This bill is based on promotion of living-related donations, according to the ministry of health. A closely matched non-related person may only provide an organ out of compassion when a genetically-related donor is unavailable. Cadaveric donation is not among the designated priorities. The edict imposes strict penalties for brokers and those indulging in unsupervised removal, storage and grafting of organs. A federal monitoring authority and evaluation committees in designated institutions have been convened. A donor from their country of origin will have to accompany non-residents if they want to avail of our services [5].

Transplant registry, a nationwide pool of potential donors, a donor card system, as well as allocation of resources for disadvantaged end-stage renal disease (ESRD) patients, donor care and follow-up are planned. Transplant institutions will only be allowed to function if they (and personnel thereof) meet prescribed licensure criteria. Limited experience (28 cadaveric grafts to date), non-existence of a brain-death law and doubts about public approval of cadaveric mode of organ harvesting preclude the optimistic notion of the Transplant Society of Pakistan that a deceased organ donation programme will help save 50 000 lives every year.

Pakistani law has global implications because of rampant transplant tourism [6]. It is consistent with contemporary trends [7]. Organ donation by relatives should be portrayed as an act of dignity. I suggest that a sustained strategy of directed donations be adopted, with more effective early identification of a genetically-related donor for each ESRD patient. A strong family setup, and motivation by specialist counsellors, may both play a critical role.

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Implementation of high-throughput screening for Fabry disease in Toronto dialysis patients

Sir,

Fabry disease is a rare X-linked lysosomal storage disorder caused by mutations in the α-galactosidase A (α-gal A) gene. Affected hemizygous males have impaired or abrogated activity of α-gal A enzyme that leads to a buildup of neutral glycosphingolipids, particularly globotriaosylceramide (Gb3), in many tissues and organs [1]. Symptoms include acroparesthesias, angiokeratomas, corneal opacities, and cardiovascular and renal complications, with death usually occurring by the fifth decade of life [1]. Females that are heterozygous carriers of an α-gal A enzyme mutation show a wide variety in the range and severity of their symptoms.

The kidney is of particular pathological importance in Fabry disease, as kidney failure due to Gb3 buildup is a major complication; along with cardiac failure it is a leading cause of death [2]. In recent years, it has been proposed that some dialysis patients could be suffering from undiagnosed Fabry disease and therefore there would be benefits to screening dialysis patients for this disease [3,4]. We carried out a pilot screening study at the Toronto General Hospital in Ontario, Canada, to implement our previously published high-throughput blood spot assay for Fabry disease [5]. Informed consent was obtained from 147 forthcoming dialysis patients to screen their blood for levels of α-gal A enzyme. Based on our blood spot assay, 141 of these patients had whole blood α-gal A enzyme activity levels within the normal range compared to normal and Fabry controls [5, and unpublished data]. For those six patients with activity below 1.5 nmol/h/ml (<65% of average enzyme activity in normal controls), secondary plasma α-gal A enzyme assays showed that all patients were within the normal range.

While no Fabry patients were identified in the relatively small participating patient population, this study shows application of our previously published high-throughput screening method. Our assay is a rapid and low-cost method for screening patients that may be suffering from undiagnosed Fabry disease. This initial screening study did not exclude any patients willing to participate, so both males and females were included. As with other symptoms, α-gal A enzyme levels in female Fabry patients vary with the individual and can even approach normal levels. We thus cannot discount the possibility that there remain undiagnosed female Fabry patients in this population. For this reason, future screening studies based on our method will likely target the male dialysis population. With the availability of enzyme replacement therapy (ERT) for lysosomal...
storage disorders such as Fabry disease, standardized screening for particular biomarkers is beginning to be considered a useful tool for diagnostics [6]. Future screening studies may help to identify Fabry patients that would gain immediate benefit from diagnosis. Screening for this disease is particularly timely in Canada, where a comparative clinical trial of currently approved ERT drugs is ongoing.

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Long-term results of a calcineurin inhibitor-free immunosuppression based on Thymoglobulin® and mycophenolate mofetil in elderly kidney transplant recipients

Sir,

The number of kidney transplant donors and recipients above 60 years of age is increasing worldwide. Kidney allografts from elderly donors are at high risk of delayed graft function (DGF), increased susceptibility to calcineurin inhibitor (CNI) nephrotoxicity and seem to be more immunogenic than those from younger donors [1]. Recipients >60 years of age have an increased risk of dying of infection, cancer or a cardiovascular disease, but have a lower risk of developing an acute rejection (AR) than younger recipients [2]. However, if they do experience an AR, this shortens both patients’ and grafts’ survivals [1]. Finding adequate immunosuppression in this population is delicate. Very scarce data regarding the long-term results of CNI-free regimen in this population are available.

We conducted a prospective pilot study between January 1999 and May 2000 in kidney transplant recipients over 60 years of age. Twelve patients (mean age 65 ± 3 years) received the first renal allograft from cadaveric donors (mean age 55 ± 19 years). They received an induction therapy by Thymoglobulin® (1 mg/kg/day for 3 days and then administered when circulating lymphocyte CD2 count was <50/mm³ during the first 10 days, total mean dose: 6.29 ± 1.25 mg/kg), mycophenolate mofetil (2 g/day) and steroids [500 mg pulse pre-transplant, and then tapered to 30 mg at 1 month (M), 10 mg at M6 and 5 mg at M12]. Patients at risk for cytomegalovirus (CMV) received valaciclovir prophylaxis for 4 months. Anti-Pneumocystis jiroveci prophylaxis was given during the first 6 months post-transplantation. Seven-year patient, kidney allograft and death-censored kidney allograft survivals were respectively 83, 58 and 75%. Two patients died with a functioning graft (CMV disease and intracranial aneurysm rupture). Three other patients underwent haemodialysis, 35, 64 and 73 months after transplantation, because of chronic allograft nephropathy. Two of them had presented an AR. Overall, four patients (33%) presented an AR episode: two steroid-sensitive and two steroid-resistant rejections treated by OKT3. Only one patient presented a DGF, defined by the requirement of a dialysis session post-transplantation. Six patients presented a CMV infection (50%) and four patients developed a severe infection (not CMV) that required hospitalization. Two patients developed sepsisemia due to acute pyelonephritis and diverticulitis, respectively. A third patient suffered from a varicella zona virus infection. The fourth patient presented consecutively an ophthalmological zona, a septicaemia and cryptococcal meningitis. The latter patient had received OKT3. Two patients developed prostate cancer at 5 years post-transplantation. At the last follow-up, kidney function was good (Figure 1). Overall, five patients required the use of CNIs, i.e. the four patients who developed an AR and one other patient who had an increase in serum creatinine level related to a biopsy-proven chronic allograft nephropathy.

Hence, using a CNI-free immunosuppressive regimen based on short induction therapy by Thymoglobulin®, followed by a dual therapy by MMF and steroids, provides acceptable long-term results in elderly kidney transplant patients. OKT3 should be avoided in these patients. The results of this strategy might be improved by using pharmacokinetic and pharmacodynamic monitoring of MMF.

Conflict of interest statement. None declared.