwent transplantation for other causes. Both boys and girls were growth retarded at transplantation without statistical significance for sex but boys showed improved posttransplantation growth performance versus girls. No correlation to graft type was identified.

**Conclusion:** We conclude that early transplantation of children who show growth retardation is optimal for restoration of growth potential and delaying transplantation in older children impedes potential growth.

**PO-841**

**PROSPECTIVE BK VIRUS MONITORING IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS: ROLE OF PROTOCOL/PRE-EMPTIVE IMMUNOSUPPRESSION REDUCTION ON THE COURSE OF INFECTION**

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**Purpose:** Polymya BK virus (BKV)-associated nephritis (PVAN) is a relevant cause of reduced renal allograft survival. Treatment of PVAN has not substantially changed the prognosis, probably due to late intervention. We performed a prospective analysis to evaluate the impact of protocol/pre-emptive immunosuppression reduction on development of PVAN in pediatric kidney recipients. 52 patients have been monitored for BK virus and viremia by quantitative PCR (median follow-up: 18 months). Thirty-nine patients (75%) developed viremia, and 5/52 (9.6%) viremia. Onset of viremia occurred within the first 6 months in 28/52 (56%) patients. Among the 11 evaluable patients with viremia (n=1 case immediate loss of graft function was shown) have functioned well for 140.4±56.2 months (mean ± SD) following transplantation. The interval from diagnosis to initiation of dialysis was significantly shorter in patients with recurrence than those without recurrence (p<0.05), but no other variables differed between these 2 groups. No recurrence of FSGS was observed in the protocol biopsy specimens at 100 days after transplantation. We believe that CYA and native nephrectomy may limit or reverse progression of recurrent FSGS in renal allografts of pediatric patients, although this is a limited study.

**PO-840**

**LONG-TERM OUTCOME OF FOCAL SEGMENTAL GLOMERULOSCLEROSIS AFTER LIVING-RELATED PEDIATRIC RENAL TRANSPLANTATION**

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**Purpose:** Focal segmental glomerulosclerosis (FSGS) is known to recur in some patients after renal transplantation. Over a decade, we followed 15 pediatric patients with FSGS whom transplant procedures had been performed from living-related donors, analyzing risk factors for recurrent disease. Bilateral native nephrectomies were performed simultaneously or prior to transplantation. Immunosuppressive induction regimen consisted of cyclosporine (CyA), mizoribine or azathioprine, methylprednisolone, anti-lymphocytic globulin or basiliximab. We examined age at onset, time in months between diagnosis and end-stage renal disease, the duration of dialysis, age at transplantation, time since nephrectomy, doses of immunosuppressive agents, and HLA mismatch. Six patients (40.0%) developed recurrent disease in the graft; all showed proteinuria within 24 h after transplantation. However almost all allografts (n=1 case immediate loss of graft function was shown) have functioned well for 140.4±56.2 months (mean ± SD) following transplantation. The interval from diagnosis to initiation of dialysis was significantly shorter in patients with recurrence than those without recurrence (p<0.05), but no other variables differed between these 2 groups. No recurrence of FSGS was observed in the protocol biopsy specimens at 100 days after transplantation. We believe that CyA and native nephrectomy may limit or reverse progression of recurrent FSGS in renal allografts of pediatric patients, although this is a limited study.

**PO-838**

**RETHROMBOCYTOPENIA PROTECTS AGAINST RENAL VEIN THROMBOSIS (RVT)**

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**Purpose:** To assess the protective effect of ATG associated thrombocytopenia against RVT in pediatric renal transplantation.

**Methods:** Between Jan 1986 and Dec 1998, 120 cadaveric kidney transplants were performed in 95 children. This comprised a control group (n=61) received ATG at day 1 and continued for 4-6 days. Platelet count prior to transplantation in older children impedes potential growth.

**Results:** We concluded new growth curves, but remained growth retarded. Growth retardation in transplant recipients with biliary atresia was less common and also showed increased growth performance after that compared with those who underwent transplantation for other causes. Both boys and girls were growth retarded at transplantation without statistical significance for sex but boys showed improved posttransplantation growth performance versus girls. No correlation to graft type was identified.

**Conclusion:** We conclude that early transplantation of children who show growth retardation is optimal for restoration of growth potential and delaying transplantation in older children impedes potential growth.
Laparoscopic donor nephrectomy is the most appropriate technique for pediatric living donor transplantation

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Laparoscopic donor nephrectomy (LDN) is widely used in the United States but remains uncommon in the UK. Concerns have been raised about higher recipient creatinine after LDN and some centres are reluctant to use the technique for paediatric recipients. However, few data exist regarding outcome after transplantation with LDN for paediatric recipients. We report our experience of the technique.

Methods: 11 donors (6 female) underwent LDN, with kidneys transplanted into paediatric recipients. All donors underwent surgery using the hand-assisted laparoscopic technique. Mean recipient age was 10 years.

Results: Donor surgery was uneventful with no conversions to open surgery and no major complications. Most donors (n=6) were discharged on the third postoperative day (4 at day 2 and 1 and day 4). All donors returned to normal activities within 1 to 3 weeks. Recipient graft survival was 100% at a mean follow-up of 4 months. All grafts had immediate primary function. Only one child had mild rejection. Mean serum creatinine at day 7 was 64 µmol/L.

Conclusion: Laparoscopic live donor nephrectomy is safe for donor and recipient in paediatric living donor transplantation. It does not appear to have a deleterious effect on recipient renal function. Fast donor recovery is important where donors are the main carers and makes laparoscopic donation the technique of choice.

PO-844

LAPAROSCOPIC DONOR NEPHRECTOMY IS THE MOST APPROPRIATE TECHNIQUE FOR PAEDIATRIC LIVING DONOR TRANSPLANTATION

3 patients cleared viremia, with serum creatinine returning to baseline levels, while viruria persists in 2/3 patients. None of the treated patients progressed to PVAN or experienced rejection episodes. In conclusion, our preliminary experience suggests that prospective BKV monitoring and immunosuppression reduction in kidney recipients with BK viremia prevents progression to overt PVAN without significantly increasing the risk of graft rejection.

PO-842

NEUROLOGIC COMPLICATIONS OF LIVER TRANSPLANTATION IN PEDIATRIC PATIENTS

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Purpose: Neurologic complications (NCs) are important source of morbidity and mortality in liver transplantation (LT). Aim of the study was to evaluate the incidence, type of NC, and associated factors in pediatric patients undergoing LT.

Methods: Data regarding NCs in 31 consecutive children (19 M, mean age, 8.4 years; (11 m-17 y) undergoing LT were analyzed.

Results: Indications for LT were fulminant hepatitis (FH) in 4, Wilson’s disease (WD) in 10, and others in 17 patients. NCs were found in 11 (35.5%) patients, the most frequent being seizures in (6/54.6%). 3 patients with seizures had posterior leukoencephalopathy findings on brain MRI and headache was associated in 2 of them. Diffuse encephalopathy was observed in 2 (18.2%) patients, which was caused by uremia and hypotension in 1 and hypoxia in another. We also observed tremor in 1 patient, acute dystonic reaction in 1 patient, and headache in 1 patient. In 7 patients, NCs were related to tacrolimus, and in 2 they were related to cyclosporine; serum drug concentrations were within normal ranges. The risk of NC increased with age (13y versus 9y) (P=0.002). Although not statistically significant, patients with WD had a higher incidence of NCs (60%) than did the other patients (23.8%). Twenty-five percent of patients with FH and 37% of patients without FH experienced an NC (P=0.05). 72% percent of NCs were encountered in first month after LT. Death unrelated to NC occurred in 1, and refractory epilepsy developed in another patient who had previous epilepsy. Mortality rates among patients with NCs and those without were similar.

Conclusions: In pediatric patients undergoing LT, the most frequent NC seen was seizure. Frequency of NCs increased with age. Immunosuppressive agents were the most frequent cause of NCs, which reversed upon discontinuation of drug.

PO-843

CALCULATED AUC VERSUS CYCLOSPORINE C0 AND C2 LEVEL MONITORING IN PEDIATRIC RENAL TRANSPLANT PATIENTS

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Purpose: Cyclosporine has highly variable pharmacokinetics. Dosing of cyclosporine has been based on the trough and 2nd hour serum levels of cyclosporine, the calculated area under the curve (AUC) and their relationship with chronic allograft dysfunction in pediatric patients.

Methods: 14 renal allograft recipients (8 M; mean age: 15.3 ± 3.9 years) on cyclosporine treatment were included in the study. Patients were grouped according to their serum creatinine and the presence of proteinuria as stable (n=10), creatinine >1.5 and no proteinuria) and chronic allograft dysfunction (n=4, creatinine >1.5 and/or daily protein excretion >4 mg/m²/24 h). Through (C0) and second hour (C2) cyclosporine serum levels were measured. AUC was calculated according to formula (AUC=C0 x 10.74 x C2 x 2.28 x tC2/C2).

Results: The mean posttransplant follow-up duration was 24.23 ± 23 months (min-max: 8-72 months). Mean cyclosporine dose was 4.8 ± 1.2 mg/kg/day. The mean C0, C2 and AUC were 91.1 ± 63.9 ng/mL, 558.2 ± 230.5 ng/mL and 3351.1 ± 1085 ng/mL, respectively. There were 3 (21.4%) patients categorized as low, 6 (42.8%) patients as intermediate and 5 (35.7%) patients as high absorption. High absorbers were found to have lower C0 levels, while low absorbers had lower C2 and AUC. The stable group had experienced fewer acute rejection episodes compared to unstable group (p = 0.05). Calculated AUC values in patients with chronic allograft dysfunction were significantly higher than in the stable patients. C0 and C2 levels did not correlate with the presence of chronic allograft dysfunction. The age, primary disease, cold ischemia time and HLA status were similar between the groups.

Conclusion: Calculated AUC values may be better parameter in the monitoring of cyclosporine dosing for the follow-up of chronic allograft dysfunction compared to C0 and C2 level alone.

PO-845

IS CYA PHARMACOKINETICS RELATED TO THE GRAFT VOLUME AFTER LIVING DONOR TRANSPLANTATION IN PEDIATRIC PATIENTS?

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Objective: In liver transplantation, Cyclosporine (CyA) is metabolized by the graft itself. Liver volume is significantly different in ages of pediatric patients. Therefore, the pharmacokinetics of CyA could be changeable by not only graft function but graft volume. We investigated the relationship between CyA pharmacokinetics and graft volume after living donor liver transplantation in pediatric patients.

Methods: Seven children, performed living donor liver transplantations (LDLT) in our institute, were assessed in this study. The graft volume was calculated using the data obtained from computed tomography (CT), performed at one week after LDLT. CyA was given intravenously and CyA blood concentrations were measured in FPIA method. As the indicator of pharmacokinetics of CyA, intravenous CyA total body clearance (CL) was calculated using the nonlinear least square program, MULT.

Result: There is a significant correlation between graft volume and CL at one week after LDLT (r=0.945, P<0.0005). The correlation coefficient of graft volume and CL is higher than that of recipient weight and CL (r=0.855, p<0.01).

Conclusion: In one of our assessed children, CT was performed at 5 and 8 postoperative days. Interestingly, there is a good correlation between graft volume and CL. While, there is a poor correlation between recipient weight and CL.

PO-846

RENAL TRANSPLANTATION IN CHILDREN

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Purpose: Hemodynamic, pharmacologic and physiologic differences in pediatric population, management of end-stage renal disease and renal transplantation has sustained several difficulties compared to the adults.

Methods: Between November 1975 to December 2004, 1523 kidney transplantations were performed by our team in Turkey.

Results: Out of 1523 we retrospectively analyzed, 44 male, 39 female (mean age 14.9±2.2 years) 86 kidney transplants (19 cadaveric (22.1%) and 67 living related (87.9%) in 83 pediatric recipients from medical charts. Fourteen morbidities have been occurred in 14 recipients. Seven (8.4%) lymphocope, 2 (2.4%) hemotoma, 1 (1.1%) urinary leakage occurred in early postoperative period. Two (2.4%) developed transplant renal artery stenosis. Two (2.4%) developed distal ureteral stenosis. Two (2.4%) developed proximal ureteral stenosis. Three (3.6%) developed hydronephrosis (21.4%) (2 with hemotoma and one with renal artery stenosis), required re-
PEDIATRIC LIVER TRANSPLANTATION IN SHIRAZ TRANSPLANT CENTER
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Purpose: Liver transplantation is a successful and useful therapy for children with chronic or end-stage liver disease. It has been done exclusively throughout Iran and some neighboring countries in our center for 12 years.

Methods: The first 150 consecutive liver transplantations were performed between April 1, 1995, and June 15, 2007 in Shiraz, Iran. We evaluated 24 pediatric liver transplantation retrospectively, using the liver transplantation database, with a minimum follow-up period of 6 months.

Results: Among 24 consecutive recipients, 3 were alive. The average recipient age was 9.7 ± 4.5 years. 15 patients had a full-size cadaveric transplant; 8 patients received graft from living donor. Only 2 cases had split liver transplantation. The operative procedure was performed in a standard manner using duct-to-duct anastomosis in 68% of the cases; piggyback technique was utilized in 9%, veno-venous bypass in the rest. Immunosuppressive regimen included Cilzocap, cyclosporine, and methylprednisolone. Major causes of liver failure included cryptogenic (41.6%), autoimmune hepatitis (20.8%), biliary atresia (20.8%). Neonatal cirrhosis (12.5%) and biliary hypoplasia (4.3%). Most cases of PVT were successfully treated with a combination of endovascular procedures and medical therapy. For the treatment of PVT, different techniques were performed, including stenting of the donor and recipient portal vein (n=3), stenting of the portal vein with access to the main portal vein (n=1), transjugular portal vein stent placement (n=1). In one patient with portal vein thrombosis, portal vein angiography was performed, which showed a large portal vein thrombus. The patient was successfully treated with anticoagulation therapy and stenting of the portal vein.

Conclusions: Liver transplantation is the preferred treatment for end stage liver disease in pediatric patients. The perfect performance of the procedure, reasonable immunosuppressive regimen, prevention and prompt therapy of complications are the keys to get satisfactory results. However, with timely recognition and active intervention, a good outcome can be achieved.

OUTCOME OF CHILDREN WITH PORTAL VEIN SEVERE STENOSIS OR THROMBOSIS AFTER LIVER TRANSPLANTATION
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Aims: Portal vein thrombosis (PVT) or stenosis (PVS) incidence and outcome were revised in 383 OLT. Prophylaxis included 1-week heparin (240 U/kg/day) followed by 1-month dipiridamol (3 mg/kg/day). Results:
1) Incidence: 21 children (5.4%) were affected.
2) PVS n=6 (1.5%)
PVT cases were mostly biliary atresia patients (73%) and 47% had post-OLT intrabdominal infection.
3) PVT was recognized in early (n=5) or medium-long term (n=10) postoperative. Early cases developed liver failure, n=3 were surgically repaired, 2 underwent retransplantation, 1 died. Survivors after thrombectomy remains good. Of 10 PVT detected in the medium-long term, heparin solved the one of PVT. All early cases developed liver failure, n=3 were surgically repaired, 2 underwent retransplantation, 1 died. Survivors after thrombectomy remains good.

Conclusions: Portal vein thrombosis and stenosis are uncommon post-OLT, leading to development of ESRD and mortality. Early diagnosis allows thrombectomy (PVT) or dilatation (PVS). PVT in medium-long term remains frequently undiagnosed due to collateral flows which preserve liver function but unusually prevent gastrointestinal bleeding.

GASTROINTESTINAL EVALUATION IN PEDIATRIC RENAL TRANSPLANTATION CANDIDATES
PO-849
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Purpose: Our objective was to determine the rate of histological gastritis and peptic ulcer and the clinical features of peptic ulcer and also the importance of gastrointestinal evaluation in pre-transplant phase in pediatrics with End-Stage Renal Disease (ESRD).

Methods: 24 children with ESRD (13 female, 11 male) on maintenance hemodialysis were included in this study. Upper gastrointestinal endoscopy was performed and two gastric antrol biopsy specimens were obtained for urease test and histological study for all patients. Gastrointestinal manifestations, underlying disease, duration of renal disease and dialysis, dysphagia frequency and oral alkali supplementation were recorded. Serum gastrin level was also measured in all patients.

Results: Gastrointestinal symptoms were present in 16 (66.6%) of 24 patients. 17 (70.8%) patients had abnormal upper gastrointestinal endoscopic findings. Abnormal endoscopic findings were found in 75% of symptomatic patients. 62.5% of symptomatic patients had urease tests positive for H. pylori infection. On the other hand, only 29.4% of asymptomatic patients had abnormal endoscopic findings, but in 56% of asymptomatic patients urease test were positive. H. pylori was detected in 12 of 17 (70.6%) patients with gastrointestinal lesions, while it was detected in 4 of 7 (50.1%) of patients with normal endoscopic examination. In the presence of H.pylori infection and oral alkali supplementation, with or without clinical symptoms, abnormal endoscopic findings occurred in 80%; while abnormal endoscopic findings were positive in 60% of symptomatic H. pylori infected cases without oral alkali supplementation. Conclusion: we found a significant number of patients with H.pylori infection. Our results emphasize the importance of gastrointestinal evaluation in these patients. Thus, endoscopic evaluation should be considered in symptomatic and also asymptomatic patients with oral alkali supplementation.

THE PHARMACOKINETIC (PK) OF MYCOGENIC ACID (MPA) IN PEDIATRIC KIDNEY RECIPIENTS RECEIVING CYCLOSPORINE MICROEMULSION (CyAIME) AND STEROIDS. RESULTS A PROSPECTIVE LONGITUDINAL STUDY
PO-850
L. Ghio, M. Ferreira, F. Ginevre, F. Perfumo, I. Fontana, L. Murer, G. Zacchello, F. Zano, L. Peruzzi, S. Tirelli, M. Belingheri, M. Cardillo, A. Edefonti. NItP, Pediatric Kidney Transplant Group Italy.

We present the results of a longitudinal study in pediatric KTx designed to investigate MPA-PK and its possible interactions with CyA. 74 children received CyAIME (500 mg/m^2 targeted on C0 levels) prednisone and MMP (300-400 mg/m^2) targeted on C0 between 1.5-3 mcg/ml. MPA PK (C0, C2, C4, C6, C8, C9, C12) and CyA PK (C0, C2, C4, C6) were obtained on pod#6, 30, 180, 360, MMP daily dose declined from pod#6 to pod#180 (913±463 vs. 874±363, n=0.05). The improved bioavailability of the MFM allowed the follow-up was confirmed by a progressive increased of full MPA-AUC obtained by parallel trapezoids rule. (pod#6: 21.6±2; pod#180: 36.5±16; pod#360: 49.6±30; p<0.05). Interestingly, in our group, the truncated AUC(0-4) was correlated with the full 10 point AUC (r=0.92; p<0.001), whereas any single time point, but CMAX, was able to predict the overall MPAs exposure. A significant influence of CyA on MPA metabolism was suggested by the inverse correlation between CyA and MPA AUCs, CyA C0 and MPA AUCs. CyA C0 and MPA Cmax and overall by CyA C2 and MPA-AUC (r=-0.37; p<0.001; r=-0.18; p=0.1; r=-0.15; p<0.05; r=0.163; p<0.03, respectively). In conclusion the interference between PK of MPA and CyAIME is an important issue. In our experience the truncated AUC(0-4) proffers riable tools to optimized MPA therapy.

KIDNEY TRANSPLANTATION IN CHILDREN WITH INFERIOR VENA CAVA THROMBOSIS, A SINGLE CENTRE EXPERIENCE
PO-851
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Background: Inferior Vena Cava (IVC) thrombosis impairs venous drainage of renal allografts, resulting in thrombosis. We describe transplantation of three children with IVC thrombosis.

Results: Case 1: a 13 year old girl with End Stage Renal Failure (ESRF) secondary to aortic and IVC thrombosis. She was commenced on dialysis at

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birth. Magnetic resonance imaging suggested an occluded IVC up to the level of the renal veins. Renal transplantation was successfully performed. The renal vessels were anastomosed to the reanalysed aorta and to the IVC above the level of the occlusion. Her graft remains functioning.

Case 2: A boy with congenital nephrotic syndrome who commenced dialysis in early infancy. Imaging confirmed an occluded IVC segment. Iliac veins were patent, with collaterals replacing the occluded IVC. His dialysis access was precarious. At the age of 7 years, weighing 15kg a kidney transplant was successfully performed. The renal vessels were anastomosed to the patent iliac vessels. His graft remains functioning.

Case 3: A 2 year old girl with ESRF secondary to dysplastic horseshoe kidneys and classical abnormalities. She commenced dialysis in early infancy. Imaging demonstrated an absent IVC to the level of the native renal veins. She had a living related transplant when she weighed 13kg. The renal vessels were anastomosed to aorta and to a small stump of IVC just below the right adrenal vein. The kidney was initially well perfused but the renal vein thrombosed two weeks later.

Conclusion: This experience shows that transplantation of children with occluded IVC is feasible provided appropriate imaging and counseling is done.

MARS AFTERSPLIT-LIVER TRANSPLANTATION IN AN INFANT

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Background: We report about the application of MARS in an infant with primary graft dysfunction after split-liver transplantation. We want to discuss the practicability and efficacy of this method as ultimate treatment or bridging - therapy to re-transplantation in this case.

Patient and methods: An infant of 15 months developed acute liver failure after bone marrow transplantation because of myeloproliferative disease. He underwent split-liver transplantation (transplantation of segments 2 and 3). Early after TX, the patient developed graft dysfunction with a significant increase of liver enzymes (asat from 1,16 to 20,76 µmol/l) and alat from 3,74 to 13,72 µmol/l) and bilirubin (from 264 to 705 µmol/l). MARS in combination with hemofiltration was performed daily. We determined liver enzymes (asat, alat) and bilirubin before and after each application.

Results: The use of MARS led to a significant decrease of bilirubin and liver enzymes bilirubin from 705 to 195 µmol/l and asat 20,76 to 0,41 µmol/l and alat 13,72 to 0,93 µmol/l. But there was no influence on parameters of function and liver synthesis.

Although adequate detoxification was maintained, because of the continued absence of any evidence of recovery of liver synthetic function, it was confirmed that immediate re-transplantation was indicated. A repeat split liver transplant was performed two weeks after the first transplant and 4 days after introduction of MARS therapy.

Conclusion: There are rare experiences with MARS after liver transplantation in infants. In our case, it proved to be practicable. In combination with intensive care, it led to clinical stabilization and thus, to retransplantation of the patient.

PERCUTANEOUS TRANSESOPHAGEAL ANGIOPLASTY FOR HEPATIC VENOUS OUTFLOW OBSTRUCTION AFTER PEDIATRIC SPIT-LIVER TRANSPLANTATION. A CASE REPORT

Davide Cintoirino, Roberto Miraglia, Roberto Miraglia, Marco Spada, Sergio Clarizia, Angelica Arevalo, Margarita Ibarra, Luis C. Rodriguez-Sanchez, Marco Vezzoli

Case 1: An infant of 15 months developed acute liver failure after bone marrow transplantation because of myeloproliferative disease. He underwent split-liver transplantation (transplantation of segments 2 and 3). Early after TX, the patient developed graft dysfunction with a significant increase of liver enzymes (asat from 1,16 to 20,76 µmol/l) and alat from 3,74 to 13,72 µmol/l) and bilirubin (from 264 to 705 µmol/l). MARS in combination with hemofiltration was performed daily. We determined liver enzymes (asat, alat) and bilirubin before and after each application.

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Conclusion: There are rare experiences with MARS after liver transplantation in infants. In our case, it proved to be practicable. In combination with intensive care, it led to clinical stabilization and thus, to retransplantation of the patient.
THE NEW PEDIATRIC LIVER TRANSPLANT PROGRAM AT ISMETT, PALERMO. PRELIMINARY EXPERIENCE

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Split liver transplantation SLTx allowed northern Italian transplant Centers to transplant all the children in need, without waiting list mortality. A policy of SLTx has been recently adopted nationwide, allowing to start a pediatric liver transplant program in the south of Italy. Twenty-one pediatric cadaveric liver transplants have been performed in 19 children. Primary diseases were: biliary atresia (12), Langherans cells histiocytosis (2), cystic fibrosis (1), tyrosinemia (1), hemangioendothelioma (1), and Alagilles syndrome (1). Mean portal vein diameter was 5.6±2.9 mm. One patient had thrombosis of the main portal vein. 10 out of 12 left lateral segment and one extended right graft from in situ split liver. Two patients were successfully treated with percutaneous balloon angioplasty for HAS. Its usefulness, especially in split liver recipients with complex vascular reconstructions, must be balanced against the risk of iatrogenic complications.

MDCT is a very accurate test to show hepatic vascular system and to evaluate liver volume in pediatric patients. Data obtained from MDCT can guide in the donor-to-recipient dimensional matching and in the choice of the surgical technique possibly reducing intra- and postoperative complications.

DOPPLER ULTRASONOGRAPHY SCREENING AND PERCUTANEOUS BALLOON ANGIOPLASTY FOR HEPATIC ARTERY STENOSIS AFTER PEDIATRIC SPLIT LIVER TRANSPLANTATION

Angelo Luca, Marco Spada, Roberto Miraglia, Davide Cintorino, Gianluca Marrone, Silvia Riva, Sergio Clarizia, Bruno Gridelli.

We report our experience using Doppler ultrasonography (DUS) for diagnosis of arterial complications and percutaneous treatment of hepatic artery stenosis (HAS) after pediatric liver transplantation (LTx).

We perform DUS daily for the first 5 days after LTx to rule out hepatic artery complications. Resistance index 0.5 cm/sec and/or systolic acceleration time 0.08 sec and/or velocity peak 200 cm/sec are used as criteria to suspect HAS. A 16 slices multidetector CT (MDCT) with multiplanar reconstructions, MIP, volume rendering imaging, and digital subtraction angiography are used to confirm complications.

Twenty pediatric LTxs were performed at our center. DUS showed a suspicious of HAS in four patients, all but one had normal liver function tests. MDCT confirmed HAS in 3 cases and in one showed a severe discrepancy between the donor and the recipient hepatic artery. The 4 patients received 3 left lateral segment and one extended right graft from in situ split liver. Two patients were successfully treated with percutaneous balloon angioplasty. In the third case, we were not able to cross the stenosis. After a median follow up time of 10 months, treated patients are alive and well with patent hepatic artery and normal graft function. The patient who underwent unsuccessful angioplasty developed a small pseudoaneurysm in the stenotic tract likely due to the manipulation, is alive and well.

After pediatric LTx, HAS has high sensitivity in detecting HAS. Percutaneous angioplasty is an effective treatment for HAS, preventing hepatic artery thrombosis. Its usefulness, especially in split liver recipients with complex vascular reconstructions, must be balanced against the risk of iatrogenic complications.

IGL-1: A MODIFIED UNIVERSITY OF WISCONSIN PRESERVATION SOLUTION PROHIBITS FATTY LIVER AGAINST ISCHEMIA-REPERFUSION INJURY IN THE RAT

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Abundant fat in the liver has been implicated in poor outcome after liver transplantation or liver surgery, but the reasons for this association are still unclear. Using an “ex vivo” isolated perfused rat liver model, we have evaluated the usefulness of a modified UW preservation solution with polyethylene glycol 35 KDa 0.23mM and high Na+/low K+ content (IGL-1; Institut Georges Lopez, France) for the preservation of fatty livers from Zucker rats. Steatotic and non-steatotic livers were preserved for 24 hr in UW and IGL-1 solutions and then perfused at 37°C during 2 hours, respectively. Perfusates transaminases and flow alterations, lipid peroxidation and bile production were determined. Fatty livers preserved in IGL-1 showed a significant diminution of AST/ALT as well as in lipid peroxidation (measured by liver MDA). Both biochemical alterations were accompanied with a remarkable amelioration of perfuse flow rate and bile production. Histological findings confirmed minimal liver damage when IGL-1 was used as preservation solution.

In summary, these results demonstrated that IGL-1-solution significantly improved all functional parameters of steatotic liver in the rat.
PO-861  EFFECTS OF POLYETHYLENE GLYCOL AND HYDROXYETHYL STARCH IN UNIVERSITY OF WISCONSIN PRESERVATION SOLUTION ON HUMAN RED BLOOD CELL-AGGREGATION AND VISCOSITY

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UW solution is considered the most effective cold storage liquid to date. Recent studies have provided evidence of the hyperaggregating effect on human red blood cells (RBC) of hydroxyethyl starch (HES) as one of the components of the UW solution. Preservation solutions containing polyethylene glycol (PEG) and HES are more useful in maintaining the integrity of the RBCs and the viability of the preserved and transplanted liver.

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PO-862  ATTENUATION OF STEATOTIC LIVER ISCHEMIA-REPERFUSION INJURY BY TRIMETAZIDINE

Ismail Ben Mosbah, Carme Xaus Rafi, Anna Serafín, Joan Roselló-Catafau, Carmen Peralta.

The shortage of organs has led centers to expand their criteria for the acceptance of marginal organs for liver transplantation such as fatty livers. It is well known that fatty livers showed lesser tolerance against ischemia-reperfusion injury than normal livers. We have evaluated the protective effect of trimetazidine (TMZ), a potent antiischemic agent, against fatty liver cold ischemia-reperfusion injury when it is added to the standard UW solution. Using an isolated perfused rat liver model, lean and fatty livers from Zucker rats were preserved for 24 hours in UW solution with or without TMZ (10-6 M) followed by 2-hours reperfusion (37°C), respectively. AST/ALT, lipid peroxidation and caspase-3 activity, as well as bile flow and bromosulfophthalein (BSP) clearance were evaluated, respectively. Histological techniques (optical and electron microscopy) were also used.

Fatty livers preserved in UW with TMZ showed a significant decrease in AST/ALT levels, lipid peroxidation and caspase-3 activity when compared to those obtained in UW solution. These beneficial effects were confirmed by an exacerbate improvement in liver functional parameters such as bile flow and BSP clearance, respectively. Moreover, histological findings revealed an efficient preservation of general hepatocyte and mitochondria morphology when TMZ is added to UW solution. These findings suggest that the presence of TMZ in UW protected fatty livers against cold ischemia-reperfusion injury being efficient liver preservation approach for steatotic grafts to be used for transplantation purposes.

Acknowledgements: This study was supported by the MCYT (BFI 2002-00704 and BFI 2003-00912 and the Agencia Española de Cooperación Internacional (AECI, grant 25/03/P project). I. Ben Mosbah is a fellow recipient from AECI.

PO-863  ENDOPLASMIC ACTIVATION DURING COLD STORAGE OR OXYGENATED MACHINE PRESERVATION OF RAT LIVERS FROM NON-HEART-BEATING DONORS

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The endoplasmic reticulum (ER) represents a subcellular target, reactive to various cytotoxic impairments. Among molecular consequences of ER stress are activation of transcription factors, recently found to be involved in several pathological processes of cellular apoptosis, and activation of membrane-bound PERK, downregulating protein translation via phosphorylation of eucaryotic initiation factor(eIF2). Here, the involvement of ER-stress in preservation injury was investigated, comparing continuous machine preservation, simple cold storage and a novel concept only temporary perfusion after procurement.

PO-864  OXYGENATED MACHINE PERFUSION OF NON-HEART-BEATING DONOR LIVERS AT DIFFERENT TEMPERATURES

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Although the use of non-heart-beating donors has the potential to increase the number of available organs, livers are used only very scarce because of the risk of primary non function. There is evidence that machine perfusion (MP) is able to improve the preservation of marginal organs. The aim of this study was to evaluate the influence of the perfusate temperature during oxygenated MP on graft function.

Livers from male wistar rats were harvested after 60 minutes warm ischemia. The portal vein was canulated and the liver flushed with Lifor® (Oncoscience AG/Lifelblood Medical Inc.) organ preservation solution for oxygenated machine perfusion (MP) at 4, 12 or 21°C. Other livers were flushed with HTK and stored at 4°C by static storage (CS). After 4 hours all livers were isolated reperfused and functional as well as structural data were collected.

Results: During machine perfusion at the same time the most significant lower portal venous resistance and higher bile production compared to livers perfused at 4°C and 12°C. Although not significant an increased leakage of ALT was observed at higher temperatures (table 1).

Table 1: Machine Perfusion Data

| Temperature | 4°C MP | 12°C MP | 21°C MP |
|-------------|--------|--------|--------|
| PVP (cm H2O) | 3.4±0.7 | 3.7±1.5 | 3.7±1.5 |
| Bile (ml/hr/L) | 0.4±0.2 | 0.8±0.5 | 0.8±0.5 |
| ALT (μl/L) | 2837±889 | 5402±2803 | 5943±1628 |

PVP (portavalous pressure); Results after 6 h machine perfusion, p < 0.05 vs 4°C MP and 12°C MP.

After preservation all machine perfused livers had a higher metabolic activity and reduced liberation of transaminases compared to livers stored by simple cold storage. MP improved the preservation of livers from NHBD. It seems that perfusion at mild hypothermia of 21°C has positive effects on the portal venous resistance and metabolic activity but this has to be balanced with an increased risk of parenchymal damage.

PO-865  PERFADEX IMPROVES EARLY LUNG FUNCTION IN BILATERAL LUNG RECIPIENTS

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Objective: To assess the influence of preservation solution types, Euro-Collins and Perfadex, on early lung function, evaluating a novel lung recipient.

Methods: A total of 74 patients underwent a bilateral lung transplant (LT) between March 1997 and December 2004 in the Marques de Valdecilla University Hospital. Lung allografts were flushed either with Euro-Collins or Perfadex. Initial graft function was assessed by measurement of PaO2/FIO2 ratio, intensive care unit (ICU) survival. Thirty-day mortality, incidence of pulmonary
reimplantation edema, length of stay in the ICU and hours of mechanical ventilation were also compared.

Results: The PaO₂/FiO₂ ratio was better in the Perfadex group at ICU admission (p < 0.01). The incidence of reimplantation edema was lower in the Perfadex group (p < 0.001). Thirty-day mortality was lower in the Perfadex group, although there was no proven significance. There were no differences in length of stay in the ICU, hours of mechanical ventilation, recipients and donor characteristics.

Conclusions: Graft preservation using Perfadex improves early lung function after bilateral LT.

PO-866 PRIMARY RENAL GRAFT FUNCTION FOLLOWING PROLONGED COLD ISCHAEMIA OF 24 HOURS OR MORE: RE-FLOW WITH UW SOLUTION PRIOR TO IMPLANTATION

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Prolonged cold ischaemia is associated with an increased incidence of delayed graft function (DGF) and primary non-function (PNF). The relationship of cold ischaemia and graft function is a linear one with increasing risk of DGF and PNF with increasing duration of cold ischaemia. Most centres in the United Kingdom do not accept or transplant kidneys from deceased heart beating donors or from deceased heart beating donors with a projected cold ischaemia time (CIT) of 24 hours or more at the time of implantation. Most of these kidneys are flushed in-situ in the donor with hyperosmolar citrate (HOC or Soltran, Baxter) and also stored in this solution. In our centre, a delayed graft function of 50% is seen following reimplantation of deceased heart beating donor kidneys with CIT of 18 hours or more. We present the results of eleven consecutive renal transplant from deceased heart beating donors with cold ischaemia time ranging from 23 hours to 43 hours. The kidneys with projected CIT > 24 hours or more at the time of implantation were re-flushed with gravity by 500-750 ml of University of Wisconsin (UW) solution (Vihaspan, Dupont) and stored in this solution until re-implantation.

All eleven kidneys transplanted using the above protocol demonstrated primary function though the rate of fall in serum creatinine was slow. The mean serum creatinine was 149 µM/l at one month and 123 µM/l at three months. We conclude that re-flush with UW confers a beneficial effect in kidneys with prolonged cold ischaemia with resultant primary graft function. This will have significant clinical and economic implication in renal transplant and may enable the use of otherwise discarded kidneys.

PO-867 EFFECTS OF ISCHEMIC PRECONDITIONING AND INTRAVENOUS ADMINISTRATION OF ASCORBIC ACID ON ISCHEMIC KIDNEY

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Prolonged and sustained ischaemia is associated with high morbidity and mortality. So that, improving the ability of organs to tolerate ischaemia and reperfusion (IR) injury would have important implications.

The aim of this study is to evaluate whether ischemic preconditioning (PC) and ascorbic acid pretreatment (AA), alone or in association, could reduce IR insults in rat kidney.

In I/R (n=10), renal pedicles were clamped for 60min then reperfused for 120min. In PC (n=9), renal pedicles undergo two cycles of 5-5 min I/R before total renal clamping. In AA (n=9), aceric acid (100 mg/kg) is intravenously administered before clamping renal pedicles. PC+AA (n=9) is the combination of ischemic and AA pretreatments, in sham (n=9), renal pedicles are only dissected.

The IR induced an increase in the plasmatic LDH activity, and tissue MDA and a decrease of Na reabsorption (RNH), urinary flow rate (GFR) and glomerular flow rate (GFR) in comparison to the sham group. Ischemic and AA preconditionings improve renal function, no statistical difference is found between sham, PC and AA groups. Compared to I/R group, the PC and AA pre-treatments diminish LDH, MDA and increase GFR and RNH. The association of these pre-treatments (PC+AA) has the same effect compared with I/R. However, PC+AA fails to improve GFR, UFR and MDA compared to the AA pre-treatment only.

Intravenous AA administration and ischemic preconditioning therefore allow rats to tolerate 0.01, 0.1 and 0.2 hours of warm ischaemia and preserve the acute renal function. However, the effects are lessened when both pre-treatments are combined.

PO-868 DETORIATION OF ENDOTHELIAL AND SMOOTH MUSCLE CELL FUNCTION AFTER COMBINED WARM AND COLD ISCHAEMIA IN A NON HEART BEATING DONOR RAT MODEL

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Introduction: Kidneys obtained from non-heart-beating donors (NHBDs) suffer from both warm and cold ischemia related injury. Immunohistochemical staining of endothelium shows an inflammatory response, however, the question remains to what extent endothelial function is compromised and how it can be optimally preserved. We studied the effects of warm and cold ischemia times (WIT/CIT) in NHBD kidneys on endothelial dependent relaxation (EDR) by acetylcholine as a functional marker, and compared preservation of the new extracellular-type cold storage (CS) solution IGL-1 with UW solution.

Methods: Six groups (n=6) of kidneys from male Fisher rats with WIT of 0, 15 and 30 minutes, with/without 24 CIT using IGL-1 or UW were studied. After nephrectomy, one kidney was immediately connected to a reperfusion model, while the contralateral kidney was reperfused after 24 h CS. Renal vascular responses were monitored with a pressure transducer. After an equilibration period of 30-45 minutes and preconstriction with phenylephrine (PE), subsequent doses of increasing amounts of acetylcholine (10⁻⁷ M to 10⁻¹ M) were given by bolus injection. The area under the curve was used to compare groups.

Results: Our data show that the combination of warm and cold ischemia has a detrimental effect on EDR. Vasodilatation to acetylcholine was reduced up to 47% after 24 hours CS with both solutions after 15 and 30 min. WIT (p < 0.05). Furthermore we found a 50% reduction in PE induced constriction after 24 h CS with either solution (p < 0.05) in all groups. This rapid decline of smooth muscle cell function might be the first step towards intimal hyperplasia as is seen in late transplant dysfunction.

PO-869 THE EFFECT OF EDARAVONE ON THE GRAFTS FROM NON-HEART-BEATING DONORS

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Background: The shortage of donors in liver transplantation has led to the consideration of marginal donor pools such as non-heart-beating donors (NHBDs). This study was designed to investigate the effects of a free radical scavenger edaravone on warm ischemia-reperfusion (IR) injury of the liver and possibility of successful liver transplantation using NHBDs.

Methods: Rat livers were isolated under heart-beating (HB group: n=5) or 30 minutes after cardiac arrest led by incision of the diaphragms (non-HB group: n=5), and reperfused with oxygenated Krebs-Henseleit bicarbonate buffer (KHB) after cold preservation in University of Wisconsin solution for 6 hours. As the third group (Ed group: n=5), livers were isolated from NHBDs, and edaravone (1mg/kg) was added into KHB.

Result: The perfusion flow of the Ed group had a tendency to be slightly higher than that of the non-HB group (450±49 mL/kg BW). Total bile production of the Ed group had significantly higher amount than that of the non-HB group (0.97±0.803 mL/kg BW, P=0.041). The levels of alanine aminotransferase (ALT), lactate dehydrogenase (LDH) and tumor necrosis factor-alpha (TNF-α) in the Ed group showed a tendency to be slightly higher than those in the non-HB group. Addition of edaravone did not influence the level of interleukin-1beta (IL-1beta).

Conclusion: Edaravone could bring some improvement of graft function on warm IR injury. Scaevenging hydroxyl radicals may be the one of tools in liver transplantation using NHBDs.

PO-870 DURATION OF MACHINE PERFUSION OF NHBD KIDNEYS

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Introduction: Many centres have expanded their donor pools by utilising non-heart beating donors (NHBD). Preservation by machine perfusion is often used to maximise organ viability, but the optimum duration of perfusion is not known.

Methods: We machine perfused pairs of kidneys from 7 consecutive NHBD, perfusing one kidney for 0.5 hours and the other, until implantation. All kidneys were transplanted locally, the kidney perfused for 4 hours being transplanted first in each case. Perfusion injury was assessed by post-perfusion weight gain.

Results: All 11 kidneys were transplanted, but 4 were implanted as dual transplants. Cold ischaemic time was shorter in the kidneys perfused for 4 hours (902±153 vs. 1344±214 minutes, p = 0.036). Perfusate glutathione-S-transferase levels did not differ significantly (126±52 vs. 133±95 IU/litre/100g). The difference in weight gain for kidneys machine perfused was not significant, with mean of 11% (S.D. ±14%) in the 4 hour group, and 4.5% (±19.3%) in the
long perfusion group; inter-donor variation in weight gain was extensive, but paired weight gains were well matched (p=0.4257). Differences in incidence (33% vs. 50%) and duration (1.5±2.9 vs. 2.1±3.1 days) of delayed graft function were non-significant, as was GFR at discharge (39.9±10.7 vs. 52.2±19.5 ml/min/1.73m²).

Conclusion: Machine perfusion until the time of implantation did not cause oedema of the kidneys, but it did not significantly improve clinical outcome, although there was a trend towards reducing effect of cold ischemic times. Although we could not demonstrate a definite benefit over a limited period of machine perfusion, we have adopted the longer period of perfusion as standard for NHBD kidneys.

PO-871 TAURINE IMPROVES HEPATIC MICROCIRCULATION AFTER WARM ISCHEMIA IN THE RAT
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Background: Reperfusion injury is characterized by both activated Kupffer cells and disturbed hepatic microperfusion. Taurine prevents activation of Kupffer cells in vitro. Thus, this study was designed to investigate its effect on both liver injury and intrahepatic microcirculation after warm ischemia.

Methods: Sprague Dawley rats were given taurine (10 mg/kg i.v.; 1.2 ml) 10 minutes prior to 60 minutes of warm ischemia of the left liver lobe. Ringer’s solution (1.2 ml) was given to controls. After reperfusion transaminases, liver histology, perfusion data of in vivo microscopy and both phagocytosis of Kupffer cells and TNF-alpha release to index cellular activation have been investigated. Further, ICAM-1 expression was shown with immunohistochemistry.

ANOVA test was used as appropriate and results are presented as mean ± SEM.

Results: Taurine significantly decreased both ALT and AST from 278±74 U/l and 392±22 U/l in controls to 129±19 U/l and 268±26 U/l, respectively eight hours after reperfusion. At the same time histological changes, i.e. neutrophil infiltration, necrotic cell death and ICAM-1 expression were markedly reduced by 14% to 34% after taurine (p<0.05). Further, taurine dramatically improved microcirculation. The number of stickers was reduced to 76% of controls in venules (p<0.05) while rolling was decreased to 37% in venules (p<0.05). Taurine significantly decreased both phagocytic activity of Kupffer cells and TNF-alpha release (p<0.05).

Conclusion: Taurine decreases liver injury after warm ischemia most likely via Kupffer cell-dependent mechanisms including leukocyte-endothelial cell interaction.

PO-872 MBT SOLUTION TO ISOLATE PANCREATIC ISLETS: AFFECTS CELL VIABILITY AND PROLONGS ALLOGRAPH SURVIVAL
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Purpose: Macobiotech-Transplant solution (MBT - Macopharma) has been shown to provide a better cell preservation in a pig renal autotransplantation model. In addition, it could reduce immunogenicity of the graft by masking cell surface antigens. The aim of the study was to compare MBT to the regular products (HBSS) used to isolate pancreatic islets.

Methods: A model of murine islet transplantation was used. Isografts (groups isoMBT and isoHBSS) were used to assess the quality of cell preservation and the function of the islets. Allografts (full mismatch combination: groups alloMBT and alloHBSS) were used to test the capacity of immunomodulation. Islets prepared with the MBT solution or HBSS were graft in diabetic mouse.

Results: Primary non function occurred in 2/6 recipients in isoHBSS group versus 0/6 in isoMBT group (p<0.05). This solution better preserves the cellular functionality (insulin secretion test and morphologic studies), and allows to decrease the islets number of the graft. Graft survival was significantly prolonged in alloMBT group (17.3±3.8 days) versus 7.3±3.8 days in alloHBSS group (p<0.05). This prolongation is due to a transitory phenomenon of immunomodulation of the antigens at the graft surface (immunofluorescence studies and murin model of acute cellular rejection).

Conclusion: Although the study failed to reach a one donor one recipient ratio are of major importance and the use of the MBT could be a major step in this regard. MBT solution delays the acute rejection occurrence by a phenomenon of immuno-camouflage.

PO-873 ADDITION OF TRIMETAZIDINE TO UNIVERSITY WISCONSIN SOLUTION PRESERVES SMALL LIVER GRAFT
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Small-for-size grafts have been associated with primary graft non-function or poor function. Organ preservation strategies are determinant to assure the graft viability after reduced-size orthotopic liver transplantation (ROLT). Previous studies have demonstrated the beneficial effects of trimetazidine (TMZ) in pig kidney cold ischemia-reperfusion injury but no investigations on the protective effect of TMZ against liver ischemia-reperfusion injury associated to ROLT have been carried out. For this purpose, we have assayed a modified University Wisconsin (UW) preservation solution enriched with trimetazidine at 10-6M concentration (UW-TMZ) which was compared to the original UW one.

Rats liver cold ischemia were performed on 15 rats which were randomly divided into 5 groups (n=3): alloMBT, alloHBSS, isoMBT, isoHBSS and UW-TMZ. The liver vascularization was assessed by in vivo microscopy. Histology, perfusion data of in vivo microscopy and both phagocytosis of Kupffer cells and TNF-alpha release to index cellular activation have been investigated. Further, ICAM-1 expression was shown with immunohistochemistry. ANOVA test was used as appropriate and results are presented as mean ± SEM.

Results: Taurine significantly decreased both ALT and AST from 278±74 U/l and 392±22 U/l in controls to 129±19 U/l and 268±26 U/l, respectively eight hours after reperfusion. At the same time histological changes, i.e. neutrophil infiltration, necrotic cell death and ICAM-1 expression were markedly reduced by 14% to 34% after taurine (p<0.05). Further, taurine dramatically improved microcirculation. The number of stickers was reduced to 76% of controls in venules (p<0.05) while rolling was decreased to 37% in venules (p<0.05). Taurine significantly decreased both phagocytic activity of Kupffer cells and TNF-alpha release (p<0.05).

Conclusion: Taurine decreases liver injury after warm ischemia most likely via Kupffer cell-dependent mechanisms including leukocyte-endothelial cell interaction.

PO-874 SIROLIMUS AMELIORATES THE IMBALANCE OF INTRACELLULAR CHOLESTEROL HOMEOSTASIS IN HUMAN VASCULAR SMOOTH MUSCLE CELLS MEDITATED BY INFLAMMATORY CYTOKINE
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Sirolimus is an immunosuppressive agent used for the prophylaxis of transplant rejection. In recent years, sirolimus was found to have an anti-atherosclerotic effect in the Apo E-knockout mice left lateral lobes and the two caudate lobes just before the harvesting of the liver, resulting in a 40% reduction of liver mass. Donor livers were flushed and preserved in cold UW and UW-TMZ solutions for 1 hour, respectively. Following, ROLT was performed according Kamada’s cuff technique.

Livers preserved in UW-TMZ solution showed lower increases in AST/ALT levels after ROLT than those observed for the livers preserved in original UW solution. This protection conferred by TMZ was also confirmed by the subsequent liver histological findings. Also, the oxidative stress associated with ROLT was prevented when UW-TMZ solution was used. This was evidenced by a significant decrease in liver MDA levels. In conclusion, the data reported here confirmed the presence of TMZ in UW preservation solution, contributed to a better liver preservation against ischemia-reperfusion injury associated with ROLT.

PO-875 ET-KYOTO SOLUTION PLUS DIBUTYRYL CAMP IS SUPERIOR TO UNIVERSITY WISCONSIN SOLUTION IN RALT LIVER PRESERVATION
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ET-Kyoto solution (ETK) is an extracellular-type organ preservation solution containing a cytoprotective disaccharide, trehalose. The efficacy of ET-K on liver preservation has been documented. Here we report the efficacy of ETK on liver preservation by comparison with University of Wisconsin (UW) solution using a rat liver transplantation (LTx) model.
INITIAL FLUSH WITH HTK AND SUBSEQUENT STORAGE IN UW SIGNIFICANTLY AMELIORATES ISCHEMIA/REPERFUSION INJURY IN AN ISOLATED RAT LIVER PERFUSION MODEL

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Prevention of graft damage by maintenance of cellular homeostasis and fluid regulation, as well as rapid cooling and microvascular clearance are major principles in organ preservation. The high concentration of cold saline account for the triple higher viscosity of UW compared to HTK, resulting in the advantage of an accelerated cooling and better wash out by using HTK solution, whereas UW derivatives may still be the best for graft storage. Aim of this study was to evaluate the effect of an initial flush with HTK and subsequent storage in UW. Male Wistar rats were used as liver donors. Preservation was performed by aortal perfusion with (1)UW, (2)HTK, or (3)initial flush with HTK, followed by back-table infusion of UW. Cold storage at 4°C was maintained for 24hs, followed by 60min of isolated perfusion in K-H buffer. Portal venous pressure, AST release, bile flow, microdialysis and histological examinations were performed.

Table 1. Tissue hypoxia was visualized by using Pimonidazole (PIM) injections (HypoxyProbe ™) and analyzed by a semiquantitative score (0-3), values displayed in median; range

| Group 1 | Group 2 | Group 3 | Group 4 | Group 5 |
|---------|---------|---------|---------|---------|
| Bile flow 2hs | 20.08±5.3 | 20.01±5.5 | 20.21±6.0 | 20.03±5.2 |
| 8hs | 20.02±5.8 | 20.01±5.9 | 20.21±6.1 | 20.03±5.3 |
| AST 2hs | 111.0±58.0 | 55.0±24.0 | 40.0±13.0 | 70.0±32.0 |
| 8hs | 111.0±58.0 | 55.0±24.0 | 40.0±13.0 | 70.0±32.0 |
| BH4 treatment significantly reduces postischemic deterioration of microcirculation and might be a promising novel strategy to attenuate IRI in clinical pancreas transplantation.

PO-878 TETRAHYDROBIOPTERIN ATTENUATES MICROVASCULAR REPERFUSION INJURY FOLLOWING MURINE PANCREAS TRANSPLANTATION

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Purpose: Tetrahydrobiopterin (BH4), is a cofactor for nitric oxide synthases and thus a critical determinant of NO production. Recently exogenous NO has been shown to reduce ischemia reperfusion injury (IRI). The role of BH4 in IRI following pancreas transplantation is still unclear.

Methods: 24 murine pancreas transplantsations were performed with a modified no-touch technique. Pancreatic grafts were subjected to different cold ischemic times (CIT) and treatment regimens: normal saline (CIT-1), S + 16h CIT-(II), BH4 50mg/kg + 16h CIT-(III). Nontransplanted animals served as controls (IV). Intravital fluorescence microscopy was used for analysis of graft microcirculation by means of functional capillary density (FCD) and capillary diameters (CD) after 2h of reperfusion. Quantitative assessment of inflammatory responses (mononuclear infiltration) and endothelial disintegration (edema formation) was done by histology-(H&E) and peroxynitrite formation assessed by nitrotyrosine-immunostaining.

Results: FCD was significantly reduced after prolonged CIT, paralleled by increased peroxynitrite formation, when compared with controls(all p<0.05). Microcirculatory changes correlated significantly with intragraft peroxynitrite generation(Spearman: r=-0.56; p<0.01). Pancreatic grafts treated with BH4 displayed markedly higher values of FCD(p<0.01) and abrogated nitrotyrosine staining (p<0.05). CD were not different in any group. Histologic evaluation showed increased inflammation, interstitial edema, hemorrhage, acinar vacuolization and focal areas of necrosis after 16h CIT in group II, which could be diminished by the administration of BH4 (p<0.05).

Conclusion: BH4 treatment significantly reduces postschismic deterioration of microcirculation and might be a promising novel strategy to attenuate IRI in clinical pancreas transplantation.

PO-879 REDUCTION OF FIG LIVER ISCHEMIA/REPERFUSION INJURY BY DIFFERENTIATED PROSTACYCLIN TREATMENT

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Purpose: Ischemia/reperfusion injury is hazardous for graft function following liver transplantation. Prostacyclin (Iloprost ™ ) therapy has the potential to beneficially influence IRI injury. Aim of this study was to determine hepatic injury and function in a (1)control group and iloprost ™ treatment groups with (2)end or pre-treatment, (3)modified preservation solution, (4)continuous infusion following graft reperfusion, and (5)combined use pre- and post-reperfusion.

Materials-Methods: German landrace pigs (n=7/group), weighted 22-26 kg, were used as liver donors. Preservation was performed by aortal perfusion with HTK solution and a cold ischemia time (4°C) of 20hs, followed by a nonthermocorporeal extracorporeal perfusion for 8hs. Iloprost ™ was given by (2)aortal (1µg/kg) injection before flushing, (3)addition (0.0125µg/ml) to HTK solution, (4)continuous infusion (0.0021µg/kg/min), and by combining (2) and (3).

Results:

| Results: | Group 1 | Group 2 | Group 3 | Group 4 | Group 5 |
|---------|---------|---------|---------|---------|---------|
| AST 2hs | 111.0±58.0 | 55.0±24.0 | 40.0±13.0 | 70.0±32.0 | 20.03±5.3 |
| 8hs | 111.0±58.0 | 55.0±24.0 | 40.0±13.0 | 70.0±32.0 | 20.03±5.3 |
| BH4 treatment significantly reduces postschismic deterioration of microcirculation and might be a promising novel strategy to attenuate IRI in clinical pancreas transplantation.
**Conclusion:** Pre-ischemia exposure to iloprost*8* by donor pre-treatment, as well as the use in the preservation solution, significantly improves graft integrity and function as measured by AST release and bile flow. The main mechanism of action appears to be the reduction of tissue hypoxia during reperfusion, which was most impressive by the combined use of iloprost*8* pre-ischemically and during graft reperfusion.

**PO-880**

**UW PREVENTS SYSTEMIC RELEASE OF OXYGEN FREE RADICALS DETECTED BY ESR SPECTROSCOPY IN EXPERIMENTAL PANCREAS TRANSPLANTATION**

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**Introduction:** Ischemia-reperfusion-injury is associated with reactive oxygen species release (ROSR). Data on the course of ROSR during early onset of reperfusion and the antioxidative effects of preservation solutions are lacking. The aim of the study was to detect ROSR using spinlabel technique combined with electronspinresonance spectroscopy (ESR).

**Methods:** Pancreata of Lewis rats (250g) were perfused with normal saline or University of Wisconsin (UW) solution and stored for 18h at 4°C before syngeneic transplantation. ROSR was quantified in arterial whole blood by ESR using i.e. CMH (1-hydroxy-3-methacrylonitrile-2,2,5,5-tetramethylpyproline, 80³g/kg/min) as spinlabel.

**Results:** Organs preserved in saline showed significantly enhanced ROSR compared to baseline 60min after reperfusion (figure 1). UW preservation led to a significant decrease 15min after reperfusion (figure 1).

**PO-881**

**A NOVEL SINGLE-CHAIN FRAGMENT VARIABLE (scFv) ANTICY-C5 ANTIBODY REDUCES APOPTOSIS AND INFLAMMATION RELATED TO ISCHEMIA/REPERFUSION IN A MURINE MODEL OF ALLOTRANSPLANT**

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We evaluate a novel anti-C5 antibody in a murine model of I/R transplant injury. This scFv anti-C5, isolated from a human phage display library, reacts with the cleavage site of C5a inhibiting the generation of C5a and C5b by the classical pathway. The C5 convertases. Heterotopic heart transplants were performed in CD rats after 24 hours) at 37°C. Cleavage of the inactive procaspase-3 to the active form was identified by western blotting. Activity was measured using the “CaspACE” colorimetric assay. Comparisons were made between cells undergoing hyoxia-reoxygenation (H-R) with and without IPC (10/10 minutes of hyoxia/reoxygenation).

**Results:**

- Warm H-R causes a significant increase in both caspase-3 cleavage and activity, compared to controls (p<0.04). Activity was increased by a factor of 5.39 and 29% mean reduction in cleavage and activity respectively, after 2 hours reoxygenation.

**Conclusions:** Normothermic preservation allows prolonged preservation of livers both with and without substantial prior warm ischemia injury. Successful outcome following transplantation can be predicted from perfusion data.

**PO-882**

**PRESERVATION AND RESUSCITATION OF LIVERS FROM NON-HEART-BEATING DONORS (NHBD) USING NORMOTHERMIC PRESERVATION**

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**Introduction:** We have assessed the use of normothermic preservation in a porcine model of liver transplantation from both heart-beating (HB) and NHBD donors. We deliberately selected a period of preservation (20 hours) which is longer than the previous maximum successful storage time reported in this model.

**Materials and methods:** Livers were transplanted following either conventional storage (cold, UW) or normothermic perfusion using a blood-based perfusate. NHBD were subjected to a period of up to 60 minutes warm ischemia immediately before retrieval. The normothermic perfusion circuit included a centrifugal pump, heat exchanger and an oxygenator, enabling physiological flows and pressures in both portal vein and hepatic artery. Bile acids, prostaclylene and parenteral nutrition were infused. Experiments were terminated (in surviving animals) at 5 days.

**Results:** Normothermic preservation was associated with a significant survival benefit for both 0 and 40min WIT and 20 hours of storage (p=0.0009). This was mirrored by lower AST, ALT and LDH levels and superior coagulation parameters. It may be of note that the best results were achieved in the 40min warm ischemia group with normothermic preservation. Outcome was predictable by measurement of haemodynamic and biochemical parameters during perfusion (massive enzyme release was noted during normothermic preservation of 60 min WIT livers).

**PO-883**

**ISCHAEMIC PRECONDITIONING LIMITS WARM HYPOXIA-REOXGENATION-INDUCED APOPTOSIS OF HUMAN SINUSOIDAL ENDOTHELIAL CELLS**

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**Background:** Ischaemia-reperfusion injury (IRI) significantly affects hepatic function following transplantation and major resection; the death of sinusoidal endothelial cells (SECs) by apoptosis plays a central role in this process. Caspase-3 is an important intracellular protease in the apoptosis pathway. Ischaemic preconditioning (IPC), a prior, brief period of vascular occlusion and reperfusion) has been shown to decrease the severity of this injury in rodent livers.

**Methods:** Primary cultures of human SECs (from hepatic resection specimens) were grown to confluence. The SECs were exposed to one hour of hypoxia (O2<0.1%) in a microaerophilic chamber, then reoxygenation (0.1,2 hours) at 37°C. Cleavage of the inactive procaspase-3 to the active form was identified by western blotting. Activity was measured using the “CaspACE” colorimetric assay. Comparisons were made between cells undergoing hyoxia-reoxygenation (H-R) with and without IPC (10/10 minutes of hyoxia/reoxygenation).

**Results:**

- H-R caused a significant increase in both caspase-3 cleavage and activity, compared to controls (p<0.04). Activity was increased by a factor of between 2- and 4-fold. IPC prior to H-R significantly reduced the degree of caspase-3 cleavage and activity (p<0.04). This amounted to a 39% and 29% mean reduction in cleavage and activity respectively, after 2 hours reoxygenation.

**Conclusions:** Warm H-R causes a significant increase in caspase-3 activity and cleavage in human SEC's in-vitro. This implies activation of the intracellular apoptotic pathway, leading ultimately to the death of SEC's by apoptosis. IPC significantly decreases the degree of caspase-3 activity and cleavage following warm H-R.
**PO-884**

**ISCHEMIC LIVER PRECONDITIONING BY DONOR HILAR CLAMPING MANEUVER DOES NOT REDUCE APOPTOTIC PHENOMENA AND PREVENT GRAFT DISFUNCTION IN LIVING DONOR LIVER TRANSPLANTATION**

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**Introduction:** Liver ischemic preconditioning (IP) has shown inhibition of cell apoptosis with less postoperative cytolysis. Pringle maneuver is claimed to be beneficial to the quality of the graft. We investigate the influence of IP on early graft outcome in LDLT.

**Methods:** Thirteen liver donors underwent heparctectomy and randomly assigned to our IP protocol. This consisted on portal triad clamping during 10 min followed by 15 min reperfusion. Donor heparctectomy was done with the USF. Recipients were divided into two groups: G1, n = 6 patients without IP, and G2, n = 7 patients with IP. Biopsies were: 1) baseline; 2) after donor IP; 3) 30 min following reperfusion (recipient). Apoptosis was evaluated by TUNEL staining and EM. Caspase 3 and 8 activity were assessed by fluorometric assay.

**Results:** Blood loss was of 421±259 ml (101-574) in G1 and 352±153 ml (200-800) in G2 (p=0.6). Cold ischemia was of 166±50 min (110-218) in G1 and 211±56 min (125-300) in G2 (p=0.23). Postoperative day 1 ACT/100 g liver was of 44±5 in G1 and 38±5 in G2 (p=0.7). One recipient in G2 displayed transient hyperbilirubinemia. Caspase 3 and 8 were not found and minimal apoptosis (10%) was found similar in both groups. ACR was 16% in G1 and 21% in G2.

**Conclusions:** The Pringle maneuver has no effects on minimizing blood loss during living donor liver resection. Donor ischemic preconditioning has no effects on tissue preservation in term of reduced apoptosis and postoperative cytolysis.

**PO-885**

**INTRAPERITONEAL LIVER INJURY DURING LIVING DONOR LIVER TRANSPANTATION (LTX)**

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**Introduction:** Postoperative hepatic dysfunction is usually attributed to volume loss and presence of micro or macro steatosis and/or fibrosis. Biochemical changes in the post-operative period, attributed to volume loss may be evolving before any loss of tissue. Factors such as injury/necrosis along the margin of resection, the re-absorption of split bile following division of the ducts causes careful examination. These findings of biochemical changes that occur prior to loss of tissue requires corroboration by other centers.

**PO-886**

**USE OF UW OR HTK IN LIVE DONOR LIVER TRANSPLANT (LTX)**

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**Availability of UW (University of Wisconsin) Lead to Better and longer preservation of solid organ allografts. Recently, HTK (Histidine-Tryptophan-Ketoglutate), has been studied in deceased donor LTX. However, data of HTK use in live donor LTX is limited.**

**Aims:** To examine the biochemical changes suggestive of hepatic dysfunction in first eight days after live donor LTX.

**Patient and Method:** Consecutive 33 patients received live donor liver allograft for end stage liver disease. In 9 cases, UW and in 24 cases HTK was used for perfusion and preservation of the allograft.

**Results:** Mean age of the recipients, MELD score, and hepatic graft recipient weight ratio was comparable in both groups (table 1). Mean AST, ALT and INR were higher on the first postoperative day in HTK compared to UW. By postoperative day 8, the were the same in both groups. Also, total bilirubin, ALK-P04 and GG TP were similar on first 8 postoperative days (table below).

| Variable       | UW (n = 9) | HTK (n = 24) |
|----------------|------------|--------------|
| MELD           | 16±8       | 50.6±11.5 (51.5 median) |
| INR            | 13±3       | 5±4 (12.5 median) |
| Day 1 GGTP     | 90±30      | 66±100       |
| Day 1 AST      | 80±20      | 20±30        |
| Day 1 ALT      | 7±5        | 5±5          |
| Day 1 INR      | 4±2        | 1±1          |
| Day 1 Bilirubin| 3±1        | 3±1          |
| Day 8 GGTP     | 212±100    | 208±100      |
| Day 8 AST      | 90±60      | 90±60        |
| Day 8 ALT      | 218±100    | 201±100      |
| Day 8 Bilirubin| 3±1        | 3±1          |
| Day 8 INR      | 12±2       | 12±2         |

**Conclusion:** Both solutions are safe in preserving the liver donor allograft. Higher values of AST, ALT and INR was observed with HTK compared to UW preserved allograft on first operative day which normalized by postoperative day 8. More prospective studies are required to establish the consistency and long-term impact of these differences.

**PO-887**

**POSSIBILITY OF CONDITIONING PREDAMAGED GRAFTS AFTER COLD PRESERVATION: RELATIVE INFLUENCE OF PERFUSATE AND TEMPERATURE**

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Grafts from non-heartbeating donors suffer from pre-preservation injury, the impact of which can be mitigated by machine perfusion or gaseous oxygenation upon harvest and during preservation. Here we wanted to evaluate the possibility to reverse deleterious priming of NHBD-grafts by oxygenated perfusion only after cold storage. Moreover, the respective role of oxygenation, nutrients, and temperature was addressed.

Livers were retrieved 30 min after cardiac arrest of male Wistar rats and preserved with HTK-solution for 18h by cold storage(CS). After 16h, some livers were put on an oxygenated machine preservation circuit for the last 2 h and conditioned by cold perfusion with either HTK (conHTK), HTK-supplemented with adenine, phosphate and glucose (conHTK+), or Williams-E solution (conWE).

Upon reperfusion in a normothermic circuit, it was found that postconditioning with any of the solutions led to a significant (3-5fold) reduction of parenchymal damage (ALT, LDH, GLDH release).

Immunohistochemical staining of adhesion molecules was prominent after CS, but a major (ICAM-1) or minor (MHC-classII antigen) reduction was achieved in the conditioned livers. Metabolic recovery (VO2) was also significantly enhanced compared to CS, with best results found after restHTK.

No signs of terminal apoptosis (TUNEL) were seen in either group. Thus oxygenation in the cold was most successful and could not be enhanced by addition of energetic substrates (HTK+) or using a nutrient solution (WE). Experimental conditioning at 22°C did not improve parenchymal recovery compared to 4°C with either solution nor were substrate enriched solutions superior to native HTK.

We conclude from these data that conditioning of predamaged livers is possible, best performed in the cold and in short term dependent mostly on oxygen rather than energetic or nutritive support.

**PO-888**

**ORGAN PRESERVATION IN HEART TRANSPLANTATION WITH UW – IMPACT OF PROLONGED ISCHEMIC TIMES OVER 5 HOURS**

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**Purpose:** Due to improvements in organ preservation and organ scareness prolonged ischemic times over 5 hours are frequently accepted in our centre. This study investigates the impact of prolonged ischemic time on myocardial damage and outcome after heart transplantation.

**Methods:** 121 heart transplant recipients (08/2000 – 08/2004, UW preservation solution) were analysed. 15% (n=18) of the donor hearts had an ischemic time of more than 5 hours (group I). They were compared to 103 patients.
ERYTHROPOIETIN EXERTS LUNG-PROTECTION AFTER ACUTE HEAD INJURY IN RATS: EFFECT ON LIPID PEROXIDATION AND MYELOPEROXIDASE LEVEL

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Purpose: To evaluate the possible protective effect of erythropoietin and methylprednisolone in lung injury following experimental head trauma.

Methods: Materials: Seventy-six female Wistar-Albino rats weighing 180-220 g were evenly allotted into ten groups. A weight-drop method was used to achieve head trauma. Samples were obtained 24 h post injury from the left lung. Lung tissue-associated myeloperoxidase activity and lipid peroxidation levels were measured. The ANOVA was applied to test for differences in the lipid peroxidation levels and myeloperoxidase activity between groups. Then, post hoc comparison was performed.

Results: First, head trauma substantially elevated the lipid peroxidation levels and the myeloperoxidase activity in lung tissue in the severe trauma group (p<0.05). Second, methylprednisolone significantly decreased lipid peroxidation levels in trauma-moderate group (p<0.05), whereas in trauma-severe group erythropoietin was superior (p<0.05). Third, erythropoietin was more effective than methylprednisolone in decreasing myeloperoxidase activity in both trauma groups (p<0.05).

Conclusion: Erythropoietin efficiently protected lung tissue against polymorphonuclear leukocytes infiltration and oxidative damage. Further studies are warranted to better elucidate the management of lung injury in brain injury并发 conditions.

SECRETORY PHOSPHOLIPASE A2 AND CYTOKINE INDUCTION IN ISCHEMIC INJURY FOLLOWING TRANSPLANTATION OF LIVERS FROM NON-BEATING DONORS: MARKERS FOR PRIMARY GRAFT NON-FUNCTION

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Secretory Phospholipase A2 (sPLA2) degrades cell membranes and plays an important role in the synthesis of pro-inflammatory mediators during inflammatory events such as ischemia-reperfusion injury (IRI). We evaluated changes in sPLA2 and pro-inflammatory cytokines in serum early after reperfusion of livers exposed to Warm Ischemia (WI) in our previously validated model of liver transplantation (LT) from non-beating donors (NHBDB).

Methods: Pig livers were exposed to 15,30,45, or 60min WI (6 in each group), procured and transplanted after 4hrs cold ischemia. Serum samples were collected prior to, and 15, 60, and 180min after reperfusion to determine sPLA2 enzymatic activity (fluorescent technique), Tumor Necrosis Factor (TNF-α) and Interleukin (IL)-6 levels (ELISA).

Results: Primary graft function (PNF) developed in 100% after 60min WI, 94.3% after 45min, 83.3% after 30min WI, and was absent after 15min WI, and was also absent after 0min WI (control). After reperfusion, sPLA2 activity in serum increased and peaked at 60min in PNF (14.59±5.47AU) vs. non-PNF recipients (10.58±7.86AU) (p<0.002). TNF-α peaked at 180min in PNF (512±79pg/ml) vs. non-PNF recipients (283±79) (p<0.0001). IL-6 peaked at 180min in PNF (3982±2291pg/ml) vs. non-PNF recipients (2102±850 pg/ml) (p=0.0034).

Conclusions: These findings indicate that an increase of sPLA2 activity 60min after reperfusion, followed by an overproduction of TNF-α and IL-6, correlates with PNF, emphasizing their potential role during IRI. Therefore, we suggest that biological interventions aimed at improving WI injury following LT (NHBDB) include the inhibition of sPLA2 activity and prevention of pro-inflammatory cytokine induction.

DELAYED GRAFT FUNCTION IN KIDNEY TRANSPLANTATION WITH CALCINEURIN INHIBITOR BASED IMMUNOSUPPRESSION

PO-891

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Aim: To assess the incidence of delayed graft function (DGF) in two groups of renal transplanted patients in treatment with calcineurin inhibitors based therapy. DGF was defined as the need for dialysis after renal transplantation (RT).

Methods: A group of 36 donors whose kidneys were transplanted into 2 groups of 36 recipients, each in therapy with CsA or tacrolimus for every donor, was identified. Cold ischemia time (CIT) and warm ischemia time (WIT) were 738 min and 56 min for CsA group, and 794 min and 55 min for Tac group (p=n.s.).

Results: We report 22% (8/36) of DGF for CsA group and 27.7% (10/36) for Tac group (p=n.s.).

Apart from immunosuppression, we found that CIT and WIT of the 18 pa-
patients with DGF compared with CIT and WIT of the 54 patients with no DGF were higher (p<0.0001 for both CIT and WIT). There was a difference ei-
ther in donors age for kidneys with DGF (51 years) vs kidney with immediate function (42 yrs) (p<0.0001), either in dobutamine administration in the donor (p<0.0001). Renal function assessed with creatinine (mg/dl) was higher for pa-
tients with DGF -1.9 and 2 (at 1 and 2 yr)- compared with patients without DGF -1.4 and 1.3 (at 1 and 2 y)- (p<0.0001 at 2 y).

Conclusions: Our data suggest that in couples of kidneys belonging to the same donor, with short CIT, there is no difference in the incidence of DGF with CsA or tacrolimus based immunosuppression. On the contrary DGF is associated with older donors age, dobutamine administration and prolonged CIT and WIT.

PORCINE LIVER HEPATOCYTES REGENERATION IN COLD AND NORTHERMIC PRESERVATION

PO-892

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Livers procured from non-beating donors (NHBDB) undergo a sequence of injuries culminating in ischaemia-reperfusion (IR) that has progressively deleterious effects (Reddy et al., transpl 157:79)(13520-32). No quantitative reports exist describing the hepatocyte proliferative response to IR. To as-

sess hepatocyte proliferative capabilities in isolated porcine perfused livers we have used alkaline-phosphatase anti-alkaline phosphatase immunohisto-

chemistry (APAAP) incorporating a monoclonal antibody Ki-67 that highlights G1, G2, S and M phases of dividing cells. Porcine livers were subject to 60 min-
utes warm-ischaemia followed by either, (1) normothermic preservation for 24 hours(Warm group, n=5); (2) 4 hours cold storage and normothermic preser-

vation for 20 hours(Cold group, n=5). Quantitation of proliferative hepatocytes by point counting using light microscopy was undertaken. Five fields in 5 lob-
ules for each tissue section (x40 magnification) were assessed in cryostat sec-
tions of snap-frozen biopsies at hepatectomy, 2, 6, 24 hours. Our results show that warm preserved livers yield significantly more dividing hepatocytes when compared to cold preserved (unpaired student’s t-test). Our results correlate well with biochemical liver function tests. In Table, ( ) = standard deviation.

Time/hours Cold group (n=5) Warm group (n=5) p-

0 49.6(9.8) 63.1(9.9) p<0.23
2 55.7(24.6) 134.5(53.2) p<0.0001
8 28.1(16.3) 183.4(62.5) p<0.0001
24 30.0(9.0) 123.7(74.4) p<0.0001

We postulate that the addition of 4 hour cold preservation to a pre-existing 60 minutes warm ischemia injury leads to a accentuated ischaemia-reperfusion injury resulting in a liver which does not recover by proliferation (ie. non-viable).

Warm preservation allows maintenance of cellular viability and subsequent proliferation.
INTRAHEPATIC PROTEIN C ACTIVATION REDUCES PHAGOCYTE ACTIVATION DURING REPERFUSION IN HUMAN LIVER TRANSPLANTATION

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AIMS: Activated protein C (APC), formed from protein C (PC) by thrombin-mediated proteolysis, exhibits both anticoagulant and anti-inflammatory effects in experimental reperfusion injury. We studied the possible anti-inflammatory role of APC during reperfusion in clinical liver transplantation (LTX).

METHODOLOGY: In 47 patients undergoing LTX, plasma levels of PC and APC and phagocyte adhesion molecules CD11b and L-selectin expressions were measured before surgery, before portal declamping, and during reperfusion. Samples of blood entering and exiting the liver were obtained during the first minute and at 5 minutes after portal declamping, and transhepatic ratio (exit/enter) was calculated.

RESULTS: Presurgery PC and APC levels were 51% (25%-111%) and 110% (78%-335%), with an increase in APC level during surgery (p<0.001). During initial reperfusion, marked portal PC entrapped occurrence within the graft (cauliflower 25% (12%-76%); portal vein 49% (20%-96%); transhepatic ratio 0.63 (0.30-1.6); p<0.001), with APC outflow from the graft (cauliflower 224% (89%-485%); portal vein 293% (97%-921%); transhepatic ratio 0.62 (0.30-3.30); p<0.12). Simultaneously, hepatic neutrophil and monocyte activation occurred, indicated by low L-selectin and high CD11b expression (transhepatic ratio all p<0.001). Transhepatic PC ratio correlated with both transhepatic neutrophil and monocyte CD11b ratio (neutrophil R=0.377; p<0.011; monocyte R=0.389; p=0.008) indicating negative correlation between PC entrapment and phagocyte activation.

CONCLUSIONS: During initial reperfusion, liver graft transiently entrapped PC without APC outflow. Simultaneously, marked phagocyte activation took place in the liver graft. The relation between PC sequestration and phagocyte activation suggests that PC activation may have a phagocyte inhibiting role during reperfusion in LTX.

OXIDATIVE STRESS INDICATORS AFTER ISCHEMIA-REPERFUSION INJURY

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PURPOSE OF THE STUDY: was to compare the oxidative stress (OxS) indicators in rat kidneys after ischemia-reperfusion injury in reperfused rat, Lsosartan-treated rat and in control rat kidneys.

METHODS: Adult Wistar rats (n=40) were studied 4 weeks (wk) after ischemia-reperfusion injury (ischemia time 45 min). Rats anesthetized with intraperitoneal ketamine and medetomidine as was assessed using following parameters: urine protein excretion rate (UproV, mg/day), awake systolic blood pressure (SBP), mmHg), serum creatinine (SCr, µM), histocompatibility (PCNA, MCP-1). Serum proteins of lipid peroxidation (LPO, µM/l) were determined together with markers of antioxidant status (concentrations of total glutathione included reduced and oxidized forms: GSSG+GSH=GSSG, µM).

RESULTS: showed that no significant elevation of renal tissue LPO level was observed in reperfused animals kidneys 4 weeks after the intervention. Lsosartan treatment did not affect the renal tissue oxidative stress markers significantly compared with rats treated without treatment.

CONCLUSION: Treatment with angiotensin II blocking agent did not change the oxidative stress status despite the favourable effects on the kidney damage.

ROLE OF NUCLEAR FACTOR KAPPA B ACTIVATION IN LIVER PRESERVATION AND ACUTE REJECTION

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The present study was undertaken to determine whether lazaroid (LZ) or nuclear factor-kappa(B) (NF-kB) decay could suppress pro-inflammatory gene up-regulation through inhibition of NF-kB activation in the liver. Lipopolysaccharide (LPS, 30 mg/kg i.p.) was administered to male ICR mice. LZ (3 mg/kg, i.v.) or NF-kB decay (2 microM, portal vein injection as hemagglutinating virus of Japan-liposome method) was administered simultaneously. Kupffer cells (KC) were isolated by collagenase perfusion. KC released both TNF-α and IL-6 after LPS addition. LZ suppressed TNF-α release in a dose-dependent manner. LZ also increased the inhibition of TNF-α mRNA expression and NF-kB activation in KC. Furthermore, LZ suppressed the degradation of I-KB proteins. LZ significantly increased survival rate after LPS injection in vivo. NF-kB activation was also observed in rat liver ischemia-reperfusion. NF-kB decay also significantly increased the survival rate and significantly inhibited the increase of TNF-α alpha release. In acute rejection model of rat liver transplantation (TX) (DA to Lewis rat), addition of NF-kB decay (2 microM) in the liver preservation solution significantly (-p<0.05)increased the survival rate of the rats and suppressed the expression of mRNA of TNF-α and IL-6 in the liver. These results suggest that inhibition of NF-kB activation of KC may be one of important strategies to liver TX and NF-kB decay are useful for the treatment of ischemic liver preservation and acute liver rejection.

MACHINE PERFUSION PRESERVATION OF THE PIG LIVER USING A NEW PRESERVATION SOLUTION, POLYSOL

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INTRODUCTION: The current gold standard method for porcine liver preservation is cold storage (CS) in a preservation solution (4°C), such as Celsior or the University of Wisconsin solution (UW). Recent studies have shown the benefits of hypothermic machine perfusion (MP) over CS. To improve the results of MP, an enriched MP preservation solution (named Polysol) was developed, which proved to be superior to the UW-Glucanate solution in a rat liver perfusion model. The aim of this study was to assess Polysol in a pre-clinical pig liver preservation model.

METHODS: Female pigs (35-40 kg) were used as liver donor. The liver was washed in i.v. using 3 L Ringer Lactate, followed by 1 L of the preservation solution (4°C). After harvesting, the liver was preserved for 24 h by either CS using Celsior (n=5) or MP using Polysol (n=5). For analysis of liver damage and function, livers were reperfused for 60 min using oxygenated Krebs-Henseleit buffer.

RESULTS: CS-Celsior resulted in significantly more damage in comparison to MP-Polysol (t=60, AST: 622 ± 215 versus 222 ± 55, ALT: 17 ± 6 versus 5 ± 1; LDH: 492 ± 100 versus 354 ± 31 IU/L). Intravascular resistance during reperfusion was significantly higher after CS-Celsior, when compared to MP-Polysol (t=0, 0.20 ± 0.01 and 0.11 ± 0.02 mmHg/ml/min, respectively). No differences were seen regarding ammonia clearance and urea production. In both groups, no bile was produced during reperfusion.

CONCLUSIONS: In an ex vivo pig-liver preservation model significantly less damage was found after machine perfusion preservation using Polysol, in comparison to cold storage using Celsior.

PRESEVERATION OF THE STEATOTIC DONOR LIVER: MACHINE PERFUSION VERSUS COLD STORAGE

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INTRODUCTION: A factor contributing to waiting lists for liver transplantation is the group of livers discarded due to steatosis. This concerns about 30-40% of all potential liver donors. These steatotic livers can be considered as sub-optimal livers. These organs have been shown to perform weakly during hypothermic static preservation, frequently resulting in primary graft non-function. However, machine perfusion preservation (MP) has been performed for donor livers instead of cold storage, resulting in superior preservation. The aim of this study was to compare CS in University of Wisconsin solution (UW) and MP using UW-Gluconate for preservation of the steatotic donor liver, using the isolated perfused rat liver model.

METHODS: Steatosis developed in male Wistar rat liver by use of a choline/ methionine-deficient diet for 2 weeks. In an isolated perfused rat liver model hepatocellular damage and liver function were assessed during reperfusion of a steatotic liver after 24 hours hypothermic CS in UW or MP using UW-G. To determine liver parenchymal damage AST, ALT, LDH levels were measured during 60 minutes of normothermic reperfusion with oxygenated KHB. Liver function was assessed by measuring bile production, ammonia clearance and urea production during perfusion.

RESULTS: All animals developed a 30-60% steatosis. Livers preserved by CS released more liver enzymes, as compared to MP-UW-G. Bile production was lower after CS as compared to MP-UW-G (± µL versus ± µL). Ammonia clearance and urea production were higher after MP-UW-G as compared to CS. Conclusion: Machine perfusion ameliorates preservation results of the steatotic livers, as compared to cold storage.
Xenotransplantation

PO-900 PREVENTION OF HYPERACUTE REJECTION IN A MODEL OF ORTHOTOPIC LIVER XENOTRANSPLANTATION FROM PIG TO BABOON USING POLYTRANSGENIC PIG LIVERS (CD55, CD59 AND H-TRANSFERASE)

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Background: The search for alternative sources for dealing with the shortage of transplant organs leads us to the search for animals an inexhaustible source of organs.

Objective: The objective of this study was to analyse whether livers from polytransgenic pigs expressing CD55 (hDAF), CD59 and H-transferase, would protect against hyperacute rejection after orthotopic liver xenotransplantation to a baboon and also to study pig liver function in a non human primate.

Methods: 9 liver transplants from pig to baboon were performed divided into two groups: a control group (n=4) with genetically unmodified pigs and an experimental group (n=5) using pigs transgenic for CD55, CD59 and H-transferase as donors. All the donating piglets were obtained through high hysterecomy and maintained in specific pathogen free conditions. The selection of transgenic pig donors was carried out following demonstration of transept gene expression using monoclonal antibodies (antiCD55, antiCD59) and immunohistological studies in liver biopsies.

Results: All the animals in the control group presented hyperacute rejection with survival rate being less than 16 hours without the transplanted livers functioning. In the experimental group none of the animals suffered hyperacute rejection. Survival in this group was between 13 and 24 hours. The livers were functional producing bile and maintaining prothrombin activity above 35%. Only in one case was there primary dysfunction of the xenograft.

Conclusion: The polytransgenic livers for complement regulatory proteins prevent hyperacute rejection when they are xenotransplanted into a baboon.

PO-901 TOLERANCE INDUCTION TO XENO-ISLETS BY ANTI-CD154 mAB AND RAPAMYCIN IS BASED ON ANERGY AND REGULATION

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Purpose: To investigate whether classical anergy and/or regulation by IL-2 dependent CD25+ T regs play a role in the induction and maintenance of tolerance in xeno-islets model.

Methods: Diabetic mice were transplanted (Tx) with rat islets. Control: islets Tx without therapy; rapamycin: 0.2mg/kg every other day to day 14; antiCD154mAb (MR1): 0.5 mg on days 0, 2 and 4; Combination therapy group with rapamycin and MR1. We then administered in addition to the combination therapy with early (from day 0 to 14 post-Tx) or late (from day 100 to 114 post-Tx) IL2, anti-IL2 mAb, and anti-CD25 mAb respectively.

Results: Rapamycin and MR1 alone prolonged graft survival compared to control (MGS (median graft survival) 34 days, 98 days vs. 17 days, p<0.001). Combination therapy allowed indefinite graft survival (MGS >120 days, p<0.001). Early IL2 induced rapid rejection in 18/18 mice (MGS 7 days), whereas in late IL2, only 3/10 developed rejection. Early anti-IL2 mAb led to rejection in 10/10 mice (MGS 42 days), whereas late anti-IL2 led to rejection in only 1/4 mice. Early anti-CD25 mAb led to rejection in 8/9 mice (MGS 49 days), whereas late anti-CD25 mAb led to rejection in only 3/7 mice.

Conclusion: Combined therapy allowed indefinite islet xenografts survival. Early IL2, anti-IL2 mAb or anti-CD25 mAb prevented tolerance induction, suggesting that classical anergy and regulation by IL-2 dependent CD25+ T regs are critical in the induction of tolerance in the post-Tx period. Delayed administration of those agents did not abrogate tolerance in most recipients, suggesting that anergy and regulatory cells are less important for the maintenance of tolerance.

PO-902 NATURAL PREGNANCY IN RABBITS WHO UNDERWENT OOPHORECTOMY AND ORTHOTOPIC ALLOGENIC OR AUTOLOGOUS OVARIAN XENOTRANSPLANTATION

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To date, most studies on the preservation of ovarian tissue have been limited to experiments with autografts. Whereas allogeneic or xenogeneic grafts have been little investigated.
The purpose of this study was to evaluate the fertility of rabbits after autologous and allogeneic ovary transplant without a vascular pedicle, in the presence of immunosuppression with cyclosporine.

Ten sexually mature California or New Zealand White female rabbits and five New Zealand male rabbits of known fertility were used. Both ovaries were transplanted from California (n = 5) rabbits to New Zealand White rabbits (n = 5) and vice-versa. All animals received 10.0 mg/kg cyclosporine through an orogastric tube, daily from one day before the operation and for nine months. Three months after the operation, the females were almost daily paired with a sexually mature male on an almost daily basis during the other six months of the study. At the end of the follow-up period, blood samples were studied for E2, P, FSH and LH, and the number of successful pregnancies were assessed. All animals recovered from surgery with the exception of one that died at the end of the operation. The other rabbits had an uneventful postoperative course and survived throughout the nine-month experimental time. Live births were recorded in five rabbits two months after the females started to be paired with a male.

Fertility in the presence of allogeneic ovary transplantation in a rabbit model was successful. A vascular pedicle was not necessary for the maintenance of ovary viability and function.

**PO-903 HBO AND PANCREAS PRESERVATION FOR ISLET ISOLATION**

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**Background:** As human islet transplantation is limited by the lack of sufficient numbers of human donor organs, xenotransplantation with the use of porcine islet cells seems to be a promising therapeutic option to cure diabetes. Recent studies showed that the two-layer method (TLM) of pancreas preservation prior to isolation significantly improved islet yield due to better oxygen supply. HBO is another possibility to improve preservation conditions and is tested in this study.

**Methods:** University of Wisconsin solution (UW), Celsior, Perfadex and NaCl are oxygenated with 100% oxygen for 50 minutes at 1.5 bar using a hyperbaric chamber. Porcine pancreata are harvested at a local slaughter house and stored in pre-oxygenated and not oxygenated preservation solutions at 4°C. Samples are taken to assess oxidative stress and organ damage.

**Results:** Amylase, lipase, MDA, ADMA and GSH/GSSG levels are significantly higher when working with Perfadex and HBO, but promising when working with the other solutions. Less apoptosis occurs using HBO in combination with Celsior and UW.

**Conclusions:** HBO has a positive impact on porcine organ preservation. As ischemically damaged islet cells are likely to undergo cell death or lose functionality due to hypoxia, the use of pre-oxygenated preservation solutions is a promising method to achieve better yields after islet isolation and transplantation.