Autopsy

1 Causes of Death in Patients with Thrombotic Thrombocytopenic Purpura (TTP): A Single Institution 22-Year Autopsy Cohort
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Background: TTP is a rare disease with a mortality rate that has gone from >90% to <20%, largely due to timely diagnosis and rapid initiation of plasmapheresis. As treatment successes in TTP patients have increased, treating disease relapses have also increased. While many successfully-treated patients with TTP die from other causes, others eventually succumb to this fatal disease. Post-mortem analysis of patients who die from or with a history of TTP are rare, we sought to characterize the clinical history, histopathologic findings, and causes of death in autopsies of patients with TTP performed over the past 22 years at our institution.

Design: A retrospective review of autopsy cases performed between 1/1/1990 and 4/30/2012 identified 19 patients with TTP in the cause of death or final diagnosis of autopsy reports. Medical records, autopsy reports, and histopathologic data were reviewed.

Results: 8 patients died directly as a result of their TTP; 11 patients died either as an indirect complication of or with a history of TTP. For all patients, the mean most abnormal laboratory values prior to death were as follows: platelets 27,000/µl (±28,000); hemoglobin 6.8 g/dl (±1.7); LDH 2002 U/L (±2138); creatinine 3.8 mg/dl (±2.0). ADAMTS13 activity testing results were available for 3 patients; activity was abnormally low (<67%) in all 3 cases and severely deficient (<10%) in 2. The mean hospital duration between admission and death was 22.5 days (±32.2). Plasmapheresis was utilized in 12 patients, with a range of 1-56 procedures performed over the hospital course prior to death. Histopathologic findings are reported in the table.

Histopathologic Findings

| Findings          | Heart | lung | Brain | Liver | Other |
|-------------------|-------|------|-------|-------|-------|
| Thrombi/Emboli    | 2     | 3    | 4     | 5     | 6     |
| Hemorrhages       | 1     | 2    | 3     | 4     | 5     |
| Malacia           | 6     | 7    | 8     | 9     | 10    |

Conclusions: Current treatments for TTP are effective at reducing mortality from this disease, and many patients do not die from causes directly related to their TTP. However, despite shorter times to diagnosis and improvements in treatment implementation, patients still die as a direct result of their TTP. We present single institution data over a 22-year period that characterizes the clinical and histopathologic findings of 19 patients who died with a diagnosis of TTP. This represents one of the largest TTP autopsy cohorts.

2 What Are We Missing? Repercussions of Declining Autopsy Rates
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Background: Autopsy is a useful tool in identifying cause of death, usually confirming or clarifying clinical diagnoses. However, in a percentage of cases, autopsy will identify previously unsuspected diagnoses, even when there is a high degree of diagnostic certainty. Information obtained at autopsy allows physicians to hone their clinical skills, recognize uncommon diseases, and potentially modify treatment in future cases. Despite these benefits, autopsy rates in the United States have dropped from 40-60% of hospital deaths to <10%. This decline has been attributed to decreased benefit of autopsy in setting of advanced diagnostic modalities, costs and increase in hospice patients. Decedents with uncertain diagnoses are currently the primary recipients of the hospital based autopsy. This study examined the effect of high versus low autopsy rates on the rate of missed diagnoses over a fifty-seven month period.

Design: In November 2007, Corizon contracted with the state of Alabama to provide health care to state prisoners. Under this contract it was agreed that University of Alabama at Birmingham (UAB) would perform autopsies on inmates that died of natural causes. The autopsy rate for the prison population was substantially higher than the current norm. After obtaining IRB approval and permission from Corizon and the prison commission, we reviewed the mortality logs of adult patients at UAB and the prison system from November 2007 through July 2012 to determine the respective autopsy rates. We then reviewed all prison autopsies performed at UAB and adult UAB autopsies during the study period to compare the rates of major missed diagnoses. A major missed diagnosis was defined as either an unsuspected cause of death or unsuspected significant morbidity, such as active tuberculosis.

Results: UAB autopsied 7.4% of adult hospital deaths, compared to a prison autopsy rate of 46% (p<0.001). Major missed diagnoses were identified in 27% of UAB cases and 19% of prison autopsies (p= 0.023). While the male to female ratio for inmates (11:1) and UAB (1.1:1) differed (p<0.001), the rate of missed diagnosis between genders was not significantly different (p=0.26).

Conclusions: Our study clearly demonstrates that despite technological advances in medicine the decline in autopsy rates has a statistically significant impact on the rate of major missed diagnoses. Performing more autopsies would yield information regarding missed diagnoses, inaccurate cause of death, and epidemiologic data. Acquiring this knowledge could have substantial impact on clinical management.

3 Intra-Uterine Fetal Demise: Autopsy and Clinical Findings amongst Different Age Groups in an Inner City Hospital
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Background: Stillbirth occurs in 1% of all pregnancies in the USA and remains largely unstudied. The use of fetal autopsy has been limited in many institutions by cost, a lack of trained pathologists, and discomfort on the part of physicians and patients in discussing or having the procedure. Here we report on clinicopathologic characteristics between different age groups in an inner city hospital.

Design: A retrospective search (2002-11) was performed to identify all women (n=163) who were diagnosed with intrauterine fetal demise in an inner city hospital. The findings were compared in three age groups: 1) under 21 (n=37), 2) 21-34 (n=104), 3) >35 (n=22). Fetal autopsy results, which included gross and microscopic morphology, were reviewed and demographic data was obtained from electronic patient charts.

Results: Under-21 stillbirths represent 23% of total stillbirths in an inner city hospital with a large racial distribution: 92% of under 21 were African American while significantly lower in >35 (54%). Gestational ages, however, were similar in all three groups. Lack of prenatal care and STD’s were the most common maternal factors in the under 21s, while diabetes, pre-eclampsia/hypertension, and previous abortions prevailed in the other age categories. Chorioretinitis was the main placental factor in all groups, followed by placental infarction in groups 1 and 2, and retroplacental hematoma in group 3. Overall, no real significant differences in the cause of death were identified, with placental causes predominating.

4 Nonthrombotic Pulmonary Embolism: New Insights – A Large Autopsy Study
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Background: Pulmonary bone marrow embolism (PBME) and pulmonary bone fragment embolism (PBFE) are two types of nonthrombotic pulmonary embolism
with a density ranging from 0.74 – 30.5 emboli/cm² with mean embolic diameter of 45.8±37.6 µm. Pathologic examination showed that a number of consent issues that were identified at the time of autopsy but not reported to risk management. Recommendations from this study include: creating a user-friendly autopsy consent form, photography was used to support and contribute to morbidity or mortality.

7 A Rare Adult Autopsy Case of Von Gierke’s Disease with Significant Atherosclerosis

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Background: Glycogen storage disease type 1a (GSD 1a), or von Gierke’s disease, is caused by a deficiency in the enzyme glucose-6-phosphatase, resulting in tissue accumulation of glycogen. Through dietary modification and pharmacologic intervention, life expectancy has greatly improved for disease suffers. Despite significant hyperlipidemia in GSD 1a patients, there remains no consensus on their risk for developing atherosclerotic disease.

Conclusion: We report a case of a 61-year-old male with known GSD 1a, complicated by cerebral infarcts, cardiomyopathy, hypertension, and end-stage kidney disease status post renal allograft, who presented with altered mental status. Inpatient work-up was most consistent with acute metabolic encephalopathy secondary to liver and kidney failure. Despite aggressive medical management, the patient expired. An unrestricted clinical autopsy was performed, using a modified Virchow approach. Formalin-fixed and alcohol-fixed tissue samples were sent for histologic processing, and additional specimens were submitted in glutaraldehyde for electron microscopy.

Results: Significant gross anatomic findings included advanced liver fibrosis, cardiomyologically, severely atrophic native kidneys, cortical necrosis of the renal allograft, and extreme calcification of cerebral, coronary, and systemic arteries. Review of the patient’s medical record revealed a diagnosis of atherosclerotic nephropathy and sciatic artery disease. Schiff stain highlighted massive focal glycogen deposits in the liver and heart. Electron microscopy showed extensive glycogen deposition in hepatocyte and cardiomyocyte nuclei, cytoplasm, and mitocondria with mitochondrial swelling, loss of cristae and lipid droplets.

Conclusions: Overall, gross, histologic, and electron microscopic findings were consistent with GSD 1a; however, most remarkable was the extent of atherosclerotic disease that likely represents the factor most contributory to this patient’s final outcome. Although longstanding hypertension contributed to the pathogenesis of calcific vascular disease, these case findings argue that accelerated atherosclerosis does occur in the setting of GSD 1a and that aggressive medical management of hyperlipidemia should be pursued in such patients.

8 Unique Autopsy and Biopsy Findings of Liver Small Cell Carcinoma – Early Identification of a Treatable Medical Emergency

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Background: Although liver small cell carcinoma is rare, it often presents as hyperacute liver failure with unknown etiology and is a medical emergency. Definitive and rapid pathologic diagnosis is therefore essential for proper treatment.

Design: Autopsy and liver biopsy cases following acute liver failure between 1992 and 2012 were identified to better characterize the morphologic and clinical features of liver small cell carcinoma. Nine cases (3 autopsy and 6 liver biopsy) were identified from patients presenting with acute liver failure secondary to hepatic infiltration by small cell carcinoma. Chart review was performed to identify any preexisting conditions that may have favored the development of small cell carcinoma and to analyze all imaging. Diagnosis of liver small cell carcinoma on autopsy or biopsy material was based on morphologic findings and confirmed by immunohistochemical stains in all cases.

Results: All autopsy cases (n=3) and all liver biopsy cases (n=6) presented with hepatomegaly, no previous diagnosis of small cell carcinoma and without a definitive mass lesion identified on imaging. Autopsy cases demonstrated marked hepatomegaly, with livers weighing 2930 - 5360 gm and containing multiple, scattered, small nodules ranging from 3 to 6 mm in size. Histopathologically, small blue neoplastic cells diffusely involved the sinusoidal spaces and almost completely replaced the liver parenchyma in all autopsy and biopsy material. Extensive necrosis was also identified. Immunohistochemistry (IHC) demonstrated that neoplastic cells were positive for CD56, synaptophysin,NSE and cytokeratin AE1/AE3, and negative for CD45 and CD99. Although a sub-carinal lymph node metastasis was identified in one autopsy case, no primary lung tumor or evidence of further metastasis was detected in the other cases on imaging or autopsy despite thorough investigation.

Conclusions: Patients with hyperacute liver failure secondary to small cell carcinoma can present with identifiable hepatomegaly, but lack discrete lesions on imaging. A diffuse small blue neoplastic cell infiltration in the liver parenchyma is a unique pathologic feature that can be identified on biopsy. Other diagnostic clues including lymphoma and peripheral neuroectodermal tumor need to be ruled out through IHC prior to diagnosing small cell carcinoma. Therefore, liver biopsy together with a rapid panel of immunostains is necessary to firmly establish a diagnosis of liver small cell carcinoma and allow clinicians to immediately implement chemotherapy.

9 Illicit Stimulant Abuse and Aortic Dissections in a Culturally Diverse Autopsy Population

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Background: Stimulants such as methamphetamine and cocaine can be cardiotoxic by increasing heart rate, oxygen demand, and ventricular contractility. They are thought
to predispose an already weakened aortic media to an aortic dissection by causing a catecholamine surge that raises the shear stress and increases the likelihood for intimal tear and dissection. Due to its relatively fixed position, a tear at the ligamentum arteriosum, resulting in a type B dissection, is thought to be more likely with stimulant drug use.

The purpose of this study is to report patients who died from acute aortic dissections in a culturally diverse autopsy population and determine if acute illicit stimulant drug use is associated with a Stanford type B dissection.

**Design:** A retrospective chart review was performed over a 33 year period in patients with aortic dissection. Among the 124 cases of dissection, clinical features, risk factors, and illicit stimulant drug abuse were determined and compared using the Stanford aortic dissection criteria. Wilcoxon rank-sum and either Fisher’s exact or chi-square test were used for continuous and categorical variables, respectively.

**Results:** Aortic dissection is more common in the 6th and 7th decade with Stanford type A being more common. Hypertension is the most common risk factor. 24.5% of patients were seen by physicians for symptoms and released prior to their dissection. Illicit stimulant-related dissections represented 5.1% of cases. All illicit stimulant-related dissections were Type A and were not statistically different from non-stimulant dissections.

**Aortic dissection characteristics**

|                          | Stanford A (n=8) | Stanford A (n=4) | p-value |
|--------------------------|-----------------|-----------------|---------|
| History of hypertension  | 74 (79)         | 74 (79)         | 0.04    |
| History of smoking      | 41 (61)         | 41 (61)         | 0.00    |
| Mean (median) age in years | 69 (48)       | 69 (48)         | 0.8 (61) |

Conclusions: All illicit stimulant-related dissections in this study were Type A. This differs from previous reports that found drug related dissections tended to be younger, Black patients and were predominantly Type B. We highlight the need for routine toxicology on all aortics dissections regardless of history to provide more insight into illicit stimulant drugs and their role in aortic dissections.

10 Hydrophilic Polymer Embolism: Incidence of a Recently Recognized Iatrogenic Disease in a Retrospective Autopsy-Based Study of 136 Patients

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**Background:** Hydrophilic polymers are commonly applied as coating on endovascular device surfaces and have the potential to dissociate from devices during endovascular manipulation, causing hydrophilic polymer emboli (HPE). Adverse events related to this phenomenon have only recently been recognized. The incidence of this iatrogenic complication is unknown.

**Design:** We conducted a retrospective autopsy study at a tertiary care hospital to evaluate the incidence of hydrophilic polymer embolism (January 1, 2010-May 31, 2012). H&E-stained sections were evaluated for the presence, total number and location(s) of HPE. Localized (single organ) versus disseminated (multiple organ system and/or bilateral lung) involvement by HPE was determined. Findings were correlated with clinical data and patient outcome.

**Results:** During this period, 136 consecutive adult and adolescent autopsies were evaluated on 63 male and 73 female patients (age range: 10-96 years). Of these, 17 cases (13%) showed histologic evidence of HPE involving the lungs (n=17), heart (n=3), and/or central nervous system (n=2). Afflicted patients included 12 men, 5 women, and 1 teenage boy (age range: 16-73 years). There were no statistically significant differences in mean age between affected and unaffected patients (53 years versus 55 years, respectively; p=0.65). Affected patients underwent central venous catheterization (n=17), peripherally inserted central catheterization (n=3), hemodialysis (n=7), continuous venovenous hemofiltration (n=2), cardiac catheterization (n=5), extracorporeal membrane oxygenation (n=4), and/or cardiac (n=1) or peripheral vascular (n=1) bypass. On clinico-pathological correlation, localized HPE was an incidental finding in 10 patients, while diffuse HPE contributed to morbidity in 7 patients, being associated with constitutional changes, coagulopathy, ischemic events, and/or vasculitis. In patients with disseminated disease, death occurred hours to weeks after suspected embolic events. Statistically significant difference in hospital length of stay was noted between the affected and unaffected patients (48 days versus 26 days, respectively; p<0.05).

**Conclusions:** Hydrophilic polymer embolism occurs relatively commonly in hospitalized patients. This phenomenon represents an under-recognized iatrogenic cause of morbidity and mortality and may occur more frequently in patients with extended hospital length of stay.

11 Undiagnosed Fatal Malignant Tumor in Adult Autopsies: A 10 Year Retrospective Study

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**Background:** Autopsy rates have declined worldwide. There is a perception that modern diagnostic imaging/laboratory techniques have made autopsy less useful. Numerous studies have shown utility of autopsy for uncovering previously undiagnosed major findings, including cancer. However, most of these studies also include incidental cancers. Few recent publications have focused on clinically unexpected malignancy as the primary cause of death in the setting of a university hospital.

**Design:** A retrospective analysis of consecutive adult hospital autopsies from January 2002 to December 2011 was done. The study includes autopsies performed on patient’s ≥ 18 years of age in which primary cause of death was malignancy which was not diagnosed prior to autopsy. The detailed autopsy report, clinical record including duration of hospital stay, radiological imaging reports and relevant laboratory results were reviewed from laboratory and hospital database.

**Results:** 821 adult autopsies were performed over a period of 10 years. Sixty nine clinically undiagnosed malignant neoplasms were found in sixty six (8%) cases. Twenty six out of these sixty six cases the undiagnosed malignant neoplasm was the primary cause of death (31%). The duration of hospital stay was <24 hours in eight (30.7%), 2-7 days in nine (34.6%) and >7 days in nine (34.6%) cases respectively. In ten out of twenty six cases (1.2%) there was suspicion of malignancy without definitive tissue diagnosis based on clinical history, radiological studies or laboratory tests (average hospital stay 4.9 days). In sixteen out of twenty six cases (1.9%), malignancy was not clinically suspected (average hospital stay 9.9 days). The clinically undiagnosed fatal malignant neoplasms were dominated by lung tumors (4 squamous cell carcinomas, 2 adenosarcomas and 2 small cell carcinomas). Other malignancies in this group included ductal carcinoma of breast, ovarian serous carcinoma, adenocarcinoma of colon and gallbladder, poorly differentiated carcinoma (in a background of polycystic liver disease) and three cases of diffuse large B cell lymphoma.

**Conclusions:** In spite of recent advances in diagnostic imaging and laboratory techniques, a subset of adult autopsies (3.1%) done in a university hospital showed clinically undiagnosed fatal malignancy and in 1.9% of these cases malignancy was not suspected despite significant hospital stay. Hospital autopsy continues to be an important auditing tool for diagnostic accuracy in the first decade of twenty first century.

12 Minimally Invasive Autopsy Employing Post-Mortem CT and Targeted Coronary Angiography: Evaluation of Its Application to a Routine Coronal Service

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**Background:** In the UK, post-mortem imaging is increasingly used as an alternative to traditional invasive medicolegal autopsy. We have developed a method of targeted CT coronary angiography in order to overcome a major weakness of cross-sectional imaging, that is diagnosis of coronary occlusion. In this study, we investigate the potential reduction in number of invasive autopsies by the application of post-mortem CT, with and without angiography, in a series of 120 adult deaths referred to HM Coroner.

**Design:** Coronial referrals were investigated by external examination and CT, with invasive autopsy performed only if there was no definite cause of death identified on imaging. The study was divided into two halves, with coronary angiography employed only in the second batch of 60 cases, in order to determine the added value of angiography. All were sudden adult deaths; case selection was performed by a single pathologist after review of the clinical history and circumstances of the death. Post-mortem imaging was interpreted by a single radiologist, and a cause of death, or requirement for invasive autopsy, determined by both pathologist and radiologist. The confidence of imaging cause of death was classified as definite (no autopsy), probable, possible or uncertain.

**Results:** Autopsy was not required in 38% of cases without coronary angiography and 70% of cases with angiography. The commonest final cause of death was ischemic heart disease (IHD), diagnosed in 48/120 (40%) cases. A definite radiological cause of death was provided in 3/20 (15%) IHD deaths without angiography and 23/28 (82%) with angiography. For all 120 cases, the confidence in imaging cause of death was definite in 65, probable in 13, possible in 37, and unascertained in 5. There was no complete agreement between autopsy and imaging causes of death in the 13 cases with a “probable” cause of death on imaging, indicating that those cases for which imaging can provide an accurate cause of death without autopsy were correctly identified. Limiting identified unsuspected injuries, including 2 cases of femoral neck fracture that were missed at autopsy.

**Conclusions:** We conclude that in sudden adult deaths, a two-thirds reduction in the number of invasive Coronial autopsies can be achieved by use of post-mortem CT with targeted coronary angiography. At the same time, inclusion of post-mortem CT into an autopsy service may improve accuracy of diagnosis, particularly for traumatic deaths.

13 Postmortem Assessment of Polysplenia and Asplenia Syndromes: What Do Complex Congenital Anomalies Tell Us about Autopsy Quality?

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**Background:** While autopsy is often cited as a quality assurance tool for hospitals, opportunities are limited for examining the quality of autopsies themselves. Polysplenia and asplenia syndromes, related congenital disorders that include splenic abnormalities and various cardiac and visceral malformations, provide a unique setting in which to
assess the completeness of autopsy practice. This study analyzed autopsied cases of polysplenia and asplenia syndromes at a large tertiary care center to determine how effectively a general autopsy service evaluates these conditions.

**Design:** A database of autopsies performed from May 28, 1889 to January 30, 2012 was searched for all cases of asplenia or polysplenia. Cases were included if there was absence of spleen or presence of multiple spleens as well as one or more other anomalies frequently associated with polysplenia or asplenia syndrome. Autopsy records were reviewed for each case, and splenic, cardiac, and visceral morphology was noted.

**Results:** 37 cases met criteria for asplenia and 58 cases for polysplenia. Reports mentioned a specific diagnosis of asplenia syndrome in 17 (46%) of cases with no spleen and polysplenia syndrome in 33 (56%) of cases with multiple spleens. A total of 26 (76%) of asplenia cases and 56 (97%) of polysplenia cases did not list any findings of normal or abnormal, for one or more commonly involved organs. Overall frequencies of missing observations ranged from 18% to 81% (see table). Additionally, frequencies of observed anomalies varied widely from previously published values.

| Absent observations | Polysplenia n(%) | Asplenia n(%) | Total n(%) |
|---------------------|------------------|--------------|-----------|
| Spleen               | 21(70)           | 53(88)       | 74(81)    |
| Liver                | 21(70)           | 53(88)       | 74(81)    |
| Cardiac position     | 21(70)           | 53(88)       | 74(81)    |

Conclusions: Polysplenia and asplenia syndromes are rare disorders that are unfamiliar to many autopsy pathologists. However, this study illustrates widespread gaps in autopsy findings that may reflect a more basic lack of completeness in postmortem examination or reporting. It also raises the question of whether standardization of autopsy practice could improve the quality of results, regardless of diagnosis. A checklist is proposed to guide pathologists in better evaluation of polysplenia and asplenia cases.

### 14 The Direct and Contributory Role of Alcohol to Mortality Rates

**Patients – A 35 Case Cohort Study**

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**Background:** Liver transplantation is the second-most common type of solid organ transplant in the USA and recipients are at risk for a variety of serious complications. In the present study, we identified 35 autopsy cases in patients with liver transplant and extensively analyzed the causes of death and major morphologic findings, in order to gain insight regarding prevalent life-ending events, and identify possible preventable complications.

**Design:** 35 full adult autopsies in patients with history of liver transplant were identified through searching the autopsy database (1996-2012). Reasons for transplantation, survival data, autopsy-determined causes of death, and major morphologic findings were assessed.

**Results:** Twenty-six patients were male and 9 were female (32-71 y/o). Mean survival was 33 months post-transplant (range 1-23 years). Reasons for transplant included viral hepatitis progressing to cirrhosis and/or hepatocellular carcinoma (18 cases), alcohol-cirrhosis (6), amyloidosis (2), primary sclerosing cholangitis (PSC) (2), non-alcoholic steatohepatitis cirrhosis (1), and cryptogenic cirrhosis (6). Twelve patients had short-term survival (<1 month), with causes of death in this group being operative complications and transplant failure (6), cardiac arrest (4), intracranial hemorrhage (1), and acute respiratory failure (1). Superimposed sepsis was seen in only 2 cases. Of 23 patients surviving >1 month, 11 expired from bacterial, viral or fungal sepsis, 5 from gastrointestinal bleeding complications, 2 from cardiac arrest, 1 from complications of esophageal carcinoma, 1 from transplant failure, and remainder (3) from multifactorial causes. Of 18 patients with viral hepatitis prior to transplant, recurrent infection was noted in 5 biopsies, although contribution to death was thought to be insignificant. Likewise, in 2 cases where rejection was noted, it was not felt to be a major death contributor. Decreased levels of coagulation factors were detectable 1-3 months antemortem in patients dying from hemorrhagic complications. Recurrent malignancies were not identified.

Conclusions: Operative complications were a relatively minor contributor to mortality, likely reflecting improvement in surgical technique. Cardiac arrest was mainly an early post-operative period cause of death, while overwhelming infections were death culprits >1 month following transplant. It is noteworthy that bleeding events were among most frequent causes of mortality, indicating that diligent attention to transplant synthetic function may be beneficial for early detection of possible fatal complications.

### 15 Causes of Death and Major Autopsy Findings in Liver Transplant Patients – A 35 Case Cohort Study

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**Background:** Excess alcohol consumption is an ever-increasing public health concern in modern society. A key area in which the health implications of alcohol can be assessed are in mortality rates, and in particular its contribution to suicide. It has been estimated by the World Health Organisation that harmful use of alcohol accounts for 3.8% of deaths annually worldwide. In this study we aim to examine the role played by alcohol in overall deaths in a single autopsy centre in a suburban area of West Dublin, with a catchment area of almost one quarter of a million people.

**Design:** This case series includes all non-forensic coronial adult autopsies performed in our institution over a 12-month period. It involved a review of all post-mortem reports with collation of data including patient demographics, location of death, toxicology results and cause of death including significant contributing factors.

**Results:** 226 autopsies were carried out (61% male; 39% female). The age of the deceased ranged from 16 to 96 years, with an average age of 61 years. 22.1% of deaths occurred in the emergency department, 22.1% in hospital, 6.1% in a community care facility and 48.7% out of hospital. Toxicology was carried out in 61% of cases. Of these, alcohol was detected in 38.4% of cases (23.4% of all autopsies). Alcohol toxicity was the primary cause of death in 1.8% of all autopsies (n=4) with death from a chronic condition directly related to alcohol abuse accounting for a further 2.2% of deaths (n=5). Alcohol was detected in 41% of deaths by suicide (n=12), 50% of road traffic collision victims (n=1), 50% of non-alcohol drug overdoses (n=8) and 13% of sudden natural deaths (n=21). Of those autopsies in which the cause of death remained undetermined, alcohol was detected in 50% of cases (n=3) and was considered of significance in 33% (n=2).

**Conclusions:** The direct and indirect contribution of acute and chronic alcohol consumption accounted for 4% of all coronial deaths in our practice autopsy. However alcohol was detected in 45% of all other unnatural deaths (suicide, RTA, non-alcohol drug overdoses). Of particular note was its presence in 41% of deaths by suicide. It also played a significant role in deaths whose cause remained unascertained. Death registration globally tends to simplify causes of mortality to the main cause and the external cause of death only. We feel that as a result of this, alcohol-related deaths, in particular the contribution of alcohol to death by suicide, are underestimated. Increased awareness of the frequent complications of alcohol in all cases of death is required to direct adequate preventative public health strategies.

### 16 Predictors of Toxicology Results in Sudden Unexpected Death Cases Released by the Medical Examiner to the Hospital

**Patients – A 35 Case Cohort Study**

B Shetuni, N Dimov, W Zhang, H Li, MS Rao, G-Y Yang. Northwestern University, Chicago, IL.

**Background:** Toxictology plays an integral role in the investigation of sudden unexpected death cases. Such cases fall into the jurisdiction of the Medical Examiner, but on occasion these cases are released to the hospital. The utility of toxicology in these cases is crucial as autopsy cases released by the Medical Examiner is unclear. Documentation of ante-mortem suspicious behavior indicating toxin use/exposure may be important. We hypothesize that documented suspicious behavior strongly correlates with positive levels of toxins.

**Design:** All sudden death cases that had toxicology test performed from February 1 to August 1 2012 were included. Cases were selected from a log book of toxicology request in the autopsy suite. All toxicology tests included a general screen, and confirmatory test if indicated. The medical record was reviewed for evidence of suspicious behavior, and the autopsy report for toxicology results and anatomic cause of death. Lethal toxin levels were considered positive, and non-lethal or negative results were called negative.

**Results:** Eleven cases were identified with a median age of 37, with the majority being female (64%). Two cases had lethal toxin levels and were determined as the immediate cause of death (18%). Both cases with lethal levels were pain medications with documented suspicious behavior of drug abuse immediately before death. The remaining 9 cases did not have documented suspicious behavior with negative toxin screens (p=0.02). In one negative case the patient had a history of heroin abuse with track marks noted on exam, but no indication of recent drug use.

**Conclusions:** Toxicology results in sudden death cases can provide the information needed for immediate cause of death in sudden death cases released by the Medical Examiner. Key information retrieved from a scene investigation and interview of family members or friends of the decedent is not available to a non Forensic Pathologist, necessitating other predictors for accidental overdose. A documented recent history of suspicious behavior suggesting toxin use/exposure may reliably predict a positive toxicology result. A history of drug abuse may not indicate an overdose as the cause of death.

### 17 Cardiovascular Pathology in Obstructive Sleep Apnea: A Prospective Autopsy Study

**Patients – A 35 Case Cohort Study**

B Shehuin, N Dimov, W Zhang, H Li, MS Rao, G-Y Yang. Northwestern University, Chicago, IL.

**Background:** Obstructive sleep apnea (OSA) results in chronic intermittent hypoxia and is associated with cardiovascular disease (CVD). Imaging studies have demonstrated increased left ventricular mass and greater coronary athersclerotic plaque burden in OSA compared to non-OSA patients. Only previous autopsy study of CVD in OSA is identified in the literature. Since obesity is a risk factor for both OSA and CVD, we compared cardiovascular pathology at autopsy in obese patients with and without documented OSA.

**Design:** Autopsy records were searched for patients with a clinical history of OSA. Of 27 patients with OSA, 23 were obese (BMI>31) and comprised the study group (n=23). The control group consisted of obese patients without documented OSA (n=25). Autopsy reports were reviewed for medical histories and gross descriptors of cardiovascular pathology. Recorded heart weights were compared to predicted heart weights for body weight and gender. Histologic sections of myocardium and arteries were reviewed in a blinded fashion.

**Results:** The two groups had no significant difference in age, gender, race, height or prevalence of ischemic heart disease, hypertension, diabetes, stroke, or history of smoking.
No statistically significant difference was found in maximum coronary artery plaque thickness or per cent occlusion of coronary arteries. Plaque morphology, including extent of calcification, number of inflammatory cells, and lipid content, was similar in the two groups.

**Conclusions:** Heart weight tended to be greater in OSA than in non-OSA patients but the difference did not reach statistical significance. However, among those patients with heart weight exceeding the upper 95% confidence limit of predicted values, excess heart weight was significantly greater in OSA patients compared to patients without OSA. We found no significant difference in ventricular wall thickness, coronary plaque burden or plaque composition between the two groups.

18 Epidemiology of Endocarditis: A 22-Year autopsy review

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**Background:** Infective endocarditis (IE) affects 10,000 to 20,000 persons in the United States every year. Epidemiologic factors include community and hospital bacterial flora and patient risk factors such as damaged native valves, prosthetic valves, intravenous drug abuse, and intracardiac catheters and devices. As the incidence of nosocomial bacteremia has increased, we hypothesized a correlative change in the epidemiology of IE at autopsy.

**Design:** Following IRB approval, a review of 6386 autopsy reports from 01/01/1990 to 09/30/2012 identified 69 cases of IE. We recorded patient demographics, clinical history, and culture results; supplemented missing data using original medical records; and calculated trends with linear regression models and hypothesis testing.

**Results:** The incidence of IE showed a modest but statistically significant increase over time (P=0.03; r²=0.16). Median age was 54; males were more affected than females (2.5:1); blacks and whites were equally affected. Endocarditis was more likely to be left-sided only (54.8%). Seven patients had left- and right-sided involvement, and 18 patients had multiple valves involved. Despite hospitalization, 21 cases (30.4%) were not diagnosed until autopsy. Nearly half of patients had a recent invasive procedure (46.2%) including cardiac surgery (6%). Risk factors included known infection (34.8%), prosthetic valves (21.7%), damaged or repaired native valves (18.8%), impaired immunity (17.4%), prior endocarditis (14.5%), and intravenous drug abuse (8.7%). Common presentations were fever (44.9%), neurologic symptoms (39.1%), dyspnea (37.7%), and pain (31.9%). Of cultured organisms, Staphylococcus aureus (SA) was most frequent (51.6%), with 21 cases being methicillin-resistant (MRSA). The incidence of MRSA increased over time (P=0.01; r²=0.30). Other causative organisms were Enterococcus (15.6%); 2 of 10 were vancomycin-resistant (VRE). They were equal numbers of coagulase negative Staphylococcus (CNS) and gram negative bacilli (6 each). Dialysis rates increased over time (P=0.01; r²=0.23). Dialysis patients grew SA (17 with 9 MRSA), Enterococcus (5 with 1 VRE) and CNS (1). SA was the causative organism at a higher rate in dialysis patients than in non-dialysis patients (P=0.01). Black patients were more likely to be dialysis-dependent (P=0.02) and have SA endocarditis (P=0.02).

**Conclusions:** Our study showed increasing incidences of endocarditis, MRSA endocarditis, and endocarditis in chronic dialysis patients. Specifically, SA was most likely to be the causative organism in black patients as well as in dialysis-dependent patients.

Bone & Soft Tissue

19 IDH1 and IDH2 Mutations in Chondrosarcoma – A Sequenom Mass Spectrometry Analysis of 53 Cases

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**Background:** Heterozygous mutations of isocitrate dehydrogenase 1 (IDH1) and isocitrate dehydrogenase 2 (IDH2) have recently been identified in cartilaginous and epithelial tumors. Mutations occur at a single amino acid residue at R132 for IDH1 and R172 and R140 for IDH2. Mutations in these genes lead to impaired ability of IDH1 and IDH2 to catalyze the conversion of isocitrate to alpha ketoglutarate. This results in neomorphic enzymatic activity leading to production of the oncometabolite 2-hydroxyglutarate (2HG). In this study, we analyzed chondrosarcoma for IDH1, IDH2 and other mutations using high-throughput Sequenom mass spectrometry.

**Design:** Fifty three chondrosarcomas were selected for the study. There were 30 females and 23 males. The age range was 18 to 77 years with a median of 55 years. Histologically, two were grade I, 4 were grade II, 6 were grade III, and 2 as Dedifferentiated chondrosarcoma. Twenty-six of 53 (50%) patients had mutations in IDH1 or IDH2. No other mutations were detected in the rest of the gene panel (AXT).