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PLATFORM and POSTER PRESENTATIONS

Autopsy

1 Impact of a Pathology Department-Based Decedent Affairs Office on Patient Death and Autopsy Related Services at a Safety Net Hospital

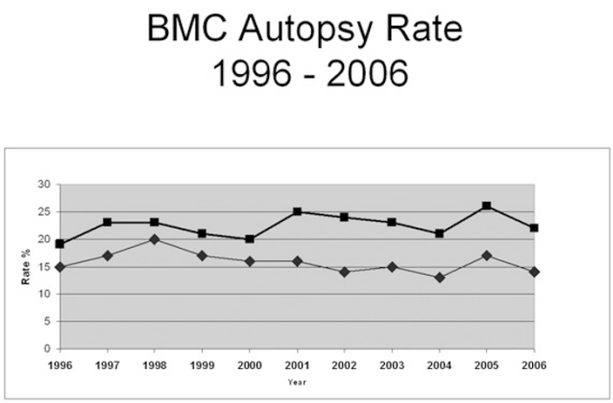
CD Andry, C Kiriakos, R Dwyer, MJ O'Brien. Boston Medical Center, Boston, MA.

Background: A decedent affairs office (DAO) was established within the department of anatomic pathology at Boston Medical Center (BMC), a 600 bed safety-net teaching hospital, in 1996. Its mission was to assure quality management of all logistical and administrative services related to patient death and family bereavement at the hospital. The aim of the present study is to report on the performance of this office as a prototypical model relative to its stated goals over a 10 year period.

Design: Departmental records, committee minutes and annual reports were reviewed to document responsibilities assumed by and added to the DAO since 1996, as well as to provide statistics and quality measures. Statistical information was also provided by the New England Organ Bank (NEOB).

Results: Measurable results that document the value of a DAO in the past 10 years include: 100% compliance with securing patient medical records; contribution to the maintenance of the BMC autopsy rate at a mean of 25% and a case reporting rate of 96-100% to the NEOB. The following service additions and improvements are also provided that were not available or systematically in place in 1996: location of relatives and notification of death for unknownpatients; procurement and secure archiving of deceased patient medical records; reporting of deaths to non-profit and state agencies; family bereavement counseling; preparation of a bereavement support guide; reporting deaths to primary care physicians; assistance with procuring of autopsy permissions; managing fetal and adult post-mortem disposition; writing and managing hospital policies related to decedent affairs; serving as a liaison with the Office of the Chief Medical Examiner and NEOB; disaster preparedness training; collating data for hospital quality assurance committees; training of clinical services residents in death reporting and death certificate preparation.

Conclusions: The performance review validated the efficacy of a pathology department based and managed office of decedent affairs in assuring excellence in the management of patient death related services in the setting of a large safety net hospital.



2 Duplicate Abstract, Withdrawn

3 Advanced Stage Pancreatic Cancers Have Distinct Morphologic and Immunolabeling Profiles Compared to Resectable Disease

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Background: Most conclusions related to pancreatic cancer have relied on surgically resected tissues. We hypothesized that a systematic review of autopsy patients with advanced stage pancreatic cancer would provide additional insight into the deadly nature of this disease.

Design: Paraffin embedded tissues of 66 pancreatic cancer patients who had rapid autopsies were collected for clinicopathologic review. E-cadherin and DPC4 immunolabeling or genomic sequencing for Kras and p53 were performed on representative samples. Frequencies were compared using a X^2-test, and parametric distributions were compared using a 2 sided T-test.

Results: The mean age was 61.9±11.5 years, 38 patients (57%) were male, and the mean overall survival was 15.6±16.4 months. Pathology from 20 patients (30%) with surgical resection were reported as adenocarcinoma (n=16), adenocarcinoma with signet ring features (n=1), mucinous/colloid carcinoma (n=2) or ampullary carcinoma (n=1). The mean tumor size was 3.2±1.4 cm, 13/20 (65%) were located in the pancreatic head and 7/20 (35%) were poorly differentiated. Of 46 patients diagnosed at an advanced stage, pathologic diagnoses from biopsy were adenocarcinoma (n=38), mucinous/colloid carcinoma (n=2), signet ring carcinoma (n=2) or carcinoma NOS (n=4). At autopsy, 59 patients had metastatic disease (most often to liver) seen as ≤10 foci (n=14), 10-99 foci (n=19), and 100-1000s foci (n=26). Review of end stage disease revealed a high frequency of anaplastic carcinoma (11/64, 17%). To determine if anaplasia was unique to our study set, 23 patients who died of pancreatic cancer were obtained from the Autopsy Pathology Archives, with 10/23 (43%) who also had anaplastic carcinoma, for an overall frequency of 21/87 (24%, $p<0.007$). There was no correlation of anaplastic carcinoma with clinicopathologic features at diagnosis, treatment or site (primary site versus metastatic deposit). Immunolabeling showed anaplastic carcinoma had a complete loss of E-cadherin (mean H score 0) compared to differentiated carcinomas (mean H score >200) ($p<0.0001$), even when present in the same tissue section. No correlation of anaplasia to DPC4, Kras or p53 mutational status was found.

Conclusions: Pancreatic carcinoma undergoes frequent de-differentiation to anaplasia during disease progression with associated loss of E-cadherin expression. De-differentiation is not correlated with treatment history or extent of metastasis at autopsy and may represent an accelerated phase of disease that culminates in rapid progression and death.

4 Multilayered Epithelium Is Present in the Developing Fetal Esophagus: an Autopsy Study of 39 Cases

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Background: Multilayered epithelium (ME) is a distinctive epithelium, with hybrid squamous and columnar features, that has been recently proposed as a specific marker of reflux injury and a precursor of Barrett's esophagus. The presence of ME in adults is indicative of an intermediate step in the transition of squamous mucosa into an intestinal phenotype in patients with gastroesophageal reflux disease. The reverse phenomenon occurs in the developing fetus whereby the original ciliated columnar esophageal epithelium progressively undergoes squamous differentiation. We analyzed the squamocolumnar junction (SCJ) and distal esophagus in fetal autopsies to ascertain whether ME is also present during this phase of columnar-squamous transformation.

Design: The SCJ and distal esophagus from 39 fetuses and neonates was evaluated. Routine sections were reviewed for presence and location of ME in relation to SCJ, character of mucin in ME, and presence of esophageal ciliated epithelium. Immunohistochemistry (IHC) for MUC2, MUC5AC, MUC5B (expressed in esophageal glands and bronchial epithelium and also in fetal esophageal columnar epithelium), p63 and Cdx-2 was performed where additional tissue was available for analysis.

Results: The gestational age of the fetuses ranged from 16-41 weeks. 26/39 cases showed foci of ME characterized by non-ciliated, columnar, gastric foveolar type cells overlying a stratified squamous epithelium. 11 of these 26 cases had columnar cells with blue-tinged, distended cytoplasm similar to that seen in ME in adults. This hybrid epithelium was present at the SCJ in 24 and proximal to the SCJ in 2 cases. IHC on 23 cases of ME showed strong cytoplasmic staining for MUC5AC in the columnar cells and a basal positivity for p63, confirming the hybrid nature of the epithelium. 3/23 cases showed faint traces of scattered MUC2 positivity in surface columnar cells. Strong MUC5B positivity was present in 10/19 cases tested. All cases were negative for Cdx-2.

Conclusions: Our findings suggest that ME appears to be a marker of epithelial "instability" and may be present when either squamous (adult) or columnar (fetal) mucosa transitions to the other phenotype. This raises the possibility that ME may also be seen in adults who respond to anti-reflux therapy and are reverting back to a normal squamous phenotype, and that ME in adults does not represent an inevitable progression to Barrett's esophagus.

5 Study of Deaths in Elderly Patients in Dublin – What Do They Die of and Where?

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Background: Death certification in the elderly provides difficulties unique to the population. Diseases which may not exist or cause the death of a young person may be fatal in an elderly person and the specific cause of death may not be straightforward. The complex health needs of the older person is an area requiring further evaluation due to population age shifts. Studies have suggested the development of criteria to aid determining whether the death of an elder is unexpected.

Design: We performed a study of deaths reported to the City Coroner over a 1 year period. Of 2192 deaths reported 1408 were in patients over the age of 65 years and 679 post-mortems were carried out on elderly patients. The place of death and immediate cause of death were noted.

Results: We found that 20.7% of elderly patients died at their family residence, 76% died in hospital, 2.3% in care homes and 1% died elsewhere. From post-mortem data the cause of death as a percentage of all cause mortality is shown in table 1.

Table 1. Cause of death and location

Cause of Death	Percentage of patients	Most Common Location
Cardiac Disease	50.9	Hospital (74.2%)
Cerebrovascular Disease	9.4	Hospital (79.7%)
Lower Respiratory Disease	2.1	Residence (50%)
Pneumonia	13	Hospital (77%)
Gastrointestinal Disease	3.5	Hospital (79.2%)
Suicide	0.7	Equivocal (40% hospital, 40% residence, 20% public place)
Malignancy	2.8	Hospital (79%)
Other	18.4	Hospital (90%)

Conclusions: Studies show that deaths in nursing homes may be underreported and that a shift in location of death from the community to hospitals and care homes has occurred. Cause and location at the time of death is fundamental to the development of end-of-life care in elderly patients. Our study examines this in an Irish setting. Whilst this study does not prove underreporting of deaths in nursing homes it emphasises the need for further investigation in this area.

6 Fatal Thromboembolic Disease in Physically Restrained Psychiatric Patients

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Background: Immobilization is commonly employed for individuals exhibiting behaviour that is deemed threatening to their own health, and those around them. Morbidity and mortality associated with physical restraint has been reported for individuals in police custody, long-term care facilities and hospital. Several mechanisms have been proposed as contributing to these events. Most recently, there have been isolated reports of fatal and non-fatal pulmonary embolism occurring in the context of physical immobilization.

Design: A retrospective review of pulmonary embolism occurring in physically restrained psychiatric patients was performed for cases at the Provincial Forensic Pathology Unit, in Toronto, Ontario, Canada.

Results: We identified three cases of fatal pulmonary embolism occurring in physically immobilized psychiatric patients. The patients were 34, 38 and 73 years of age; two were male and one female. The first two patients had bipolar disorder, the latter Alzheimer's disease. The patients were immobilized by 4 point, 3-to-5 point, and waist restraint respectively; the period of immobilization ranged from 3 to 5 days. On autopsy, one case had a saddle embolus, two showed occlusive thromboemboli in secondary and tertiary arterial branches. In two cases deep vein thrombosis of the legs were demonstrable. None of the individuals had previously recognized coagulopathies, or significant risk factors for deep vein thrombosis. Postmortem genetic studies for Factor V and prothrombin mutations were negative.

Conclusions: We report three cases of fatal thromboembolic disease occurring in physically restrained psychiatric patients without significant risk factors for thrombosis. Deep vein thrombosis may be an under recognized occurrence in physically restrained patients, including those under psychiatric care. We propose that deep vein thrombosis and pulmonary embolism be recognized as a potential risk factor for physically restrained psychiatric patients. Further research into the pathogenesis and prevention of this adverse outcome is indicated.

7 Major and Unique Autopsy Findings in Liver Transplant Patients – A Single Institution Study of 31 Cases

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Background: Liver transplantation is an efficient therapy for end stage liver disease. Although the surgical techniques and management have been improved, the immunosuppression puts the patients at risk for multiple complications, including infection, rejection and recurrent disease. We evaluated the autopsy findings in liver transplant recipients in order to investigate the cause of death, and correlate morphology and clinical data.

Design: Retrospective study of autopsies of liver recipients from 1996 to 2007. A total of 31 cases- 24 males (mean age 54.4) and 7 females (mean age 50.3) were found. Reasons for transplantation, survival data, major causes of death and selected clinical data were assessed.

Results: Transplantations were performed for viral infections progressing to cirrhosis and hepatocellular carcinoma (14 cases), alcohol-related disease (8), amyloidosis (2), autoimmune diseases (2), cryptogenic cirrhosis or unknown (5). The mean survival was 27 months (range 1 day to 15 years). Twelve patients (39%) survived less than 1 month; major causes of death were operative complications and transplant failure (50%), cardiac arrest (42%) and intracranial hemorrhage (8%). Two patients developed sepsis, one had acute cellular rejection. Laboratory data showed severely impaired transplant function in all patients. Of the 6 patients with cardiac arrest, 5 survived less than 1 month. Transfusion reactions and reperfusion injury were contributing factors. The most common findings in the 19 long term survivors were bacterial, viral or fungal sepsis (47%). Intracranial (16%) and gastro-intestinal hemorrhages (16%) were the cause of death in patients with transplant failure of undetermined etiology. All had decreased albumin and/or coagulation factors, detectable more than 3 months antemortem. Respiratory failure was lethal for 16% of patients. One patient developed lymphoproliferative disorder. No recurrent malignancies were found.

Conclusions: Our findings confirm that infectious complications are the most common cause of death of transplant recipients. Cardiac arrest and respiratory failure contributed to the mortality in these patients. Significant finding in this study is that gastrointestinal and intracranial hemorrhages due to impaired liver function are common cause of mortality, particularly in long- term survivors. Our findings indicate that laboratory monitoring of the synthetic function of the transplant and early detection of infections are clinical approaches for improving the survival after transplantation.

8 Pistachio Green Brain Discoloration Associated with Methylene Blue Use: An Autopsy Series

EA Douglas, D Mahajan, RA Prayson. Cleveland Clinic, Cleveland.

Background: Methylene blue is a heterocyclic aromatic chemical compound widely used as a redox indicator in analytical chemistry. Solutions of this substance are blue when in an oxidizing environment, but will turn colorless if exposed to a reducing agent. In clinical medicine, methylene blue is used in the treatment of methemoglobinemia as well as a dye in diagnostic procedures such as fistula detection and for the delineation of certain body tissues during surgery. Its use as a pressor agent for catecholamine-refractory vasoplegia in post-cardiopulmonary bypass patients has also been described in the anesthesia and cardiothoracic surgery literature. It is known to give the urine and stools a blue-green color, and possibly the skin and nails. However, discoloration of the tissues of the central nervous system is not described in the literature.

Design: Retrospective clinicopathologic review of three autopsy cases.

Results: Three patients, ages 55, 60 and 61 years old, underwent cardiac-related surgery-two for coronary artery bypass grafting and aortic valve replacement surgery and the third for orthotopic heart transplant. All three patients developed catecholamine resistant vasoplegia in the setting of sepsis and multi-system organ failure in the post-operative setting for which a trial of methylene blue was administered. At autopsy, a pistachio-green discoloration of the gray matter was noted in all cases. No abnormal deposition of pigments was noted upon histologic examination of the brains. In one case, the brain was bisected in the fresh state to reveal that the unexposed gray matter retained its usual coloration. Over a period of approximately 30-45 seconds the cut surface assumed a similar blue-green hue to the previously exposed cortical surfaces.

Conclusions: A green discoloration of the gray matter of the central nervous system may be observed in catecholamine-refractory vasopelegic patients treated with methylene blue. The coloration appears to be elicited upon exposure to the air (oxidation).

9 Fatal Pulmonary Fat Embolism in a Liver Transplant Patient

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Background: End-stage liver disease requiring liver transplantation is becoming an increasingly prevalent problem in the United States. Peri-operative respiratory distress, including acute pulmonary edema and acute respiratory distress syndrome, have been described in the literature as a relatively common complication occurring in liver transplant patients. Transfusion-related acute lung injury (TRALI) is frequently reported as the etiology of such respiratory compromise. In this work, we describe fat embolism as the etiology of peri-operative acute respiratory distress syndrome in a liver transplant patient. This is the second published report, and the first detailed report, of such a case.

Design: The reported patient was a 64 year-old Caucasian female with a history of end-stage liver disease secondary to Laennec's cirrhosis. The patient was admitted for an orthotopic liver transplant. The donor liver had a reported 15-20% macrosteatosis. During liver transplant surgery the patient clinically developed acute respiratory distress syndrome in addition to significant ischemia and reperfusion injury of the donor liver. In the immediate post-operative period, the patient went into asystolic cardiac arrest, followed by death. Permission was granted for a full autopsy.

Results: Microscopic examination of frozen sectioning the lungs with an Oil Red O stain demonstrated diffuse intravascular and extravascular lipid droplets. Hematoxylin and eosin-stained slides of the lungs demonstrated diffuse pulmonary edema and vascular congestion. Microscopic examination of the donor liver demonstrated massive centrilobular hemorrhage and coagulative necrosis with coalescence of fat droplets, in addition to macrosteatosis and macrosteatosis of the viable liver parenchyma.

Conclusions: We present a case of fatal pulmonary fat embolism in the peri-operative period of an orthotopic liver transplant surgery. While clinical suspicion was directed toward the frequently reported TRALI as the etiology of the patient's respiratory distress, Oil Red O stain demonstrated diffuse intravascular lipid droplets within the patient's pulmonary microvasculature. The fat emboli were likely secondary to ischemia and reperfusion injury to the steatotic donor liver. It is recommended that when there is respiratory distress in a liver transplant patient, on autopsy an Oil Red O stain should be performed to assess for fat embolism as an etiology.

10 Clinically Undetected Invasive Fungal Disease at a Teritary Care Medical Center: A Post-Mortem Analysis of 26 Cases

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Background: Invasive fungal infections are serious complications of patients suffering from malignancy, organ transplantation, AIDS and other immunosuppressed conditions. Timely and accurate pre-mortem diagnosis is critical, as these infections can be rapidly progressive, with widespread invasion and fatal outcomes. We delineate the clinicopathologic features of 26 cases of clinically unsuspected invasive fungal infections which were discovered at the time of autopsy.

Design: The records of 963 autopsy cases performed at Cedars-Sinai Medical Center (CSMC) from 2000 through 2007 were screened to identify cases of invasive fungal disease found at autopsy. For all fungal cases, autopsy and clinical records were reviewed, from which clinical and pathologic data were collected for analysis. Only cases in which invasive fungal infection was not considered as a pre-mortem clinical suspicion or diagnosis were included in the study.

Results: All 963 autopsies were performed at one institution (CSMC), which represented a mix of adult (71%) and pediatric/perinatal (29%) cases. Autopsy case types reflected the disease processes experienced at CSMC, which included a broad range of oncologic, organ and bone marrow transplantation, cardiovascular, hepatic and HIV/AIDS-related pathology. In 26 cases (2.7% of total), invasive fungal infections were discovered at the time of autopsy, which had not been clinically suspected before death. These included 19 men and 7 women with an age range of 22-80 years. Significant underlying disease processes included solid and hematologic malignancies (n=12), hepatic disease (n=7), organ or bone marrow transplantation (n=5), cardiovascular disease (n=6), HIV/AIDS (n=5) and others (n=3). Fungal organisms included aspergillus (n=16), zygomycetes (n=3), candida (n=3), coccidiomycosis (n=2), and cryptococcus (n=2). In 85% of cases, multiple organs were involved (lung involvement in 85% of cases; brain 46%, heart 38%, spleen 35%, kidneys 31%, and others). Angioinvasion was a common pattern of fungal dissemination.

Conclusions: The clinicopathologic features of clinically unsuspected invasive fungal disease in a large tertiary care medical center are described. 2.7% of all autopsies revealed clinically unsuspected invasive fungal infections. All patients suffered from serious underlying disease and/or immunosuppressed states. The value of the autopsy as a tool for medical education and quality improvement is further underscored.

11 Individuals with Ruptured Cerebral Berry Aneurysms Arising from the Posterior Circulation Have an Increased Mortality Rate Compared to Ruptured Aneurysms Arising from the Anterior Circulation of the Brain

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Background: Ruptured cerebral berry aneurysms produce subarachnoid hemorrhage and have a 35% mortality rate. Review of the current literature reveals that 95% of cerebral berry aneurysms arise from the anterior circulation, whereas, only 5% of berry aneurysms arise from the posterior circulation.

Design: We have observed an increased number of fatalities occuring in ruptured cerebral aneurysms arising from the posterior circulation in autopsies performed in our local medical examiner's office. We conducted a preliminary review of autopsies performed during 2000 - 2007 at the Alabama Department of Forensic Sciences in Mobile, Alabama, and discovered a total of forty fatal ruptured cerebral berry aneurysms.

Results: Ten (25%) of these cases, a number far greater than expected, were ruptured posterior circulation berry aneurysms.

Conclusions: A possible explanation for the increased mortality rate for ruptured berry aneurysms of the posterior circulation is subarachnoid hemorrhage and compression of the brainstem. We are currently expanding our data collection to include earlier cases, as well as, combine our data with the Office of the Chief Medical Examiner in Louisville, Kentucky.

12 Utility of C4D Immunohistochemistry in Acute Myocardial Infarction

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Background: The pathologic presence of acute myocardial infarction (AMI) is determined by gross and histological examination. These findings are generally not seen early in the course of an AMI (<9-12 hours). The earliest indication of cell death is contraction band necrosis, which can be seen within minutes of reperfusion. However, it is often absent in typical infarction and is considered an artifact in endomyocardial biopsies. C4d (and C3d) is an end-product of the classical complement cascade which covalently binds the target tissue. The utility of C4d immunohistochemistry (IHC) is well described in the evaluation of antibody-mediated rejection of cardiac allografts. Full activation and involvement of the complement pathway following AMI has been shown. The aim of our study is to determine the specificity and potential timeline in C4d detection on necrotic myocytes following an AMI.

Design: Sixteen autopsy cases with a total of 26 areas of infarcted myocardium were reviewed. The clinical record and microscopic examination of H&E slides showed that the areas of infarction ranged from a few hours to months in age. IHC was performed on paraffin sections of formalin-fixed tissue using the ABC/peroxidase method with C4d. Staining patterns and intensity were recorded. Five cases without evidence of infarction were used as controls and histologically normal myocardium functioned as an internal control.

Results: C4d antibody strongly and diffusely stained necrotic myocytes in all cases of 8 to 48 hours in age (10/10). Adjacent histologically normal myocytes were nonreactive, resulting in clear delineation of damaged myocardium by C4d. Four cases with only scattered contraction band necrosis showed focal to no C4d reactivity, indicating that contraction bands may not be specific for necrotic myocytes. Three cases with 3-7 day old infarcts showed variable staining. Areas of fragmented myocytes showed focal weak staining. Infarctions of >1-2 months and negative controls were nonreactive. The use of C4d provided new diagnoses in two cases, including evidence of reinfarction and a newly diagnosed AMI.

Conclusions: C4d is specific for necrotic myocytes as areas of histologically apparent necrosis stained strongly for C4d and normal appearing myocytes did not. C4d staining of necrotic myocytes is apparent prior to the influx of inflammatory cells making this a useful diagnostic tool in the event of uncertainty. The contrast achieved by IHC impressively creates a clear delineation between viable and necrotic myocytes, making C4d an efficient diagnostic tool.

13 Sudden Cardiac Death in Non-Cardiac Primary Hematolymphoid Malignancy

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Background: Cardiac involvement by lymphoid or leukemia may be underdiagnosed and directly responsible for significant morbidity and mortality. We describe five patients with non-cardiac primary hematolymphoid malignancy who experienced sudden cardiac death. All had extensive cardiac involvement by tumor identified at autopsy, clinically unrecognized in four of the cases.

Design: Autopsy was performed in four cases with en bloc removal of the organs, dissection of the heart and evaluation of the coronary arteries and conduction system. One case was limited to solid organ biopsies through a small posterior incision. Routine histochemical staining was performed using standard methods.

Results:

Case	Age (years)	Tumor	Clinical Findings	Autopsy Cardiac Findings
1	59	Burkitt lymphoma	Restrictive cardiomyopathy; bradyarrythmia	Extensive interstitial and epicardial lymphoma, also involving sino-atrial node
2	60	Burkitt-like high grade lymphoma	Syncope	Extensive interstitial and epicardial lymphoma compressing the left circumflex artery resulting in 75% luminal stenosis
3	44	Acute myeloid leukemia	Chest pain; tachycardia	Extensive interstitial and epicardial leukemic infiltrate; fibrinous epicarditis; right atrial and left ventricular hemorrhages
4	78	Diffuse large B-cell lymphoma (DLBL)	Dyspnea; hypotension; pericardial effusion	Intravascular lymphoma with interstitial infiltrate and myocardial infarction
5	73	DLBL	Chest pain; mediastinal and cardiac mass on MRI	Extensive interstitial lymphoma with rupture of ventricular free wall

Conclusions: The majority of cardiac tumors are metastatic, of which hematolymphoid metastases are frequent and may lead to sudden cardiac death by different mechanisms as illustrated in this case series. Patient 1 had a restrictive cardiomyopathy and refractory bradyarrhythmia with lymphoma involving the sinoatrial node. Patient 2 had syncope with severe coronary artery compression associated with epicardial and interstitial lymphoma. Patient 3 had features of diastolic dysfunction and tamponade with an epicardial leukemic infiltrate. Patient 4 had intravascular and interstitial lymphoma with myocardial infarction, and patient 5 had interstitial lymphoma with ventricular rupture, illustrating the variable distribution and pathophysiology of DLBL involving the heart. Importantly, cardiac involvement by tumor was unrecognized until the autopsy for patients 1 through 4, reflecting a clinical diagnostic gap that may be improved with greater awareness and earlier recognition of cardiac involvement in patients with lymphoma or leukemia.

14 An Effortless and Highly Effective Method of Positive Reinforcement for Meeting Autopsy Turnaround Time

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Background: Timeliness of reporting of autopsies is a difficult goal to meet at most departments of pathology even though there are several reasons why reasonable turnaround time brings many benefits to the family of the deceased and the clinicians requesting the autopsy, not to mention compliance requirements to national guidelines for accreditation of pathology laboratories. In too many hospitals, there is a culture of lack of adhesion to agreed upon standards and new approaches and methods for creating a change are necessary.

Design: For several years, a significant percentage of autopsies did not meet the 30 consecutive days turnaround time for the final autopsy report and the 45 consecutive days turnaround time for the neuropathology final autopsy report at our University Hospital. Two consecutive steps were adopted: As a "New Year Resolution" for the entire department, residents and attending pathologists were asked to have all the late autopsy reports finished by the end of the month of January 2007. On February 1st the first e-mail congratulating everyone involved was sent by the director of the autopsy service. Every week after that, a new e-mail was sent again, stating how many weeks or months the autopsy service was "accident free". Monitoring of turnaround time was performed for the six months before (n= 62) and after February 1st (n=46).

Results: The incidence of overdue reports went from 20 % before implementation of the positive reinforcement method to 4 % for the next 6 months 9 (p=0.025; chi-square test). The only cases that missed the deadline were one complex case that got signed out two days late, and one non-complex case that got signed out one day late. All the neuropathology reports were on time after the change was implemented.

Conclusions: In positive reinforcement methods, one avoids terms such as "zero-tolerance", "non-compliance" and "delinquency", which are terms that have a negative connotation. Instead, congratulations for work well done are frequently used and publicly stated. Previous, only partially effective methods at our hospital included weekly e-mail reminders of autopsies which were overdue or close to being overdue, and frequent

telephone calls. The business administration literature is replete with reports on the advantages of positive reinforcement methods. Our experience suggests that this approach should also be applied to quality assurance in the pathology laboratory.

15 Characterization of Melamine-Containing Crystals and Calcium Oxalate Crystals in the Kidneys of Two Domestic Cats by Histopathology, Infrared Spectroscopy and Scanning Electron Microscopy with Energy Dispersive X-Ray Analysis

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Background: In March 2007 a recall of melamine-contaminated pet food was announced by a Canadian manufacturer supplying the US pet food market. Acute renal failure arising in dogs and cats was reported by veterinarians in multiple states. Canadian investigators identified melamine-containing crystals in cat urine, and published the crystals' infrared spectra on the internet.

Design: Renal tissue obtained at necropsy from two domestic cats that had developed acute renal failure shortly after the melamine-contaminated pet food recall, was sent to the Department of Veterinary Pathology at the AFIP for consultation. Both animals had a reported history of ingesting pet food listed in the recall. The material was examined histologically, histochemically, with infrared (IR) spectroscopy, and with scanning electron microscopy with energy dispersive X-ray analysis, (SEM-EDXA).

Results: Case 1 was a 1-year-old neutered domestic shorthair cat. The renal tissue contained intratubular birefringent crystals, of two types. The first were smooth-surfaced, colorless, plate-like crystals and the second had a rough surface, were occasionally lamellated and were pale brown. The rough crystals stained with a 72 hour Oil red O, and had the IR spectral characteristics of the melamine-containing crystals published on the internet. The smooth crystals stained with von Kossa, but not Alizarin red, and had the IR spectral characteristics of calcium oxalate monohydrate. Case 2 was a 5-year-old neutered domestic longhair cat. The renal tissue contained intratubular birefringent crystals with smooth surfaces which had the IR spectral characteristics of calcium oxalate monohydrate. The owner reportedly had another cat that had died of ethylene glycol poisoning.

Conclusions: Both calcium oxalate and the melamine-containing crystals identified in the kidneys of domestic cats have characteristic morphological and histochemical features. Despite similar clinical presentations, renal deposition of melamine-containing crystals was demonstrated in only one of these two cases. When necessary, crystal characterization by IR spectroscopy can be valuable. It is important for pathologists to recognize this form of melamine-containing crystal, as similar contamination may eventually present in humans.

16 Hydrops Fetalis: A Fifteen Year Review

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Background: Hydrops fetalis (HF) is a serious fetal condition defined as abnormal accumulation of fluid in two or more body compartments, including ascites, pleural effusion, pericardial effusion, and/or subcutaneous edema. Predominate causes include cardiovascular and chromosomal abnormalities, fetal anemia, thoracic lesions, and twin-to-twin transfusion. Infections reported to cause ~5% of HF, result in high death rates. Nonimmune-mediated etiologies account for about 87% of cases in developed countries. HF can be fatal due to progressive lymphatic obstruction, capillary leakage, fetal anemia, and/or hypoproteinemia and high output cardiac failure. Identification of the underlying etiology in a given case has important implications for determining genetic recurrence and pre-currence risks of any structural anomalies or syndromes; assessing the efficacy of any treatment interventions; and contributes to ongoing epidemiologic studies to assess rate shifts in the causes of HF.

Design: We performed a review of autopsy files from our hospital from January 1992 through March 2007 for cases of HF to determine (1) to what extent the postmortem examination either confirmed the antenatal diagnoses or identified the unknown cause of HF; (2) the most frequent causes of death in HF; (3) if the causes of HF changed during this interval; (4) in what percentage of cases did the autopsy identify a structural anomaly(s) that had significant implications for genetic counseling.

Results: We identified 51 cases of HF among 732 perinatal autopsies performed in our hospital (7%); 50/51 cases were due to nonimmune etiologies (98%). Only one was due to an immune-mediated mechanisim (2%) from maternal anti-c antibody. Clinical diagnosis of HF was made in 31 cases (60.7%) via prenatal ultrasound, but etiology was not identified in the majority (67.7%) of these cases. Autopsy confirmed all the prenatal etiologic diagnoses and further identified the causes in the remaining 72.5 %.

Conclusions: Autopsy identified the etiology in ~92%, confirming its crucial role in the evaluation of perinatal death in HF. The overwhelming majority of death in HF was of non-immune type with structural anomalies, especially cardiovascular (11.76%) and urologic (11.76%) malformations, and infection (23.53%) accounting for the largest number of cases. Parvovirus B19 was the most common infectious agent found, but death due to Parvovirus B19 was not identified after 1996. Conservative assessment revealed 47% of cases had causes with increased risks of recurrence (structural, chromosomal mosaicism, immune-mediated).

17 Risk Factors for Intrauterine Fetal Demise (IUFD) in the Bronx, NY from 2000-2006

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Background: IUFD sadly affects women of low socioeconomic status. The Bronx is home to a low-income minority population. We previously reported that chorioamnionitis (CA), placental malperfusion, & oligohydramnios have increased in incidence among IUFD autopsies at Montefiore Medical Center (MMC) over the last decade (USCAP San Diego, 2007). To date no study has compared these IUFD factors to those among live deliveries to determine which impact fetal heath in the Bronx. Here we hypothesize that DM & hypertension (HTN) are tied to IUFD.

Design: The reports of IUFD autopsies (n=117) at MMC from 2000-2006 were reviewed & compared to records of live-birth control deliveries (n=222) randomly selected at MMC from 2000-2006.

Results: IUFD cases were 53.1% Hispanic & 37.2% Black; live-birth controls were 42.4% Hispanic & 38.7% Black. The incidence of DM (gestational, Type II) was significantly greater among IUFDs than controls (13.0% v. 6.8%, Fisher's Exact, p=0.045). The incidence of HTN was greater among IUFDs (12.2% v. 5.9%, p=0.037). The following factors had a significantly greater incidence among IUFDs ($p<0.05$): advanced maternal age (AMA), CA, small placenta for gestational age (SGA), placental abruption, placental hemorrhage, SGA fetus, fetal hydrops, oligohydramnios, & polyhydramnios (see Table). By contrast, there were significantly more control cases with mothers + for *Group-B Streptococcus* (GBS, p=0.00035).

IUFD Risk Factors in the Bronx from 2000-2006

Factor	% Incidence, IUFDs (n=117)	% Incidence, Controls (n=222)	p-Value*
DM	13.0	6.8	0.045
HTN	12.2	5.9	0.037
AMA	23.3	13.1	0.013
CA	21.4	1.4	0.00000000075
SGA Placenta	24.5	0	0.0015
Placental Abruption	11.6	1.4	0.000085
Placental Hemorrhage	22.3	1.8	0.0000000013
SGA Fetus	7.8	0.9	0.0015
Hydrops	6.0	0	0.00052
Oligohydramnios	12.3	4.1	0.0057
Polyhydramnios	2.6	0	0.038
GBS+	8.7	23.9	0.00035

*by Fisher's Exact

Conclusions: Our live-birth data has elucidated the significant impact that DM, HTN, & CA have on fetal outcome in the Bronx. The higher incidence of GBS among controls warrants the need for prenatal screening & antibiotic treatment at delivery. These findings can be used to promote prenatal programs in low-income areas & to guide obstetric care for minority women.

18 The Septic Autopsy: A Human Morphologic Model of Sepsis Based on Review of the Literature and Study of 16 Adult Autopsy Cases

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Background: Sepsis has been intensively studied throughout the world literature leading to a dramatic increase in our understanding of disease pathogenesis. Despite several detailed clinical classification schemas there exists no pathologic correlative characterizing the morphologic changes in sepsis and the sepsis-related syndromes to validate these clinical schemas. The purpose of the current study is to describe a human morphologic model of sepsis for the first time and to apply this model to a small autopsy study set.

Design: Search Strategy: A search of Ovid Medline 1950 - present using the terms "SIRS, MODS, sepsis, septic shock, systemic inflammation, or systemic infection" in combination with "histology, morphology, or pathology" limited to the English language and adult studies yielded 1114 articles. Studies were excluded based on a lack of detailed morphologic descriptions, lack of critically ill non-septic controls, or unrelated search terms. The search yielded 4 human studies documenting statistically significant findings in the heart, spleen and colon. Three additional human studies documented changes in the brain, heart, lung, liver, kidney and adrenal glands without statistical analysis. Five animal studies with appropriate controls confirming the human data were included in our review. Study Set: A diagnostic table of significant findings in sepsis was created and the criteria were applied to 16 adult autopsies performed from October 2004 to October 2006 at Robert Wood Johnson University Hospital (IRB approved).

Results: Table 1: Morphologic Changes Observed in Septic versus Non-Septic Autopsies

Organ	Morphology	Sepsis (8)	Critically Ill (4)	Sudden Death (4)
Brain	Perivascular parenchymal PMNs	37.5%	25%	0
	Hemorrhage with PMN Infiltrate	25%	25%	0
	Foci of Liquifactive Necrosis with PMNs	25%	25%	0
Heart	Macrophage Infiltration	50%	25%	25%
	Myocardial Apoptosis	0	25%	0
	Subendocardial Hemorrhage	0	25%	25%
Spleen	B cell Follicle Loss	75%	0	0
Lung	Diffuse Alveolar Damage with Interstitial PMNs	25%	0	0
	Diffuse Alveolar Damage without Interstitial PMNs	25%* (1 neutropenic patient)	25%	25%
Liver	Hepatocyte Degeneration	75%	50%	0
	Inflammatory Cell Infiltrate of Sinusoids	50%	25%	0
	Kupffer Cell Hyperplasia	25%	25%	0
GI Tract	Hemorrhagic Enteropathy	62.5%	0	25%
	Apoptosis	autolyzed	autolyzed	autolyzed
Kidneys	Interstitial Inflammatory Infiltrate	50%	25%	0
	Acute Tubular Necrosis with Interstitial Inflammatory Infiltrate	37.5%	25%	0
	Apoptosis	autolyzed	autolyzed	autolyzed
Adrenals	Hemorrhage	62.5%	50%	50%
	Cortical cell lipid depletion	87.5%	0	50%
Systemic	Microabscesses	50%	50%	0
	Microthrombi	87.5%	50%	25%

Conclusions: This is the first study to examine a human morphologic model of sepsis. The strongest trend observed was in the spleen, with a marked reduction in B cell follicle size and number compared to the controls. A larger scale study to statistically validate our proposed model and to further distinguish the subtle differences amongst the sepsis-related syndromes is warranted.

19 Antemortem Diagnosis of Asbestosis by Screening Chest Radiograph Correlated with Postmortem Histologic Features of Asbestosis: A Study of 274 Cases

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Background: Accuracy in the clinical diagnosis of asbestosis has significant implications for the future health of affected patients as well as serious medicolegal implications for both patients and asbestos-associated industries. The radiographic gold-standard for diagnosis of asbestosis has been the plain chest radiograph, and in many asbestosis-screening clinics, chest radiograph abnormalities in conjunction with a history of asbestos exposure have been the mainstay of diagnosis. No studies have yet compared the antemortem chest radiographic diagnosis of asbestosis with the subsequent presence of pulmonary fibrosis and lung tissue ferruginous bodies at autopsy.

Design: Records were reviewed from 274 autopsies performed to investigate asbestosis over an 11-year period. Accrued data included age and gender as well as the presence or absence of the following: occupational exposure to asbestos, antemortem clinical diagnosis of asbestosis by chest radiograph, fibrous pleural plaques, peribronchiolar or interstitial pulmonary fibrosis, ferruginous bodies in histologic sections of lung tissue, and ferruginous bodies in digested lung tissue.

Results: 241 cases with the antemortem radiographic diagnosis of asbestosis (study group) were identified. 31 additional autopsies had been requested based on history of asbestos exposure without radiographic documentation of asbestosis (control group). Comparison of the two groups showed a statistically significant increase in the association of chest radiograph-diagnosed asbestosis and the presence at autopsy of pleural plaques ($p=0.0109$), peribronchiolar or interstitial pulmonary fibrosis ($p=0.0472$), and histologically-diagnostic asbestosis ($p=0.0021$). At autopsy, histologically-diagnostic asbestosis was confirmed in only 90 of the 243 study group cases. Comparison of individual parameters within the 243 study group cases showed a statistically significant correlation between the presence of fibrous pleural plaques and histologically-proven pulmonary fibrosis ($p=0.0025$) as well as the subsequent histologic diagnosis of asbestosis ($p<0.0001$).

Conclusions: Clinical diagnosis of asbestosis by screening chest radiograph is more predictive of the postmortem presence of fibrous pleural plaques, pulmonary fibrosis, and histologically-proven asbestosis than is occupational exposure history alone. However, chest radiograph-based diagnosis of asbestosis significantly overpredicts the subsequent histologic diagnosis of asbestosis.

20 Post-Transplant Lymphoproliferative Disorder Mimicking Acute Antibody Mediated Rejection and Vasculitis in Heart Transplantation

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Background: The histopathology of post-transplant lymphoproliferative disorder (PTLD) encompasses a spectrum from reactive lymphoid hyperplasia to frank lymphoma. Histopathologic manifestations of antibody mediated rejection (AMR) in cardiac allografts include endothelial cell swelling, intravascular macrophage infiltration, and rarely transmural vasculitis. Distinguishing between PTLD and AMR is critical since management strategies are diametrically opposed.

Design: We report the findings of an unusual autopsy case demonstrating a previously undescribed pattern of PTLD, presenting morphologically as transmural arteritis without significant myocardial involvement, mimicking AMR.

Results: A 63-year-old man, 13 months post heart transplantation for giant cell myocarditis presented with heart failure. Echocardiogram revealed an ejection fraction of 40% with regional wall motion abnormalities. Coronary angiography revealed slow flow in the distal vessels without major obstruction. Endomyocardial biopsies were negative for rejection and staining for C4d was negative. Refractory heart failure with vasculitis and absent cellular rejection led to a clinical impression of AMR. Despite aggressive therapy including plasmapheresis and OKT3, the patient expired and an autopsy was permitted. Grossly, the heart showed thickened porcelain-like epicardium. Coronary arteries were without significant obstruction, though a distal shallow LAD thrombus was present. Microscopically, the coronary arteries showed segmental transmural lymphocytic infiltration with medial smooth muscle damage. The lymphocytes were polymorphic, with large atypical forms and demonstrated a CD3 (-), CD20 (+), CD79a (+), PAX5 (-), MUM1 (-) phenotype with polytypic immunoglobulin light chain expression. In-situ hybridization for EBV was diffusely positive in these cells. Similar findings were present focally in intramyocardial muscular arteries. The myocardium showed only focal acute ischemic changes without significant lymphocytic inflammation. There was no involvement of the bone marrow or any other organ.

Conclusions: This case highlights a pattern of involvement by PTLD in a cardiac allograft, mimicking coronary vasculitis and AMR and expands the histological spectrum and clinical manifestation of PTLD. PTLD should be considered in the differential diagnosis when vasculitis is present in cardiac allograft specimens as well as cardiac specimens from all patients at risk for PTLD.

21 Cellular Prion Protein Is a Fetal Protein of Pancreatic Duct and Is Over-Expressed in Pancreatic Adenocarcinoma

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Background: Cellular prior protein (PrP^C) has recently been shown to be over-expressed in many tumor cells in vitro, including gastric, breast and pancreatic cancers. The mutant form of prion protein is responsible for prion disease. However, the normal form of PrP^C can be found in blood cells, neurons and other cells. PrP^C is a glycosyl-phosphatidylinositol anchored membrane protein. The role of PrP^C in cancer has not been elucidated; however, it may be related to its cell adhesive or apoptotic regulatory activities. In this study, we would like to evaluate the protein expression status of PrP^C in different stages of pancreatic development from autopsy and surgical samples, comparing endocrine and ductal markers.

Design: Twenty three consecutive fetal autopsy cases between years 2005-2007 were retrieved from our surgical pathology archives. Normal pancreatic tissue resected for non-pancreatic neoplasms in 20 patients, 25 to 77 years of age, were retrieved as well. The gestational ages of the fetal autopsies ranged from 14 to 40 weeks. In addition, 20 randomly selected resected pancreatic adenocarcinomas from patients 55 to 80 years of age were utilized for cancer controls. Immunohistochemical study was performed using monoclonal antibodies specific for PrP^C, Ngn3 (endocrine lineage specific transcriptional factor), and AE1/AE3, respectively.

Results: Starting at 14 weeks of gestational age, the fetal pancreas showed well developed lobular architecture with identifiable islets of Largerhans and ducts. In fetal pancreas, PrP^C were positively immuno-labeled on precursor cells, morphologically similar to centroacinar cells, in all of the 23 fetal pancreatic samples. None of the well-developed ductal or acinar cells were immunolabeled by PrP^C in all fetuses. The PrP^C positive cells were also positive for AE1/AE3, and 30% of these positive cells overlapped with Ngn 3 staining. In adults, very rare centroacinar cells could be detected by PrP^C in non-neoplastic pancreatic tissues. In contrast, 55% (11/20) of pancreatic adenocarcinoma showed diffuse strong positive immuno-labeling of PrP^C.

Conclusions: Our data indicate that the PrP^C is a fetal protein expressed on precursor cells in all normal fetal pancreas. Many pancreatic ductal adenocarcinomas re-express their fetal protein, PrP^C. The exact role of PrP^C in the pancreatic carcinogenesis is not been fully understood. However, it might give us a new marker for early detection of pancreatic cancer.

22 Trends in the Mortality of HIV in the Era of Highly Active Antiretroviral Therapy: An Autopsy Study

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Background: In the mid 1990's, amidst an epidemic of HIV-related deaths, the advent of highly active antiretroviral therapy (HAART) transformed HIV from a relatively rapid fatal disease to a chronic progressive albeit terminal illness. As survival has increased and therapies have improved, the morbidity and mortality in the HIV+ population may be shifting away from obvious HIV related infections to more mainstream causes of death (COD). While there have been population-based studies based on death certificates, which lack specificity in the underlying cause of death, in the United States no population-based studies have been done utilizing autopsy findings to evaluate HIV-related morbidity and mortality.

Design: A computer search for the terms "human immunodeficiency virus", and "acquired immunodeficiency syndrome" was performed on all autopsies performed at Bellevue Hospital, New York City, between June, 1994 and September, 2007. These autopsy reports were then evaluated for immediate COD, HIV-related cause of death, final anatomical diagnoses, age at death, date of death, sex, race, duration of final hospitalization, last reported CD4 count, and other pertinent clinical history.

Results: In 79 autopsy reports reviewed thus far, the COD was determined to be HIV-related in 58 cases (73.4%) versus 21 unrelated to HIV (26.6%). Of the HIV-related COD, 48 cases were attributed to infection (82.8%), with 33 of all infections being respiratory infections (68.8%); lymphoma accounted for 8 (13.8%) and Kaposi's sarcoma accounted for 2 (3.4%). Positive correlations were observed for higher CD4 count and more recent date of death ($R=0.0467$). The COD is increasingly unrelated to HIV in relation to more recent date of death ($R=0.0324$). Positive correlations were observed between higher CD4 counts and more advanced age at death ($R=0.0367$) and recent date of death ($R=0.0265$). There is an increase in non-infectious COD compared to infectious related to more recent date of death in the HIV-positive population ($R=0.0111$).

Conclusions: With the advent of HAART, non-HIV-related causes of death are increasing in recent years in the HIV+ population. People with HIV are living longer with HAART and are dying with increasingly higher CD4 counts. Although, infection is still a significant cause of HIV-related mortality, non-infectious causes of death are emerging as a major cause of mortality in the HIV+ population. This report underscores the importance of autopsies in monitoring mortality trends.

23 The Largest Ever Reported Liver: A Case of Metastatic Squamous Cell Carcinoma

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Background: We present a very unusual case of massive hepatomegaly, which to our best knowledge is the largest liver ever reported in the literature.

Design: A 46 year-old Caucasian male with a history of smoking and alcohol abuse for 20 years (not drinking for the past 5 years) was referred to our center with abdominal pain and elevated liver enzymes for three weeks. He had no significant past medical history. Abdominal CT scan revealed an ill-defined hypoattenuating mass involving almost the entire right lobe and smaller hypoattenuating lesions within the left lobe of the liver, suspicious for multifocal hepatoma or metastases. The patient condition gradually deteriorated and he eventually expired on the 7th day of hospital stay due to multiple organ failure.

Results: Major postmortem examination findings included: 1) massive hepatomegaly (15,710 grams) with very large irregular soft mass in right lobe and multiple metastatic smaller masses in left lobe; 2) an ulcerated mass with raised border in posterior wall of hypopharynx measuring 4 x 3 x 1 cm; 3) pulmonary congestion and edema (right lung: 1410 grams; left lung: 1450 grams), and 4) splenomegaly (330 grams). Histologic examination of hypopharyngeal mass showed poorly differentiated squamous cell carcinoma. Sections of liver and spleen revealed metastatic poorly differentiated squamous cell carcinoma. Finally, histologic examination of lung showed multiple tumor emboli. Morphology of all metastatic carcinomas closely resembled the hypopharyngeal mass, which was considered as the primary origin.

Conclusions: We believe that clinical presentation and histopathological findings in this case are unique and worth reporting for following reasons: 1) Distant and delayed metastases of hypopharyngeal cancers are more common in advanced primary lesions and those with nodal involvement. However, the case presented here had no previous

symptoms related to his hypopharyngeal cancer. Also, his chief complaint was not directly related to his primary cancer and it was only at the time of autopsy that the hypopharyngeal mass was identified; 2) To our best knowledge, this is the heaviest liver ever reported for any primary or metastatic cancer. The patient did not have any risk factor for liver disease and although he had the history of alcohol abuse, there was no histologic evidence of cirrhosis in the liver in postmortem examination. Primary clinical presentation and ultimate cause of death were all attributed to metastatic squamous cell carcinoma with hypopharyngeal cancer as the primary origin.

24 A Case of Pulmonary Zygomycosis Associated with Calcium Oxalate Deposition within Bronchial Cartilage

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Background: The deposition of calcium oxalate crystals associated with fungal infection, especially, *Aspergillus niger* is well known and is considered an important diagnostic feature. It is seen in pulmonary and extra-pulmonary sites. Crystals of calcium oxalate are thought to be formed from oxalic acid produced by the fungus and calcium present in the tissue. Thus, they are usually seen at site of infection. Oxalic acid may cause local tissue damage and vascular involvement may cause hemorrhage. We report a case of pulmonary zygomycosis with calcium carbonate and calcium oxalate crystal deposition, the latter showing unusual involvement of bronchial cartilage.

Design: We reviewed the clinical and pathological results from an autopsy case of pulmonary zygomycosis. Lung tissue was examined by light microscopy, scanning electron microscopy with energy dispersive X-ray analysis (SEM/EDXA), and infrared spectroscopy (IR).

Results: A 75 year old white female with acute onset of shortness of breath, cough, and hemoptysis was treated for community acquired pneumonia, but despite intensive therapy had an unfavorable hospital course and expired 16 days after admission. An autopsy revealed multifocal necrotizing pneumonia associated with mixed herpes virus and fungal infection, and diffuse alveolar damage. Fungal elements displayed broad-based, branching, hyaline, septate hyphae consistent with *Zygomycetes spp*. Fungal lung culture grew *Rhizopus spp*. Brightly birefringent particles were seen in association with fungi. Unusually, some of the particles were present within bronchial cartilage. These particles stained with Von-Kossa but not with alizarin red, consistent with calcium oxalate. SEM/EDXA mapping demonstrated areas of calcium, oxygen, (and carbon) collocation within the cartilage. By infrared spectroscopy, birefringent crystals in the bronchial cartilage had the spectral characteristic of calcium oxalate monohydrate. Calcium oxalate dihydrate was identified in other locations, and calcium carbonate was present in fungus-invaded vascular walls.

Conclusions: This case documents an unusual association of pulmonary zygomycosis with tissue deposition of calcium oxalate, where the calcium oxalate crystals were deposited within bronchial cartilage. As the fungus infected tissue is the presumed source of the oxalate, it may be that the availability of calcium facilitates crystal deposition within the bronchial cartilage.

25 Clinical Setting Does Not Predict Discrepancy between Clinical and Autopsy Diagnoses

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Background: Autopsy rates in the United States and worldwide have continued to decrease in recent years. A number of factors, including financial concerns, fears of malpractice litigation, difficulty and inexperience in approaching families and advancing diagnostic technology have resulted in a cultural change in Medicine regarding the autopsy. Despite this, a number of important studies have shown that the discrepancy rate between clinical diagnoses and postmortem findings has not changed significantly. (Goldman, 1983) (Vincent, 2004).

Design: The purpose of this study was to determine whether the discrepancy rate between clinical and autopsy diagnoses differed between patients that had either (1) the benefit of intensive medical evaluation, (2) those that underwent recent surgery, and (3) those that did not have the benefit of such evaluation. A retrospective comparison of clinically and post-mortem determined primary cause of death and level of discrepancy for patients treated in the medical intensive care unit (MICU), patients that had undergone recent surgical procedures (SURG) and patients autopsied from affiliate nursing homes (NH) was made. Associations between diagnostic discrepancy and age, sex, and year of diagnosis were also examined.

Results: From 2003 to 2006, 562 adult autopsies were performed at our institution. Of these, 285 expired in one of the 3 clinical settings considered in this study (MICU:108, SURG:97, NH:80). The overall diagnostic discrepancy rate was 27% and was not significantly different between the 3 groups (p=0.828). Diagnostic errors were classified in two broad categories according to criteria established by Goldman, et al. Class I discrepancies included missed major diagnoses that, if detected prior to death, could have influenced management and might have resulted in prolonged survival. Class II discrepancies included major diagnoses that would not have altered management. Of the discrepancies, 65% were Class I and 35% were Class II and this did not vary between groups (p=0.728). Diagnostic discrepancy was also not associated with age (p=0.265), sex (p=0.425), or year of expiration (p=0.937).

Conclusions: Discrepancy rates of postmortem diagnoses and antemortem clinical diagnoses did not differ significantly among the three patient populations and were independent of clinical setting, level of antemortem evaluation, age, sex and year of expiration.

26 Prevalence of Respiratory Pathology in a Cohort of 784 Adult Autopsies

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Background: Respiratory pathology findings are said to be common in autopsy populations but their nature and prevalence are not well documented. The purpose of this study was two fold: First, to ascertain the overall prevalence of respiratory disease in a large cohort of autopsied patients and second, to investigate the possible impact of newer diagnostic technologies (ie, spiral chest ct) and therapies (ie, last generation antimicrobials) on the mortality of a subset of patients, whose deaths were directly attributable to pneumonia.

Design: We reviewed the autopsy protocols of 1107 autopsies performed over a period of 10 years. Autopsies performed in fetuses and children (n199) and restricted autopsies (such as heart only) (n124) were excluded, leaving a pool of 784 cases; 440 men, 344 women, mean age 62 years. In this pool, respiratory disease was categorized according to major etiologies (ie, malignancy, pneumonia, thromboemboli). For comparative analysis, patients identified as dying primarily of pneumonia were divided into 2 consecutive five year periods.

Results: Respiratory abnormalities were found in 703 (89.6%) of the 784 autopsies. Of the 703 cases, 191 had pleural abnormalities and 17 were tracheobronchial cases. The remaining 475 cases had parenchymal lung disease with pneumonia (n 241), thromboemboli (n 144), malignant neoplasms (n 93) and diffuse alveolar damage (n 91); as the leading disease entities. Of the 241 cases with of pneumonia, 204 had comprehensive documentation and of those 71 (34.8%) had deaths directly attributable to pneumonia. In 133 cases, pneumonia was interpreted as a major co-morbidity but not directly associated with death. Among the 71 patients with deaths attributable to pneumonia, 32 occurred during the first 5 year period and 39 during the second 5 year period (p=0.3132 by Poisson test).

Conclusions: This study documents an extraordinarily high prevalence of respiratory disease among a large cohort of adult autopsied patients. Among the various diagnostic groups, pneumonia represented the single largest group of parenchymal lung disease. Our findings re-affirm the notion that pneumonia ranks highly as a major cause of morbidity and mortality in hospitalized patients. Newer diagnostic technologies and/or therapies appeared to have had no significant impact when pneumonia mortality data for the two 5 year study periods were compared with one another.

27 The Decline of Clinical Autopsy Severely Impairs Healthcare Quality Assurance

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Background: Clinical autopsy provides the basis for education of medical professionals, recognition of environmental influences, infections and occupational toxicity, validation and reliability control of morbidity and mortality statistics. In addition, it is crucial for assessment of diagnostic procedures and therapy, as well as recognition of unexpected complications. Despite the progress of diagnostic technology, the discrepancies between clinical and autopsy diagnosis are acknowledged in medical literature. Our object is to evaluate the status quo of clinical autopsies and the consequences of negligence of postmortem studies on healthcare.

Design: Clinical autopsy data from multiple countries are reviewed. Autopsy frequencies are compared between countries and it tendency is assessed. The discrepancies between clinical and autopsy diagnosis is analyzed. The relationship between medical error rate and autopsy frequency is investigated.

Results: The frequency of autopsies in Germany decreased within the ten year period of 1985 to 1995 from 5.6% to about 1% of all patients deceased in hospital. During the five year period of 1995 to 1999, an additional reduction by 10.7% - 51.3% was registered in the individual German states. Similar trends are noted in the United States and in other Western countries from 1970's to 2004. Cancer, myocardial infarction, strokes, pulmonary embolism, endocarditis, peritonitis, vascular insufficiency of the bowel, lung abscess, duodenal or gastric ulcer, aortic aneurysm and various infections were among frequently missed diagnoses. Fifty eight percent of infectious diseases of adults at a community hospital in the USA were unknown before death. The average frequency of major errors in clinical diagnoses has increased during the same time period. Opposite developments have only been reported from Zurich, Switzerland, where the autopsy frequencies remained at a high level of about 90% of patients deceased in the hospital, and clinical error rates were reduced to about one third.

Conclusions: Autopsy numbers of patients deceased in hospitals have dropped to record lows in Western countries, which severely interfere with the quality evaluation of healthcare. Clinical autopsy discovers missed clinical diagnosis and provides crucial assessment of healthcare quality assurance. In order to keep healthcare at high standards, clinical necropsy ought to be a standard procedure at this time of highly specialized diagnostics and therapy.

Bone & Soft Tissue

28 *BRAF* Mutations Are Present in a Subset of Small Bowel Gastrointestinal Stromal Tumors (GISTs)

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Background: Although most GISTs show activating mutations in either *KIT* or *PDGFRA*, about 10% of cases have a wild-type genotype for these genes. Recently *KIT* mutations have been described in certain subsets of melanomas, which more commonly harbor *BRAF* mutations concentrated in two hot spots, exons' 11 and 15. It