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PLATFORM and POSTER PRESENTATIONS

Autopsy

1 Multiple Site Culture Is Useful for Evaluation of Diagnostic and Therapeutic Efficacy in the Hospital Pediatric Autopsy Population Irrespective of Post Mortem Interval and Antibiotic Use

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Background: In the era of cost containment, the utility of all diagnostic and therapeutic modalities must be supported by practice guidelines and peer-reviewed literature. Post-mortem (PM) examination can provide information as to the cause and mechanism of death, however it has been underutilized in recent years. The literature has been sparse regarding the utility of cultures in the hospitalized pediatric autopsy population.

Design: We reviewed pediatric autopsy reports and ante mortem (AM) culture data from two tertiary care centers, each for a four year interval. We wanted to determine: contamination rate, the effect of PM interval, and the effect of AM antibiotic use. We evaluated a total of 380 consecutive pediatric and perinatal autopsies, defined as any PM between the ages of 0 days to 17 years. The 111 cases with PM culture data were reviewed. We examined AM culture status, antibiotic use, PM interval, and the use of multiple site cultures PM. We defined a positive culture as isolation of a pathogen. A contaminant was defined as growth of normal flora, non-pathogens or many species. Utility, in this context, is all culture data, excluding contaminated cases.

Results: PM interval > 12 hours did not increase the contamination rate. Single site culture was positive in 9.5% of cases, negative in 69%, and contaminated in 21%. Multiple site culture was positive in 64%, negative in 22% and contaminated in 14%. Cases with antibiotic treatment had positive PM cultures in 51%, negative in 35%, and contaminated in 14%. Patients without antibiotic treatment were PM culture positive in 16%, negative in 59% and contaminated in 25%. Patients with positive AM cultures had positive PM cultures in 74%, negative in 19%, and contamination in 6%. Patients with negative AM cultures had positive PM cultures in 21%, negative in 53%, and contamination in 26%. We found that 82% of cultures had diagnostic utility.

Conclusions: PM culture in this population is not affected by increasing PM interval. Multiple site culture is more effective in retrieval of pathogen(s) than single site culture, which may reflect sampling or tropism. There is a high percentage of positive PM cultures with antibiotic treatment, which suggests treatment failure due to temporal factors or resistance. A low percentage of positive cultures is seen without antibiotic treatment, which supports the clinical impression AM. Thus, PM culture provides valuable information to clinicians.

2 Factitious Intravascular Crystaline Granulomata: *Sudden Death in "Closet" Intravenous Drug Abusers*

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Background: Microcrystalline cellulose is a stable, physiologically inert naturally occurring polymer of glucose. Its physical features allow its use as a superior filler in pharmaceutical tablet manufacture. When tablets, crushed and suspended in water, are injected intravenously, they may embolize to the pulmonary arterial tree with dangerous, even fatal consequences. We describe four medical patients who used their intravenous access lines to self-administer medicinal tablets in aqueous solutions and had sudden fatal outcomes.

Design: Four women from 37 to 51 years of age, died unexpectedly, two in hospital, and two at home. All had intravenous access lines for medication or hyperalimentation due to severe gastroparesis, complications of small bowel surgery, Crohn's disease, or acute myelogenous leukemia. All had elevated blood levels of medications including hydrocodone, oxycodone, buproprion, or sertraline. At autopsy two had toxic levels of hydrocodone or oxycodone that had not been prescribed for them, the others had elevated levels of antidepressants. Lung samples from each case and the filters and tubing from two hyperalimentation units were analyzed.

Results: At autopsy, all had diffusely gritty lungs that histologically contained myriad intravascular and transmural granulomata which partly or completely obstructed small pulmonary arteries at the bronchiolar level. The granulomata surrounded colorless polarizeable crystals, that had no reaction with routine histochemistry. No such granulomata were found in other arteries of the body and no crystals were present in alveoli. The polarizeable crystals in the lungs and in the filter and tubing were comparable, by light and scanning electron microscopy. In energy dispersive x-ray spectroscopy, they consisted of carbon, nitrogen, and oxygen, and were considered organic products. By infrared microspectroscopy with spectral subtraction, they were consistent with microcrystalline cellulose. No specimen had any chacacteristics of talc.

Conclusions: These patients inappropriately used medications that contained the same cellulosic filler. Their diffuse pulmonary arterial disease suggested that they had been injecting aqueous suspensions of their pills, undetected, for moderate periods of time. Sudden death of patients with long term indwelling catheters should be evaluated with suspicion of possible intravenous self medication. All tubing and filters should accompany the patient to autopsy and be included in toxicology studies.

3 Diagnostic Errors in Outpatient Medical Care Detected by Autopsy

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Background: Despite advances in medicine and technology, discrepancies between clinical diagnoses and findings at autopsy are well documented. Studies reviewing such discrepancies have primarily focused on error in hospitalized patients. Our objective was to estimate the correlation between clinical diagnoses and autopsy findings in outpatient and acute care settings.

Design: A two-year (2000-2001) retrospective review was completed. The study group included all naturally occurring deaths within Sacramento County, California in which an autopsy was performed. Autopsy findings were compared with clinical diagnosis and treatment at the healthcare visit prior to death.

Results: Of 692 cases studied, 53 (7.7%) autopsies detected clinically-missed diagnoses involving a primary cause of death (major error), with 45 (6.5%) cases likely to have had an adverse impact on patient survival (class I errors). The vast majority of missed diagnoses documented at autopsy were complications of atherosclerotic cardiovascular disease.

Conclusions: The results of this study show that autopsies are useful in medical audits of deaths occurring in outpatient and acute care settings.

4 Congestive Heart Failure in Patients with Severe Coronary Atherosclerosis without Myocardial Infarction: Combined Ischemic and Dilated Cardiomyopathies or a Unique Form of Ischemic Cardiomyopathy? A Report of Six Patients

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Background: A few studies have delineated a unique subset of patients exhibiting the co-existence of features of a dilated cardiomyopathy (DCM) with congestive heart failure (CHF) plus severe coronary atherosclerosis (CAD). Since DCM is diagnosed by exclusion of all other known cardiac diseases, including ischemic heart disease (IHD), the coexistence of CAD precludes a positive diagnosis of DCM in such patients. We report clinicopathologic features in 6 patients with coexistent pathologic features of DCM-CAD.

Design: A review of the 567 autopsy records for the years 2002-September 2006 yielded 6 patients (1.1%) who had CHF associated with greater than 50% coronary luminal narrowing and generalized chamber hypertrophy and dilatation without evidence of myocardial necrosis. The following was recorded: age, sex, duration of CHF, systemic hypertension, diabetes mellitus, alcoholism, heart weight, LVFW thickness, degree of narrowing of all 3 major coronary arteries, myocardial histology, bypass grafting, presence of emboli and mode of death.

Results: Six patients, 5 females and 1male, mean age 63.3 years (range= 50-84, SD= 12.0) were encountered. Mean heart weight was 586.7 grams (range= 370-850, SD= 185.6). All hearts showed generalized chamber dilatation and hypertrophy reminiscent of DCM. Mean LV thickness was 1.4 cm (range= 1.0-1.6, SD= 0.24). Apart from scanty subendocardial fibrosis in the LV of all cases, none of the hearts showed healed or acute myocardial infarction. The 18 coronary arteries in these 6 patients showed a

mean stenosis of 66.7% (range= 0-95%, SD= 34.3%). None of the myocardial sections showed wavy myocytes or features suggestive of stunned or hibernating myocardium; only myocyte hypertrophy similar to that noted in DCM was present. Three patients had undergone coronary bypass grafting. Mode of death was cardiac (3), metabolic (1), infection (1) and drug overdose (1).

Conclusions: Until a means of positively diagnosing DCM becomes available, the separation of DCM and IHD without infarction will remain problematical. Pathologic evidence tilts towards the coexistence of DCM and CAD in our patients. Contrary to two earlier studies our patients showed a much lower incidence of diabetes mellitus and alcoholism. Once genetic markers become available for DCM they could be profitably be applied to this group of patients.

5 Neutrophil Aggregates and Complement Fixation in Amniotic Fluid Embolism Syndrome

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Background: Amniotic fluid embolism syndrome, also called the anaphylactoid syndrome of pregnancy, is the most common cause of maternal perinatal death. There is devastating vascular collapse with hypoxia, often ARDS, then DIC. Many cases have fetal squames or other emboli in the pulmonary vasculature, but other clinically similar cases do not. Hypocomplementemia is noted clinically, but the immunologic mechanism has not been studied pathologically.

Design: Three autopsy cases of amniotic fluid embolism with squamous emboli, two clinically similar cases without emboli, and seven control cases (maternal perinatal deaths from other causes) were studied. Immunoperoxidase staining for complement component C9 (clone 10A6, Vector Labs) were performed on selected blocks. The slides were reviewed in a blinded manner. Lung tissue from two cases of amniotic fluid embolism were studied by electron microscopy.

Results: The five cases that had the clinical syndrome, either with or without amniotic emboli at autopsy, had large, predominantly neutrophil aggregates in the pulmonary microvasculature, often not associated with the squamous emboli. These changes were not seen in the seven controls ($p<0.01$, Fisher exact test). Strong complement C9 immunostaining was present on the squamous emboli in the pulmonary microvasculature in the amniotic fluid embolism cases. In two cases with squamous emboli in the lungs, electron microscopy confirmed the presence of neutrophil aggregates and showed neutrophil degranulation in the lungs and a marked increase in the pulmonary capillary endothelial cell pinocytotic vesicles.

Conclusions: Neutrophil aggregation in the pulmonary microvasculature was seen in patients with the clinical syndrome associated with amniotic fluid embolism, whether or not emboli were found. This suggests that a common immunologic mechanism could be present in this distinctive clinical syndrome whether or not there are recognizable emboli. We hypothesize that those cases lacking recognizable emboli could have emboli consisting of small cellular or membrane fragments that cannot be identfied by morphology alone. Intravascular complement deposition and activation on the embolized material provides a mechanism, via soluble complement factors C3a and C5a, for intravascular neutrophil activation and aggregation. Complement activation, presumably induced by maternal antibodies to the embolized fetal material, could explain the shock and ARDS-like changes found in amniotic fluid embolism syndrome. Further work is needed to determine the complete mechanism active in this syndrome.

6 Use of a Comprehensive Authorization Form Does Not Impact the Number and Diagnostic Potential of Autopsies

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Background: The Alder Hey Hospital organ retention scandal changed the way Autopsy Authorization Forms (AAF) are obtained. In the wake of the scandal, it became a duty for the clinician to ensure that the next-of-kin understands exactly what methods and procedures are involved during autopsy. To meet this duty, our facility implemented in May 2000 a detailed template for the AAF, which also offered ample possibility to limit the procedure. However, there were concerns that the new template would make families less likely to give their permission, and that limited autopsies would be of little clinical and educational benefit. The objective of this study is to evaluate the impact of this comprehensive AAF in the volume of autopsies performed by our department, as well as whether the limited autopsies had a lower diagnostic potential.

Design: We collected data on all autopsies performed between 1996 and 2005. Using the Student t-test, we compared the average number of autopsies performed before and after the implementation of the new AAF. 2000 was a transitional year and was excluded from the study. Adult autopsies performed in the second period were then classified as seen in table 1. A possible association between limited autopsies and undetermined causes of death at the final diagnosis was analyzed by chi-square.

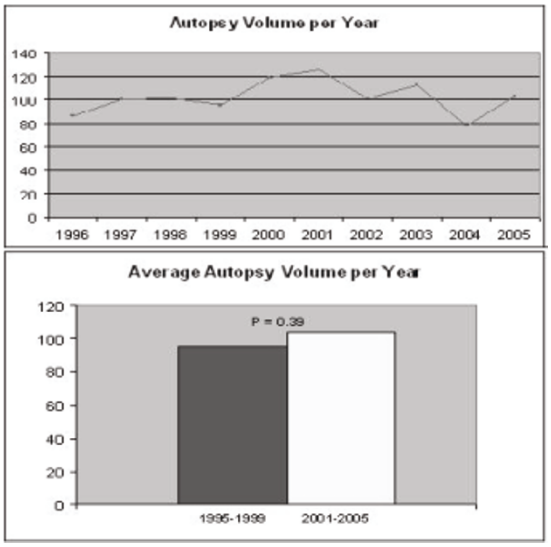
Results: There was no statistically significant difference in the average number of autopsies performed yearly in both study periods (Fig 1). Chi-square analysis of adult autopsies performed in the second period did not show an association between autopsy limitations and the rate of undetermined causes of death (Table 1).

Conclusions: In conclusion, implementation of a comprehensive AAF did not appear to interfere with the autopsy volume. Furthermore, offering the next-of-kin ample opportunity to limit the autopsy had little impact in the final determination of the cause of death. These findings are especially reassuring for teaching hospitals, which need autopsies both for their educational value and to meet board requirements.

Adult Autopsy Limitations x Cause of Death (COD)

	Undetermined COD	Determined COD	
Limited Autopsies	11	173	184
Unlimited Autopsies	16	263	279
	27	436	463

Chi-Square, p=0.91



7 The Importance of the Postmortem Radiograph in Perinatal Autopsies: An Algorithm for Common Lethal Skeletal Dysplasias

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Background: Lethal skeletal dysplasias are developmental disorders of chondro-osseous tissue that lead to death in utero or shortly after birth. Many have a known genetic basis and accurate diagnosis at autopsy has important implications for recurrence and precurrence risks. Regardless of the type of genetic transmission, the aberrant gene produces changes in all anatomic sites in which the gene is expressed. Thus, anomalies throughout the skeleton can be accurately predicted, making postmortem radiographic images a useful diagnostic tool. This is especially true in instances when patient history is unknown or death is unexpected. Development of a sequential approach for interpretation of postmortem radiographs is useful in categorizing skeletal dysplasias and potentially leads to higher yield histologic sampling, prediction of internal visceral anomalies, and more accurate diagnosis.

Design: Using postmortem radiographs of known cases of skeletal dysplasia from perinatal autopsies performed by the Department of Pathology at University of Alabama at Birmingham, a systematic approach was taken to characterize the different bone abnormalities seen in five common lethal skeletal dysplasias.

Results: We propose use of an algorithm to aid in the development of a differential diagnosis of common lethal skeletal dysplasias (osteogenesis imperfecta, type II; achondrogenesis; thanatophoric dysplasia; lethal hypophosphatasia; and campomelic dysplasia).

Conclusions: Postmortem radiographs are critical diagnostic aids in the evaluation of common lethal skeletal dysplasias. Since the frequency of all skeletal dysplasias is low, only 15.7 per 100,000 births, the diagnosis can be problematic to the general pathologist. Our algorithm provides a practical schema to differentiate among them.

8 Spectrum of Pulmonary Pathology in Solid Organ Transplant Recipients: An Autopsy Study

ND Dimov, DL Zynger, AV Yeldandi. Northwestern University, Chicago, IL.

Background: Improved surgical techniques and supportive care have led to a significant increase in solid organ transplantation (SOT) as the definitive treatment for end stage organ damage. The lungs of SOT recipients are frequently affected by various infectious and non-infectious pathological processes, possibly contributing to preventable causes of mortality. Pulmonary findings in SOT patients at autopsy have not been described. We evaluated post-mortem lung pathology of SOT recipients in order to evaluate the impact on survival.

Design: Autopsy reports and histological lung sections from SOT patients from 1996 to 2006 were reviewed. A total of 70 SOT cases- 47 males (mean 52.9 years) and 23 females (mean 50.5 years), received 47 renal, 34 liver, 8 pancreas, 1 heart and 1 small bowel allografts. Survival data, pulmonary findings and major cause of death were assessed.

Results: The mean survival was 35.4 months post-transplantation, with 29 patients (44%) surviving less than 100 days. Frequently encountered specific changes were diffuse alveolar damage (61%) and diffuse alveolar hemorrhage (59%). Bronchopneumonia (27%), lobar pneumonia pattern (6%), and respiratory bronchiolitis (3%) were identified. Fungi were observed in more than 10% (Aspergillus, 9%; Candida 1.5%), bacteria in 11%, CMV inclusions in 7.5%, and noncaseating granulomata in 3%. Variable vascular changes were present in 36%, and pleuritis and subpleural edema in 21% of patients. Nonspecific interstitial pneumonia (8%), usual interstitial pneumonia (5%), and organizing pneumonia (5%) were encountered. Other findings included pulmonary edema (50%), microthrombi (30%), and previously undiagnosed primary adenocarcinoma (2%). While pulmonary abnormalities were detected pre-mortem by imaging studies in 30% of patients, lung pathology was present in 95% at autopsy. Respiratory failure was considered the major cause of death of 34 (49%) patients, of which only 19 (56%) had radiologic findings. Potentially treatable conditions among these patients included early bronchopneumonia (9), lobar pneumonia (3), CMV (4), Aspergillus (3), and Candida (1).

Conclusions: Post-mortem pulmonary pathology in SOT patients encompasses a spectrum of morphological presentations. In our study, pulmonary complications were the major cause of mortality in half of SOT recipients, and 59% of those were infectious processes. Timely invasive diagnostic procedures for histological and microbiological evaluation could be beneficial for appropriate management of pulmonary complications to improve the survival of SOT recipients.

9 A Comparative Autopsy Study of Pulmonary Pathology in Solid Organ and Stem Cell Transplant Patients

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Background: While solid organ transplantation (SOT) is the definitive treatment for end stage organ damage, peripheral stem cells transplantation (SCT) is being used for patients with malignancies, as well as immune disorders. The mortality of transplant recipients may be increased due to the pulmonary pathology. As the level of immunosuppression varies according to the type of transplant, the aim of the study was to compare infectious and malignant processes within the lung upon autopsy of SOT and SCT patients.

Design: Retrospective review of autopsies, performed between 1996 and 2006, revealed 68 SOT and 33 SCT patients. The SOT cohort received 47 renal, 34 liver, 7 pancreas and 1 small bowel allografts and the SCT group included 18 autotransplants and 15 allotransplants. Autopsy reports, histological lung sections and major cause of death were reviewed.

Results: Mean survival was 35.4 months for SOT and 15.0 months for SCT. Respiratory failure was considered the major cause of death in 49% of SOT and 67% of SCT. Aspergillus was identified in 7 to 8% of single organ transplants but was seen in 27 to 28% of SCT. Frequency of CMV inclusions (<10%) was similar for all types of transplant patients. Pneumonia with a lobar pattern was most common in allo-SCT (14%). Surprisingly, bronchopneumonia was encountered more in SOT, most frequently in renal transplant patients (34%). Pulmonary involvement by lymphoma/ PTLD (17%) or metastatic carcinoma (11%) occurred in a considerable portion of auto-SCT.

Conclusions: The frequency of pulmonary complications varies based on type of transplant, which might relate to different degree of immunosupression. While the overall level of CMV infections was relatively low, possibly reflecting adequate prophylaxis, invasive Aspergillosis was frequent in SCT and multi-organ SOT recipients. Awareness of the differences could allow further patient stratification resulting in an earlier detection of pulmonary pathologic processes and thus improved survival.

	Aspergillus	CMV	Broncho-pneumonia	Lobar Pneumonia Pattern	Lymphoma/ PTLD	Carcinoma
Renal Transplant (n=29)	2 (7%)	1 (3%)	10 (34%)	2 (7%)	0	1 (3%)
Liver Transplant (n=26)	2 (8%)	2 (8%)	4 (15%)	2 (8%)	0	0
Muli-organ Transplant (n=13)	2 (15%)	1 (8%)	4 (31%)	0	0	0
Auto-SCT (n=18)	5 (28%)	1 (6%)	4 (22%)	2 (11%)	3 (17%)	2 (11%)
Allo-SCT (n=15)	4 (27%)	1 (7%)	2 (13%)	2 (14%)	1 (7%)	0

10 A Retrospective Correlation of Primary Cancers with Their Metastatic Sites at Autopsy

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Background: While metastasis is a well-known phenomenon among most primary cancers, few comprehensive studies have compared metastatic patterns among different primary cancers. Large-scale postmortem analyses of these patterns would be of clinical value, both for anticipating the metastatic behavior of specific cancers, and for locating primary cancers among patients with metastases from unknown primary sites.

Design: Archival data from 4,012 (2,108 male and 1,904 female) autopsies performed between 1914 and 1943 at Ponderville, Palmer, Westfield, Harvard, and Huntington Medical Centers were examined. A total of 3,792 autopsies, comprising 43 primary neoplasms, were analyzed. For each set of patients with a given primary neoplasm, metastases at each of 30 different anatomic sites were quantified, for a total of 9,394 metastases. We address several key questions: (1) How frequent was each primary cancer; (2) how often did the different cancers generate metastases; (3) which metastatic sites were associated with each primary, and with what relative frequency; and (4) with what relative frequency were different metastatic sites targeted?

Results: The most common primary neoplasm was rectum (437 primaries, 11.5% of the total) and the least common was pleura (1 primary, 0.03% of the total). Mediastinal cancers were most likely to metastasize (6.3 metastases per primary), while duodenal cancers were least likely (0.6 metatases per primary). The most common metastatic target was regional lymph nodes (1,939 metastases, 20.6% of total), while the least common was testes (11 metastases, 0.1% of total). Preferred metastatic sites varied among the primary cancers analyzed.

Conclusions: Surprisingly few large-scale comparative studies of cancer metastasis are available in the recent literature. The most current study we encountered analogous to our own was a 1950 investigation involving 1,000 autopsies. While our own analysis relies on autopsies performed many years ago, it nonetheless represents the largest of its kind of which we are aware, and demonstrates the utility of this approach in generating hypotheses for future research. We hope to extend our analysis, using current autopsy material, to study shifts in metastatic patterns that may have resulted from more recent practices in cancer treatment.

11 A Novel Autopsy and Gross Dissection Training Program: A Pilot Study

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Background: The post-mortem examination has been considered an essential tool in developing knowledge in surgical dissection skills necessary for anatomic pathology. There has been a gradual decrease in the number of autopsies performed at universities and private/community hospitals. With this decline, the opportunity for residents to learn from autopsies has also decreased. We hypothesized that the development of these skills is possible through a novel introductory training course in autopsy and gross dissection using sheep organ blocks to simulate a portion of the post-mortem examination. The goal of this project was to introduce first and second year (junior) residents to autopsy and gross dissection techniques, particularly the modified Rokitansky method. These residents compared to more experienced third and fourth year (senior) residents.

Design: A general questionnaire was distributed to all residents to assess individual experience and a self-assessment of competency in the autopsy dissection. Junior residents performed three organ block dissections with the first two being didactic sessions with staff supervision. The third and final dissection was completed without supervision and used as a measure of retention of skills and effectiveness of teaching. Senior residents completed a single dissection representing an assessment of prior training and competency. An objective measure scale was created to determine the completeness of the dissection (0=No, 1=Incomplete and 4=Yes). Based on this measurement, a score greater than or equal to 150 was considered a complete dissection.

Results: Overall, junior residents had higher performance scores than senior residents with median scores of 115 and 73, respectively and those residents who received training performed a more complete dissection (see Table 1).

Conclusions: Based on these findings, residents who received specific training performed more complete autopsy dissections when compared to a more experienced group that had not received such training. On average, the experience of the resident did not correlate with a complete autopsy dissection. These findings indicate that a dedicated and systemic approach to autopsy/gross dissection will ensure that residents obtain the necessary grossing skills applicable to anatomic and autopsy pathology.

Table 1: Overall Performance/Assessment

Junior Resident Performance	Median scores
PGY-1	113 (range 28-123)
PGY-2	140 (range 102-156)
Combined (PGY-1/2)	115
Senior Resident Assessment	
PGY-3	69 (range 45-103)
PGY-4	77 (range 25-122)
Combined (PGY-3/4)	73

12 Comparison of Autopsy Findings in Lung Transplant Patients over a 17 Year Period: The Methodist Hospital Experience

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Background: Lung transplantation is a treatment option for end-stage lung disease. Transplant recipients remain at high risk for morbidity and mortality. Few studies have addressed factors contributing to mortality based on autopsy cases. Comparison of autopsy findings in double and single lung transplant recipients was made over a period of 17 years in a single institution.

Design: From 2003 to 2006, 20 autopsies were performed on 13 male and 7 female lung transplant recipients (15 double lung; 5 single lung). Autopsy reports were reviewed and demographic and clinical data was collected. Current autopsy findings were compared to previous published data from Methodist Hospital autopsy experience from 1985 to 1989.

Results: Mean age was 48 years (26-70). Indications for transplantation were idiopathic pulmonary fibrosis (8), COPD (4), cystic fibrosis (3), primary pulmonary hypertension (2), alpha-1 antitrypsin deficiency (1), and sarcoidosis (1). Three patients died during the early post transplant period (< 30 days) and 17 patients died after 30 day period. Graft failure and gram-negative bacterial infections accounted for deaths in the early post transplant period. In remainder of the cases, bronchiolitis obliterans (BO) and infections were the main cause of death. One case of Cytomegalovirus (CMV) and a case of cryptococcal infection was identified. Findings other than BO included patchy/diffuse interstitial fibrosis (6), pulmonary edema (4), necrotic areas with microabcess formation (4), thrombus in blood vessels (2) and acute bronchitis(1). Majority of the cases (18) showed chronic rejection with only two cases exhibiting mild acute rejection. Mean survival after transplant was 45.3 months (range: 10 days to 8 years). In comparison, the mean postoperative survival period was 23 days (range: 2 days to 6 weeks) in the previously published study (1989). CMV infection (3) with gram-negative bacterial pneumonia and sepsis were the most prevalent contributing factors to death in lung transplant patients in the previous series.

Conclusions: Current autopsy findings compared to previous autopsy experience show no significant differences despite new surgical techniques and treatment modalities. Bronchiolitis obliterans syndrome and infections are still the most common cause of morbidity and morality. Our study found that infections and graft failure were responsible for the early posttransplant mortality. Chronic rejection was a major cause of death in more than half of the patients who survived beyond 3 months.

13 Short-Term Survival in Patients with Systemic Lupus Erythematosus: An Autopsy Study of 13 Cases

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Background: The prognosis of SLE has significantly improved with more than 90% of patients surviving for more than 10 years. In these patients, the clinical manifestations and causes of death are typically infections, as a result of medication side effects, or thrombotic events. In our study, a unique group of 13 autopsy cases having short survival times (less than 5 years after diagnosis) was analyzed to determine the most common clinical presentations, autopsy findings and causes of death.

Design: In the time interval between 1992 and 2006, 13 autopsy cases of SLE from Emory's Department of Pathology were identified and retrospectively studied. The causes of death and frequency of specific organ involvement were analyzed and correlated with pertinent clinical, laboratory and demographic data.

Results: The following demographic data was extracted from our autopsy files: average age was 36 years (range 22-51 years); 10 patients were female (76.92%) and 3 were males (23.08%); 11 were African American (84.62%), 2 were Caucasian (15.38%). The most common clinical presentation was respiratory illness with SOB/dyspnea observed in 7 cases (53.85%), followed by sepsis (6 cases, 46.15%), coagulopathy (4 cases, 30.77%), altered mental status (3 cases, 23.07%) and fatigue/myalgia (3 cases, 23.07%). Duration of illness ranged from 3 days to 5 years. The leading causes of death were as follows: infections including sepsis/pneumonia (10 cases, 76.92%); diffuse alveolar damage (DAD) (6 cases, 46.15%); renal failure (2 cases, 15.38%), and coagulopathy with stroke (2 cases, 15.38%). Surprisingly, a higher number of neurologic and gastrointestinal clinical symptoms and/or autopsy findings were identified in our study group; 7 cases (53.85%) with neurologic manifestations and 9 cases (69.23%) with gastrointestinal findings.

Conclusions: The prevalence of clinical manifestations and causes of death in SLE patients varies depending on the phase of the disease. Active SLE and infections predominate as the most common causes of death during the initial 5 years, while thrombotic events dominate in the latter phase. In our study group, infection remains the leading cause of death, with high rate of lupus/coagulopathy-related neurological findings. These neurologic findings are typically observed in patients surviving for greater than 10 years. The decreased survival time in our group of patients can be explained by socioeconomic factors and related poor patient compliance.

14 Robust Immunohistochemical Staining of Several Classes of Proteins in Tissues Subjected to Autolysis

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Background: Despite the common use of immunohistochemistry in autopsy tissues, the stability of most proteins over extended time periods is unknown. The traditional belief is that proteins rapidly degrade in devitalized tissues, although this has never been proven.

Design: The robustness of signal for sixteen proteins (MMP1, MMP2, MMP3, MMP9, TIMP1, TIMP2, TIMP3, AGER, MSR, SCARB1, OLR1, CD36, LTF, LGALS3, LYZ, and DDOST) and two measures of advanced glycation end products (AGE, CML) was evaluated. Two formalin-fixed paraffin embedded human tissue arrays containing sixteen tissues each were created to evaluate up to 48 hours of autolysis in a warm or cold environment. Analysis was performed by two independent observers and confirmed for a subset of proteins by digital analysis and western blotting.

Results: For these 16 proteins, we saw no systemic diminution of signal intensity through 24 hours. Overall signal intensity loss was 10%, 7%, 5% and 18% for time points 0, 12, 24, and 48 hours respectively. Only 4 samples showed appreciable signal intensity loss at 48 hours (DDOST, LGALS3, MMP9, OLR1). There were no significant differences in intensity loss based on temperatures. Observer scoring and digital scoring analysis showed strong correlation (R^2= 0.83) and western blot data confirmed the presence of these proteins and a lack of significant degradation.

Conclusions: We conclude that this large set of proteins generally degrades slowly and maintains faithfully their IHC characteristics over at least a 24 hour time interval in autolyzed tissues. This study supports the use of autopsy tissues with short postmortem intervals for IHC and further dispels the traditional belief of poor protein preservation in devitalized tissues.

15 Temporal Histopathologic Changes of Noncompaction of the Heart

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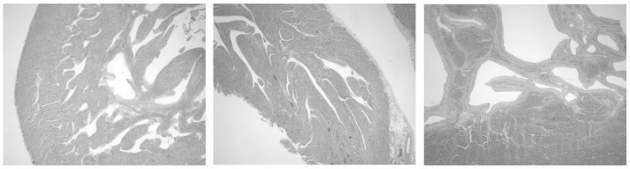
Background: Noncompaction of the heart is a rare condition in which the loose spongy meshwork of interwoven myofibers and vascular channels of the ventricles fails to compress down into firm, dense myocardium during embryogenesis . This abnormal compaction results in the presence of prominent trabeculae and deep intertrabecular recesses in the endomyocardium that remain connected with the ventricular cavity. These changes can result in variable symptoms and outcomes that range from clinically silent disease to rapidly evolving heart failure, arrhythmias, and death. While there has been much interest in the echocardiographic findings seen with noncompaction of the heart, we were interested in the less noted histopathologic changes that occur over time.

Design: We examined and compared the histopathology of three cases of noncompaction of the heart from patients of differing ages. The cases included hearts from a fetus (< 20 weeks gestational age; products of conception, Figure 1 left panel), a 16 week old infant (autopsy, Figure 1 middle panel), and a 21 year old adult (explanted heart, Figure 1, right panel). Microscopic examination was performed with standard hematoxylin and eosin stained tissue sections.

Results: Grossly there was noncompaction of the inner myocardium in the left ventricles of the fetal and adult cases, whereas the infant case had patchy noncompaction of both left and right ventricles. Microscopically, in all cases the inner ventricular myocardium was characterized by a spongy, loose layer of myocardium that contained deep intertrabecular recesses lined by endocardium, with the ratio of noncompacted to compacted myocardium > 2 (Figure 1). With increasing age there was evidence of progressively prevalent subendocardial fibrosis of the noncompacted areas. Further, there was evidence of progressive myocyte hypertrophy in both the noncompacted and immediately adjacent compacted myocardium.

Conclusions: The temporal histopathologic changes seen with noncompaction of the heart include progressive subendocardial fibrosis and myocyte hypertrophy. Further study is warranted to elucidate a better understanding of the variable clinical course and pathologic changes that occur with this disease.



16 Recognition of Infectious Disease at Autopsy of Organ Donors and Its Potential Impact on Clinical Outcomes: A Ten Year Review

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Background: Transmission of infectious diseases to recipients has been a concern since the advent of organ transplantation. While screening for common infectious diseases is standard, less common organisms still pose a risk to transplant recipients. Statistics indicate that these infections are rare but result in severe outcomes. We report four cases involving organ transplant that resulted in vastly different clinical outcomes for the recipients.

Design: We reviewed the autopsies from our hospital between 1995-2005 for cases of transplant donor related infectious diseases.

Results: We report four cases involving organ transplantation from infected donors. The first case was a heart transplant patient who died three weeks post transplant of presumed bacterial sepsis. Autopsy showed disseminated toxoplasmosis and the donor was subsequently identified as having had acute infection with *T. gondii*. The second and third cases were liver and kidney transplant patients who died 2 weeks post transplant of presumed bacterial sepsis. Autopsy revealed disseminated coccidiomycosis. The donor had presented to a local hospital complaining of headache and near syncope. There was a remote history of coccidiomycosis. He developed anoxic brain injury following cardiac arrest. After organ harvesting, autopsy revealed cloudy meninges and cardiomegaly. Histologic examination of the brain and meninges one month later revealed meningitis with fungal organisms consistent with *C. immitis*. The fourth case was a donor who died of a closed head injury. After harvesting of the heart, liver and kidneys, autopsy revealed changes in the lungs consistent with active granulomatous inflammation, confirmed by frozen section. Fungal forms consistent with Histoplasma were subsequently identified by GMS. Based on this finding, timely antifungal therapy was given to the liver and heart recipients and the kidneys were not transplanted.

Conclusions: Prompt recognition of infectious disease at autopsy can have a major impact on the clinical course of transplant recipients. These cases highlight that autopsy can be of the utmost benefit to clinicians caring for transplant recipients. Early detection of infectious disease at autopsy requires a thorough review of the clinical history, a keen eye, and a high index of suspicion. Although rare, these inapparent infections can have severe consequences for the transplant recipient. Autopsy offers an opportunity to identify infectious diseases in the donor that might change the outcome for the recipients.

17 Risk Factors for Intra-Uterine Fetal Demise (IUFD) in the Bronx, NY

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Background: Despite the decline in US autopsies performed annually, the rate of IUFD cases has remained steady. Risk factors for IUFD include chorioamnionitis, diabetes mellitus (DM), and hypertension (HTN). To date no study has evaluated these factors in the predominantly low-income, medically underserved minority community of the Bronx, NY. We hypothesize that in this region, cases with these factors have increased in incidence over the last decade.

Design: One hundred forty-nine IUFD cases performed from 1996-2005 at the Montefiore Medical Center (MMC) in the Bronx were divided into 2 groups by date and compared.

Results: Group 1 (1996-2000, n=62): Hispanic (26/58), Black (16/58), male (36/62), and female (26/62). Group 2 (2001-2005, n=87): Hispanic (41/83), Black (34/83), male (42/87), and female (45/87). Between groups, the number of IUFD autopsies increased by 40.3%. The prevalence of cases >27 wks gestational age = 75.2% (109/145). The incidence of cases with chorioamnionitis increased significantly from 10.5% (6/57) to 20.9% (18/86) (Fisher exact, $p<0.05$). None of the group 1 cases and only 5 of the group 2 cases (27.8%) were associated with known maternal infection; 3 of the latter 5 cases (60%) were linked to Group-B Strep (GBS). Cases of placental malperfusion increased in incidence from 16.1% to 34.5% ($p<0.001$). Placental infarction had a greater overall prevalence = 27.1%; the prevalence of abruption = 12.9%. The incidence of cases with maternal history of therapeutic abortion decreased significantly from 35.1% to 17.8% ($p<0.05$). Cases with large fetal weight for gestation decreased from 35.5% to 10.5% ($p<0.001$). The incidence of oligohydramnios increased from 4.8% to 15.0% ($p<0.05$). The incidence of maternal DM (gestational, Type I or II) increased from 4.8% to 7.0% ($p=0.24$), but not significantly. The incidence of maternal chronic HTN increased insignificantly from 3.2% to 8.0% ($p=0.14$). The prevalence of pre-eclampsia = 3.4%.

Conclusions: The number of autopsies and the incidences of cases with chorioamnionitis, placental malperfusion, and oligohydramnios have increased at MMC over the last decade. These findings are concerning because they underscore the growing impact of prenatal disease on maternal-fetal outcomes; they likely reflect the need for improved medical care in this area. Our results can be used to foster and guide prenatal care programs in the Bronx and other low-income regions. As a result, the provision of systematic GBS screening and the treatment of maternal DM and HTN will likely diminish IUFD risk. More factor and statistical assessments with 2006 data are underway.

18 GVHD in Solid Organ Transplantation

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Background: Graft versus host disease (GVHD) is a pathological process seen in patients who receive biological material (graft) that contains lymphocytes capable of proliferating and attacking the recipient (host). GVHD is typically seen in patients with impaired immune function who cannot mount an immune response to the attacking lymphocytes. The lymphocytes that cause GVHD attack the skin, gastrointestinal tract, and liver of the host. Clinical findings include skin rash, diarrhea, and/or hepatic insufficiency, which may occur individually or in any combination; the severity also varies from patient to patient. Similar symptoms can be caused by other factors, including infections, drug reactions and reaction to therapeutic interventions (e.g a rash after total body irradiation).

Design: We reviewed our archives for histologic material from solid organ transplant recipients who had died. In particular we reviewed biopsy, surgical and autopsy sections from liver, skin and the gastrointestinal tract. Medical history, including type of transplant, skin rash, diarrhea, hepatic insufficiency and HLA match was noted. Based on histologic criteria, cases suspicious for GVHD were selected and these selected cases were further analyzed by immunohistochemistry for CMV and class I HLA antigens. The final data was then analyzed.

Results: We reviewed the histologic material from 180 deceased solid organ transplant patients. Based on the histologic criteria, a total of 29 possible GVHD cases were identified, all were from cadaveric donors. Results are presented in the table. Most patients had donors with 4 to 6 HLA antigen mismatch. All patients received blood product transfusions; no transfusions were irradiated. Each patient had at least one of the clinical symptoms of rash, diarrhea or hepatic dysfunction. Immunohistochemical analysis for CMV was negative in all cases.

Conclusions: Findings suggestive of GVHD were found in 16% of patients who died after solid organ transplant. None of these cases were positive for CMV by immunohistochemical stain. Evidence of humoral rejection as an explanation for the histological findings was suggested in only one of 24 cases. Though histiologic findings of GVHD are specific, a similar pattern can be seen in other conditions such as drug reactions and viral infections. Demonstration of donor lymphocytes in the involved organ helps support the diagnosis of GVHD in questionable cases.

GVHD in Transplant

Type of Transplant	#(%) cases of suspected GVHD	# of cases reviewed
Liver	11(73)	15
Lung	5(16)	32
Kidney	3(8)	36
Heart	10(13)	79
Heart-Lung	1(6)	18
Total	29(16)	180

19 Rituximab-Induced Changes in Lymphoid Tissues. An Autopsy Study

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Background: Rituximab, an anti-CD20 monoclonal antibody, was approved by the FDA in Nov 1997 as the first therapeutic antibody for cancer treatment. It is indicated for the treatment of patients with relapsed or refractory, low-grade CD20-positive, B-cell non-Hodgkin's lymphoma (NHL) and for diffuse large B-cell, CD20-positive NHL in combination with CHOP regimen (R-CHOP). We have studied the tissue effects of rituximab treatment on lymphohematopoietic tissues collected at autopsy.

Design: We reviewed our computerized records for autopsies performed on patients with lymphoma or post-transplant lymphoproliferative disorder (PTLD) that had received R-CHOP therapy. Pre-1997 autopsy cases of patients with lymphomas treated with CHOP as well as randomly selected autopsy cases of patients without lymphoma that died of other causes, including cases of transplant patients that were immunosuppressed served as a control. After review of the slides, immunoperoxidase stains for the following monoclonal antibodies: CD3 (clone SP7), CD20 (clone L26), CD22 (clone FPC1), all from LabVision, and CD79a (clone JCB117, CellMarque) were performed on all lymph node (LN), spleen and bone marrow blocks available. The relative number of cells staining was scored semi-quantitatively from 0 to 3+ for each antibody by two pathologists blinded to the clinical information.

Results: We reviewed the immunostaining pattern of lymph nodes and spleens from 10 autopsies of patients who received R-CHOP. we compared the results with those of 11 autopsy cases of patients treated with CHOP and 8 randomly selected autopsies of patients without lymphoma. We arbitrarily considered as positive the immunostains that scored at least 2+.

	R-CHOP		CHOP		Control	
	LN	Spleen	LN	Spleen	LN	Spleen
CD3	75% (n=8)	12.5% (n=8)	50% (n=8)	29% (n=7)	80% (n=5)	20% (n=5)
CD20	25% (n=8)	0% (n=8)	62.5% (n=8)	43% (n=7)	80% (n=5)	100% (n=5)
CD79a	25% (n=8)	0% (n=8)	50% (n=8)	57% (n=7)	60% (n=5)	100% (n=5)
CD22	0% (n=3)	0% (n=8)	25% (n=4)	14% (n=7)	67% (n=3)	100% (n=5)

Conclusions: Patients with lymphoma or PTLD that had received R-CHOP therapy had a significantly lower percentage of CD20+ B-cells (25% LN and 0% spleen) when compared to patients treated with CHOP alone (62.5% LN and 43% spleen) or control patients without lymphoma (80% LN and 100% spleen).

20 Unilateral Regression of Cavopulmonary Anastomosis-Induced Pulmonary Arteriovenous Malformations Following Hepatic Vein to Pulmonary Artery Conduit

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Background: Pulmonary arteriovenous malformations (PAVM) occurring after cavopulmonary anastomosis (CVPA) may be due to diversion of labile anti-angiogenic hepatic factor(s) from the pulmonary circulation, and vasodilation in PAVM has been linked to nitric oxide (NO). We report the autopsy morphometric and immunohistochemical findings of a child with heterotaxy syndrome and PAVM following CVPA, in whom angiography showed evidence of ipsilateral regression of the PAVM following a left Fontan. The unilateral regression enabled a novel study of gross and histomorphometric changes of Fontan-associated regression of CVPA-induced PAVM and the role of NO in vasodilation in PAVM.

Design: A 4-year old girl with functional single ventricle and interrupted inferior vena cava with azygous continuation underwent a Glenn (CVPA) procedure at age 4 months. At 21 months, bilateral PAVM were noted, and a left Fontan performed. At 4 years, angiography showed ***complete*** regression of the left lung PAVM, but progression of the right. A right Fontan was performed, but she died shortly thereafter. Postmortem evaluation included vascular morphometry on CD31-stained sections, and comparison of endothelial nitric oxide synthase (eNOS) and endothelin-B receptor (ETBR) staining to 2 age-matched controls.

Results: Grossly, multiple ectatic vessels were seen bilaterally, most prominent in the right hilum and lower lobe. Microscopically, dilated, irregular, thin-walled vessels were seen next to proximal airways and were more numerous in the right lung. Peripheral lung had complex chains of ectatic, but smaller vessels. Morphometric analysis confirmed increased vessel number in the right vs left lung (121 vs 83/lpf, $p<0.0001$). Right hilar mean vascular perimeter was also larger (570 vs. 379 µm, $p<0.01$). ETBR and eNOS staining was bilaterally similar, but greater than that in the controls.

Conclusions: Our study confirms the liver plays a role in development of PAVM after CVPA. The left PAVM regressed angiographically following the Fontan, while right PAVM increased in number, a finding that was morphometrically confirmed. Functional regression and lower vascular number, but not size, in the left lung likely reflected restoration of hepatic factors, but not differences in NO. To our knowledge, this is the first report demonstrating that angiographic regression does not fully correlate with histologic attenuation.

21 Hurricane Katrina: The Final New Orleans Mortality Data

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Background: Hurricane Katrina has been recorded as the largest natural disaster in our nation's history. Until recently, mortality information from the Greater New Orleans area has been contentious with public opinion divided on the storm's disparate impact on various racial groups. Final mortality data has just now been released.

Design: Pathologists from LSUHSC-NO were responsible for post-mortem examinations following Hurricane Katrina for the primary purpose of identification of the dead. Operations were centrally organized by the Disaster Mortuary Operational Response Team (DMORT). Examinations included field case notes, personal effects, fingerprints, dental, x-ray, autopsy findings, DNA, and anthropology. 910 post-mortem files including >1,000 dental charts and >30,000 images have been compiled and stored digitally. Pre-Katrina US Census data was analyzed for comparison.

Results: 820 autopsies (56%) were performed. 96% of deaths were storm-related and 97% of individuals were positively identified. 28% were identified using autopsy findings alone, comprising the single most successfully utilized identification technique. 73% of victims resided in Orleans parish. Victims ranged from 5-75 years, with 64% > 65 years. The racial distribution was: 56% African-American, 40% Caucasian, 4% Asian, 4% Native American, and 2% Hispanic. The most recent pre-Katrina Census revealed the Orleans parish population to be 454,863 individuals, with 12% > 65 years. The racial distribution was: 68% African American, 29% Caucasian, 3% Hispanic, 2% Asian, and 0.2% Native American. 26% of families were below the national poverty line.

Conclusions: With more than 1.3million residents of the Gulf Coast displaced, and 1,464 deaths of those left behind, New Orleans still struggles to comprehend such devastation. Both national as well as public opinion about the disparate impact of the hurricane have been divided. Final data do not substantiate the belief that the hurricane disproportionately destroyed any one race. In fact, deaths among Caucasian, Asian and Native Americans were all overrepresented relative to Census data; while the African-American and Hispanic populations were less impacted. Under appreciated is the fact that our elderly and poor populations, regardless of race, were the most devastated; and a lesson learned is about those left behind due to lack of physical or financial means. Our experience also concludes that pathological examination is a remarkably successful human identification method when combined with detailed demographic data.

22 Autopsy Findings in a Patient with Homozygous Mutations in *NEUROG3*

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Background: NEUROG3 is required for endocrine cell development in the small intestine, colon and pancreas. In mice, *Neurog3-/-* do not develop endocrine cells in the small intestine or pancreas. Diseases of NEUROG3 in humans are rare and are only recently described. Three patients known to have homozygous point mutations in *NEUROG3* have all been previously shown to have markedly reduced endocrine cells in the small bowel and colon. This resulted in a profound malabsorptive disorder. The status of the pancreatic endocrine development in these patients is a mystery, and the relationship to the findings in mice is incomplete. Two patients developed type 1 diabetes, but only after several years of life. The third patient underwent combined

liver and small bowel transplantation secondary to malabsorption and TPN induced cholestatic liver disease. Nearly one year after transplantation, at age 2y 10 mos, this patient expired from an apparent episode of sepsis. This patient did not yet demonstrate type 1 diabetes.

Design: An autopsy was performed with attention to the cause of death, identification of any qualitative gross developmental abnormalities, microscopic abnormalities, disorders of selected endocrine tissues, and a comparison of graft intestine with residual native intestine. Immunohistochemistry for various endocrine markers was performed. The pancreas was additionally studied for quantitative differences in endocrine development compared to age matched controls.

Results: The autopsy cultures revealed *E. coli* in the blood; *E. coli, K. pneumoniae*, and enterococcus species from the central line; and all the above plus *S. viridans* in the lungs. Chromogranin A immunohistochemistry identified endocrine cells in the pituitary, trachea, bronchi, stomach, graft small bowel, and pancreas. Endocrine cells of the residual native small bowel were not detected, and were only rarely found in the residual native colon. The pancreas demonstrated a markedly reduced number of islet cells.

Conclusions: The most likely cause of death was from line sepsis. The intestinal endocrine cell deficiency persisted in the native intestine and the deficiency did not occur in the transplanted intestine. The defective NEUROG3 resulted in an endocrine cell deficiency in the human pancreas.

23 Kidney Injury Molecule-1 Is a Specific Biomarker Which Enables Diagnosis of Pre-Mortem Acute Tubular Necrosis in the Presence of Autolytic Artifacts in Cadaver Kidneys

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Background: KIM-1 is a specific biomarker that can identify acute tubular necrosis (ATN) in native and transplant renal biopsies. In kidneys studied on autopsy it is usually difficult to differentiate ATN from renal autolysis. In this study we determined whether KIM-1 staining could identify pre-morbid ATN in cadaver kidneys, even when autolysis was present.

Design: Forty-three autopsy kidneys were stained by immunohistochemistry for KIM-1 with AKG-7 anti-KIM-1 monoclonal antibody. The staining intensity scores of KIM-1 along proximal tubular membranes (0 to 3+) were recorded and correlated with renal functional indices present prior to death. Phosphorylated (p)-mTOR and p-p70S6K (two downstream signals of growth factors) were also identified using immunohistochemical techniques.

Results: KIM-1 staining scores were significantly positively correlated with antemortem blood urea nitrogen (BUN, $r = 0.53$, $p < 0.003$) and serum creatinine ($r = 0.63$, $p < 0.0001$) and negatively correlated with estimated glomerular filtration rate ($r = 0.52$, $p < 0.0064$), despite prominent autolysis in one half of cases. Cases were divided into three groups: group 1 (multiple causes of death, n = 23); group 2 (acute myocardial infarction, n = 8); and group 3 (cirrhosis with liver failure, n = 12). Groups 2 and 3 had significantly higher scores of kidney KIM-1 staining when compared to group 1 ($p<0.05$). KIM-1 positive staining was found in 52%, 88% and 92% of kidneys in Groups 1, 2 and 3 respectively. Upregulated KIM-1 in injured proximal tubules was seen concurrently with enhanced expression of p-mTOR and p-p70S6K and membranous KIM-1 protein co-localized with translocated p-p70S6K in the nuclei by a double staining method.

Conclusions: Whether or not autolysis is present, KIM-1 expression is a specific biomarker for proximal tubular injury and is significantly correlated with renal dysfunction. KIM-1 may regulate the m-TOR-pp70S6K growth pathway. The high degree of KIM-1 expression in group 2 is consistent with a high degree of renal ischemia following myocardial infarction. In group 3, the high percent of positive KIM-1 staining suggests that liver disease is often associated with ATN and not purely a functional kidney defect.

24 An Analysis of Pediatric Autopsy Findings through Text Mining

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Background: Few collective analyses of pediatric autopsies are in literature. This study aims to a better understanding of the etiology in pediatric deaths.

Design: Retrospective review of pediatric autopsies performed during November 1996 to March 2006 at our Children's And Women's Hospital. Autopsy reports were programmatically extracted from LIS and parsed into relational database for statistics by text mining using Visual Basic and SQL. A structured report template of our department enabled text mining to successfully retrieve relevant information from reports. All text mining results were manually verified.

Results: 228 pediatric autopsies were found in the reviewed period, with decreasing numbers performed each year since 1999. 125 cases occurred as intrauterine fetal demise (IUFD). The male/female ratio was 136/92 in all deaths, and 71/54 in IUFD. While sepsis still the most common etiology, it has declined from 72.5% in 1997 to 22.2% in 2005. Among congenital diseases, 5 were Turner's syndrome, all IUFD around 2nd trimester. There were 1 case of Trisomy 13 (IUFD at 32 wk), 1 case of Trisomy 18 (IUFD at 26+ wk), 1 case of Trisomy 21 (died at 1 day of age), all confirmed by cytogenetic studies. In both Trisomy 13 and Trisomy 18 cases, mothers were sickle cell traits. The 4 tumor cases were of children aged 2 to 15 yo with nasopharyngeal carcinoma (15 yo), neuroblastoma (3 yo), rhabdoid tumor arising from the prostate (8 yo), or primitive neuroectodermal tumor (2 yo), respectively. Only 7% of all deaths, or 4% of IUFD, were signed out as unknown etiology.

Conclusions: Determining causes of pediatric deaths can be challenging. A thorough autopsy can usually identify the etiology and additional diagnosis, which will serve as better guidance and consultation for the subsequent pregnancies. Text mining provides an effective tool to analyze free text reports for trend and new insights. A well structured report template helps to yield high quality text mining results.

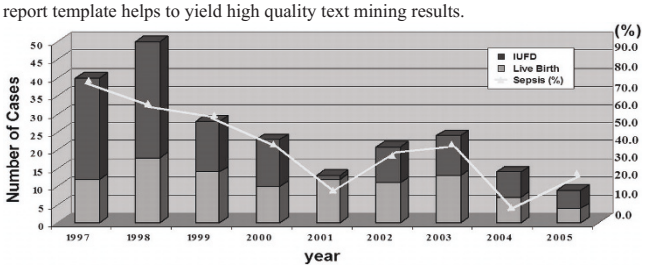

Table 1. Common etiology and frequency found in pediatric autopsies.

Etiology	All Deaths (n=228)		IUFD (n=125)	
	Cases	%	Cases	%
Sepsis	106	46.49	65	52.00
Congenital Disease	45	19.74	18	14.40
Twin Pregnancy	24	10.53	8	6.40
Pulmonary Hypoplasia	10	4.39	0	0.00
Tumor	4	1.75	0	0.00
Uteroplacental Insufficiency	25	10.96	21	16.80
Abruptio Placenta	15	6.58	12	9.60
Cervical Incompetence	2	0.88	0	0.00
Maternal Diabetes	18	7.89	9	7.20
Maternal Obesity	25	10.96	18	14.40
Maternal Sickle Cell Trait	12	5.26	9	7.20
Pre-eclampsia	8	3.51	6	4.80
Antiphospholipid Antibody Syndrome	1	0.44	1	0.80
Unknown	7	3.07	4	3.20

Bone & Soft Tissue

25 Comparative Gene Expression Profiling of Chordoma and Chondrosarcoma

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Background: Chordoma and chondrosarcoma are malignant bone tumors characterized by their production of abundant extracellular matrix. These two tumor types are similar in their resistance to conventional therapeutic modalities, including radiation and systemic chemotherapy. Our goal was to delineate the gene expression profile of chondrosarcoma and chordoma tumors, in order to identify potential molecular therapeutic targets.

Design: A HG-U133A Affymetrix Chip platform was used to determine the variability of gene expression in 6 conventional chordomas and 14 conventional chondrosarcomas, which was compared to a control group of 45 soft tissue sarcomas. Statistical analyses were performed to identify discriminatory gene lists and Venn diagram was used to select non-overlapping, differentially expressed genes among gene lists. Validation of selected genes was performed by qPCR and immunohistochemistry on an extended subset of chondrosarcoma and chordoma tumors.

Results: By unsupervised hierarchical clustering, chordomas and chondrosarcomas grouped together in a genomic cluster distinct from a broad set of soft tissue sarcomas. They shared overexpression of many extracellular matrix genes including: *aggrecan, type II & type X collagen, fibronectin, connective tissue growth factor, fibromodulin, matrillin 3, chondroitin sulfate proteoglycan 4 (CSPG4), MMP-9, and MMP-19*. In contrast, *T Brachyury* and *CD24* are distinctly expressed in chordomas, as are *Keratins' 8,13,15,18 and 19*. Chondrosarcomas are distinguished by the high expression of *type IX* and *XI collagen*. Among these genes, *CSPG4* stands out as a promising therapeutic target, having already been extensively used as an immunotherapy target in patients with melanoma. Immunohistochemical analysis with CSPG4 mAb revealed positive staining in 48% and 62% of the chondrosarcoma and chordoma tumors, respectively.

Conclusions: Chordomas and chondrosarcomas share a similar gene expression profile, based on the overexpression of a significant number of extracellular matrix genes. *CSPG4* is one among numerous potential candidate genes, which can be further exploited for targeted therapy.

26 Is GLUT-1 a Specific Marker of Perineurial Differentiation? An Evaluation of GLUT-1 Expression in 82 Mesenchymal Tumors

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Background: GLUT-1, an erythrocyte-type glucose transporter protein expressed in juvenile hemangiomas, has recently been shown to be a sensitive marker of perineurial cells and their tumors, in a small number of cases. GLUT-1 expression has not, however, been systematically examined in other mesenchymal neoplasms. Importantly, GLUT-1 is known to play a critical role in the cellular response to hypoxia, as a downstream target of HIF1-alpha. Prompted by a recent report of GLUT-1 expression in epithelioid sarcoma, a tumor not generally felt to show perineurial differentiation, we examined GLUT-1 expression in a wide variety of mesenchymal tumors, specifically including tumors with spontaneous and/or therapy-related necrosis.