United States and Canadian Academy of Pathology

Annual Meeting, Washington, DC March 20 - March 26, 2010

PLATFORM and POSTER PRESENTATIONS

Autopsy

1 The Autopsy Findings of 29 Cases with Prenatally Diagnosed Renal Anomalies

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Background: Renal anomalies are common congenital anomalies, with diverse morphological and etiopathogenic features. The aim of the study was to compare the consistency of renal anomalies detected by second trimester prenatal ultrasound examination with the findings in fetal autopsies following the termination of pregnancy (TOP) in the second trimester.

Design: In a 4-year long prospective study, the study included 29 cases with renal anomalies out of 107 second-trimester TOP was performed due to fetal malformation diagnosed by second trimester-ultrasound examination at a tertiary referral center. Ultrasound findings were compared with fetal autopsy findings.

Results: There were 107 prenatally diagnosed malformed fetuses that were analyzed following the TOP. There were 29 (27%) renal anomalies (isolated n = 10, multiple anomalies n = 19). The mean maternal age was 26 years (range 19–40). The mean gestational age at the time of termination was 20 weeks (range 13–28). The most common renal malformation was cystic renal disease (n = 27) including infantile type polycystic kidney disease (n=23) and cystic renal dysplasia (n=4). There was a case with bilateral renal agenesis, and another case with horseshoe kidney. Eight cases with cystic renal diseases had associated malformations including encephalocele and polydactly consistent with Meckel-Gruber syndrome. There were one case with polycystic kidney together with Prune-Belly syndrome and another case with cystic renal dysplasia was associated with sirenomelia. There were polydactly (n=10), central nervous system anomalies (n=12) and cardiac anomalies (n=4) in fetuses with cystic renal diseases (n=19). All fetal anomalies were detected by prenatal sonography and fetal autopsy confirmed these anomalies.

Conclusions: Fetal autopsy including histopathological examination of kidney is important to establish definitive diagnosis. It's important to distinguish between infantile type polycystic kidney disease and cystic dysplastic kidney as recurrence risk is 3% in case of cystic renal dysplasia in contrast to 25% in case of infantile type polycystic kidney disease. Gross examination may point toward syndromic diagnosis like Meckel-Gruber syndrome. This study confirms that developmental anomalies of the kidney are frequent and that ultrasound diagnoses are in good concordance with the autopsy diagnoses.

2 Acute Aortic Dissection: Changing Spectrum of Clinicopathologic Findings at Autopsy

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Background: Acute aortic dissection continues to be a life-threatening medical emergency with a high mortality rate despite progress in surgical techniques. Death may occur as a direct result of the dissection or as a complication related to the extent of dissection. This study was undertaken to describe the clinicopathologic findings of in-hospital mortality due to acute aortic dissection.

Design: All autopsy cases of acute aortic dissection were retrieved from the pathology archives from January 1993 to June 2009. Relevant clinical and pathologic data, including patient demographics, type of dissection (DeBakey classification), predisposing factors, histopathology findings and cause of death were recorded for analysis. Cases with isolated dissections of branches of the aorta including coronary arteries were excluded from the study.

Results: There were a total of 72 cases with 49 (68 %) males and 23 (32%) females. The age range was from 19-83 years with a median of 65 years. In 22 cases, acute dissection occurred in aortas that already had chronic dissection including 10 that were aneurysmal. Type I dissections were seen in 35 (49%) cases, while 13 (18%) were type II and 24 (33%) were type III. The most common predisposing factor was systemic hypertension (57%), followed by previous cardiovascular surgery (32%) including coronary artery bypass grafting, aortic valve replacement, aneurysm and dissection repair. Other associated risk factors include Marfan's syndrome, Ehler Danlos syndrome, rheumatoid aortitis, giant cell aortitis, and cocaine abuse. Only 18 cases (25%) had cystic medial degeneration on histology. Rupture of the aortic dissection (46%) leading to hemopericardium (16 cases), hemothorax (9) and hemoperitoneum (8) was the most frequent cause of death. Other causes of death included myocardial ischemia, mesenteric ischemia, multiorgan failure and sepsis.

Conclusions: Hypertension remains the most common associated disease in patients presenting with acute aortic dissection at autopsy. However, iatrogenic and postsurgical dissections are seen with increasing frequency and accounts for the second largest group of patients who experienced aortic dissections. A third group of patients at risk for aortic dissection are those with connective tissue disorders and inflammatory aortopathy. Cause of death is often multifactorial, but rupture of dissection most often causes sudden and unexpected demise.

3 Documentation of the Small Intestine Atresias: A Single Institution Experience in Turkey [22 Cases]

U Bayol, D Etit, F Aktas, D Altinel, S Cumurcu, R Beyhan, B Sahin. Tepecik Training and Research Hospital, Izmir, Turkey.

Background: Atresia is the loss of continuity of the small bowel lumen and is accompanied with intestinal obstruction, whilst stenosis is a localized luminal narrowing which may produce a partial obstruction to passage of intestinal contents. The duodenum is the most commonly affected segment, its incidence being about 1 in 5000 live births. Involvement of the jejunum and ileum are less common.

Design: Retrospective study of neonatal autopsies of small intestine atresias (SIA) in a 22 consecutive cases in Izmir Tepecik Training and Research Hospital. A total of 22 cases with a mean age of 29 days, 9 were males and 13 females. In the current study, anomalies associated with SIA were grouped into several categories as cardiac, genitourinary, hepatobiliary and central nervous system anomalies.

Results: According to our series; out 22 SIA cases, 2 (10%) were associated with cardiac anomalies including heart and large vessel disorders. 2 (10%) cases had genitourinary system abnormalities, while 3 (13%) had hepatobiliary and 5 (22%) had central nervous system disorders.

Conclusions: SIA was a significant gastrointestinal tract abnormality among the perinatal autopsy cases in our institutional archives. SIA s were accompanied with central nervous, hepatobiliary, cardiac and genitourinary system disorders consequently.

4 Contribution of Perinatal Autopsy to the Assessment of Intrauterine Fetal Demise

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Background: Fetal autopsy is one of the tools available for the determination of the cause of intrauterine fetal death (IUFD). The purpose of this study was to evaluate the contribution of perinatal autopsy in the assessment of the cause of IUFD.

Design: Perinatal autopsies performed at MHMC from January 2002 to December 2007 were reviewed. The causes of death as determined by perinatal autopsy were compared with the available clinical information.

Results: Among all 619 autopsies performed from 2002 to 2007, 95 (15.3%) were perinatal. The male/female ratio was 1:1. The mean gestational age was 27.7 weeks, ranging from 16 to 42 weeks. Chromosomal abnormalities were found in four cases (4.2 %) including trisomy 21 (2), trisomy 18 (1) and 46, XY der(17) t(8:17) (1). Osteogenesis imperfecta and twin to twin transfusion syndrome were found in two cases. The remaining cases showed isolated anomalies including bilateral renal agenesis, bilateral club feet, cleft palate, esophageal atresia, hypoplasia of fingers and hypoplasia of right testicle, without associated chromosomal abnormalities. Examination of the placenta revealed acute chorioamnionitis in 50 cases (52.6%), abruptio placentae (12) and placental infarcts (10). Microbiological cultures from fetal organs and placenta were positive for Group B-Streptococcus (15 cases), Enterococcus (2) and Escherichia coli (1). Umbilical cord prolapse was observed clinically in two cases. Maternal factors contributing to IUFD included premature rupture of membranes (8 cases), cervical incompetence (6), pre-eclampsia (5), Hepatitis B (1) and HIV (1) infections, cocaine abuse (1) and antiphospholipid syndrome (1). In sixteen cases (16.8%) the cause of death could not be determined. Autopsy findings, including cytogenetics and microbiological cultures established the cause of IUFD in 83.2% of cases (79/95).

Conclusions: Perinatal autopsy along with placental examination, cytogenetic studies and bacteriological cultures proved to be a valuable tool in the determination of the cause of IUFD in the majority of our cases (83.2%). It is recommended that permission for autopsy should be strongly encouraged in cases of IUFD.

5 Autopsy Rates – Contributory Factors at an Urban Teaching Hospital

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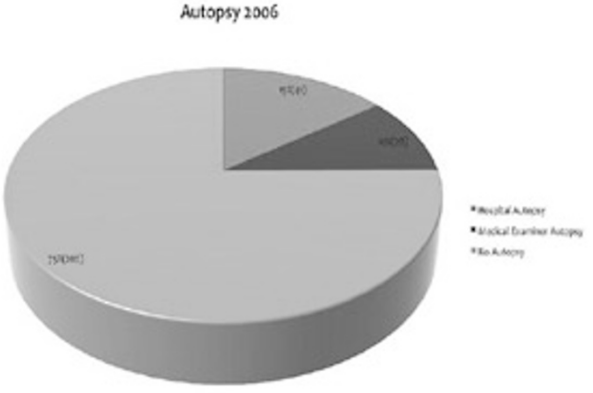
Background: There has been a worldwide decline in hospital autopsy rates, which has been attributed to many factors. The detrimental effect of this dwindling autopsy rate on quality health care delivery is well documented. The aim of this study is to identify contributory factors to declining autopsy rates at an urban teaching hospital, and to suggest methodologies to reverse this trend.

Design: A retrospective review of hospital death notices and autopsy reports to ascertain causative factors and attitudes which help determine autopsy rates at an urban teaching hospital was performed. This study examined whether pre-analytic autopsy practices influenced the frequency at which autopsies were performed. Information obtained from the Notice of Death (NOD) forms which was reviewed include length of hospital stay, attending physician for the deceased, age of decedent, and next of kin notified. The turn around time to final autopsy sign out was also examined.

Results: For the year under review the majority of admitted patients who expired did not undergo postmortem examination.



Our results indicate that the decedent's next of kin who was notified; the post mortem interval and the completeness of NOD forms are important factors that determine whether or not an autopsy is performed on the deceased. The age of decedent; length of hospital stay and the treating attending physician did not influence the incidence of autopsy.

Conclusions: There is a need for re-defining hospital policies and procedures regarding autopsies. These may include: stricter monitoring of methods used to request autopsies, compliance to death notice form requisite, better performance expectation for post-mortem examination and reporting, and dissemination of educational material to patient families & health care professionals. Some of the causative factors to the declining autopsy rate are reversible and hospitals can implement guidelines to help alleviate some of these issues and thus improve declining autopsy rates.

6 Sudden Unexplained, Non-Traumatic Death in ≤35 Year Olds: An Irish Coroner's Autopsy Population Based Study

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Background: The prevalence and cause of sudden unexplained, non-traumatic death varies with age and is most prevalent from 0-6months and 45-75years due to Sudden Infant Death Syndrome(SIDS) and Coronary Artery Disease(CAD) respectively. It is less well categorized in the younger adult population. The aim of this study was to evaluate the incidence and categorize the causes of sudden unexplained, non-traumatic death in ≤35year olds within an Irish Coroner's autopsy population, with particular interest in cardiac causes and Sudden Adult Death Syndrome(SADS).

Design: Retrospective analysis of autopsies performed on ≤35year olds in the Cork / Kerry region from July 2001 to June 2009. The ≤35year old regional population is approximately 324,000. Autopsy reports were reviewed for circumstances of death, histology, toxicology, microbiology and cause of death. All traumatic and suicide deaths were excluded.

Results: 252 (164 males; 88 females) cases met the study criteria with the following age distribution: 0-1year = 52; >1-17years = 37; 18-35years = 163. 47(18.7%) deaths had a cardiac cause including CAD, hypertrophy, cardiomyopathy, arrhythmia, myocarditis, Congenital Heart Disease(CHD), tamponade and fibroma. 11(4.4%) cases were SADS. 164(65.1%) deaths were drug/alcohol related, 34(13.5%) had CNS causes, 27(10.7%) respiratory causes and 6(2.4%) GI causes. 35(13.9%) deaths were SIDS with 9(25.7%) documented co-sleepers. Remaining deaths were due to diabetes mellitus, sickle cell disease, connective tissue disease, hypersensitivity and stillbirth. Cause was unascertained in 8(3.2%) cases.

Conclusions: The incidence of sudden unexplained, non-traumatic death in this population was 0.08%. Deaths occurred mainly in males(65.1%) in the 18-35 age group (median age 26.8) and were alcohol, cocaine or heroin related. A notable increase in heroin use was seen in the last two years. Cardiac deaths were most frequent in males in the 18-35 age group (median age 32.2) with CAD(27.7%) leading. CHD was the main cardiac cause in 0-1year olds although overall SIDS was the leading cause of death in this group. In the >1-17age group CNS causes were commonest. Interestingly, dual cause of death was identified in 5(1.9%) cases where CAD, myocardial infarction, myocarditis(x2) and intracerebral haemorrhge(ICH) were associated with toxic levels of drugs/alcohol. SADS incidence was similar to prior studies at 4.3% (median age 27.4) but as distinct to documented figures the male to female ratio was 0.57:1.

7 Anomalous Placement of the Coronary Arteries as a Cause of Sudden Cardiac Death in Athletes

MW Cruise, TS Giles, TJ Green, RL Legallo. University of Virginia, Charlottesville, VA.

Background: Sudden cardiac death in previously healthy adolescents is rare; the estimated prevalence of athletic field related deaths is 0.5:100,000. In the United States, the most common cause of these deaths are hypertrophic cardiomyopathy, while in Europe it is reported to be arrythmogenic right ventricular cardiomyopathy. Sports physicals with ECG can help identify patients at risk for these afflictions. However, other minor structural abnormalities, such as coronary artery abnormalities can not typically be appreciated by standard methods.

Design: Case Report: A previously healthy 12-year-old gifted athlete, with no pertinent personal or family medical history, experienced his first syncopal episode while playing soccer. A subsequent neurological examination was normal. Six months later, he developed a similar episode while playing soccer and a cardiac workup demonstrated a normal ECG, echocardiogram, and treadmill stress test. A third syncopal episode occurred, again during physical exertion, with a quick recovery and no other findings. Fifteen months after the patient's first syncopal episode, the patient experienced a fourth syncopal episode and collapsed while playing soccer. An AED applied showed wide complex tachycardia without pulses. Resuscitative efforts were attempted immediately, however the patient remained pulses and apneic.

Results: At autopsy, the decedent was a well developed 13 year-old with BMI=18. The heart was structurally normal aside from anomalous coronary arteries. There was rotational insertion of the right and left coronary arteries; the right coronary ostia was located in the posterior right cusp and the left coronary ostia was located in the anterior portion of the right cusp just behind the commisure. This resulted in an acute angle take-off of the left coronary artery from the aorta with a reduced-sized orifice and a left coronary path between the aorta and pulmonary artery. Microscopically the cardiac tissue contained patchy myocardial fibrosis as well as subendocardial contraction band necrosis consistent with both new and old ischemic events.

Conclusions: The patient's death was due to an arrhythmic event initiated by intermittent occlusion of the left coronary artery and the resulting episodic ischemia. Given that this condition is surgically repairable, it is important to identify these patients. In the face of normal neurological, psychological, and cardiac workup with continued syncopal episodes, it may be appropriate to consider additional imaging studies such as thin section CT, cardiac MRI, or aortogram.

8 Profile of Sudden Death in an Irish Adult Population (1999-2008)

MR Downes, J Thorne, HA Hassan, TN Tengku Khalid, M Leader. Beaumont Hospital, Dublin, Ireland; Royal College of Surgeons, Dublin, Ireland.

Background: Sudden death is the sudden and unexpected death of a person within 24 hours of symptom onset. The majority of these cases are cardiac in origin. We analysed over 1000 autopsy cases performed over one decade (1999-2008) to identify and subclassify the causes of death in an Irish adult population within the catchment area of a university affiliated, tertiary referral hospital. The autopsies all fell under the remit of the Coronial service.

Design: A retrospective audit was conducted on all autopsies performed over a ten year period to identify those ascribed as sudden deaths. All adult patients (16 years of age or older) found dead and brought to the hospital who had been seen alive in the prior 24 hours and those that died within 24 hours of admission to the Accident and Emergency department were include. Autopsy log books, computer records and Coroners Authorisation forms were utilised to identify our cohort. The results were analysed according to age and organ system involved.

Results: A total of 2,809 post mortems were performed in the defined review period, 1,230 of which were within the study parameters. The majority of subjects were over forty (86%, n= 1,057) and overall males outnumbered females in a 2:1 ratio. In 2.8% of cases (n= 35) a definitive cause of death was not found. Cardiovascular deaths dominated in the over forties. Overall 63% (n= 775) of all sudden deaths were ascribed to a cardiovascular cause (two thirds of which were myocardial infarction/severe coronary artery disease). Death due to a respiratory cause was the second commonest listed cause of death at 13% (n=158). Accidental death was the third commonest cause of death (11%, n= 138) and the commonest in the under forties.

Conclusions: The results from our cohort demonstrate that the vast majority of sudden adult death is cardiac in nature, mainly due to underlying coronary artery disease. This autopsy series of over 1,000 cases successfully identified a cause of death in 97.2% (n= 1,195) of cases. This is the first Irish study to examine all sudden deaths in an adult population and subclassify these according to age and organ system. Nine cases of the under 40's age group had an unidentifiable cause of death. The recent literature regarding sudden cardiac death in the structurally (and microscopically) normal heart raise the possibility of a potential genetic aetiology having been overlooked. This highlights the value of such retrospective audits in informing future clinical practice.

9 Aortic Rupture Due to Clostridium septicum: A Cause of Cardiac Tamponade

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Background: Clostridium septicum is a Gram-positive, anaerobic bacillus that rarely causes clinical disease, classically in the setting of malignancy. Eight percent of C. septicum infections are vascular, and these convey high rates of morbidity and mortality. To date, 29 cases of aortitis due to C. septicum have been reported, including 24 mycotic aneurysms and 6 cases of aortic dissection, one of which produced hemopericardium. Detection of aortic involvement and surgical repair are necessary for patient survival.

Design: A 74-year-old man presented with malaise, chest pain, and pain in the left neck and head. Workup showed small pleural and pericardial effusions, iron-deficiency

anemia, IgA-kappa monoclonal gammopathy, and a previously undetected rectal adenocarcinoma. Blood cultures were positive for bacteria, initially identified as Gram-negative bacilli. Computerized tomography and transthoracic echocardiography showed no abnormality of the aorta. Treatment consisted of antibiotics and blood transfusion. After initial improvement, the patient had sudden cardiac arrest with pulseless electrical activity on the 7th hospital day, and could not be resuscitated.
Results: Autopsy showed a 2.5 x 3.5 cm rupture in the ascending aorta, communicating with the pericardial sac. Microscopic exam revealed an aortic abscess at the site of rupture. The pericardium contained 400 ml of blood, and showed organizing fibrinous pericarditis. Other findings were atherosclerotic cardiovascular disease, rectal adenocarcinoma with metastases to the left lung, and plasma cell myeloma. Following the patient's death, bacteria in blood cultures were identified as C. septicum. Two polymerase chain reaction (PCR) assays, each complemented with cycle sequencing of PCR amplicons, demonstrated C. septicum DNA in abscessed aorta, but not in unaffected aorta or in the rectal carcinoma.
Conclusions: We present a unique case of fatal C. septicum aortic abscess in which aortic aneurysm and dissection were not present, and cardiac tamponade was the mechanism of death. Antemortem imaging of the aorta showed no abnormalities, indicating that a C. septicum aortic abscess may be difficult to diagnose. This case underscores the association of C. septicum infection with colonic and hematologic malignancies. PCR is a useful tool in tissue diagnosis of C. septicum vascular infection, particularly in patients who have undergone antibiotic treatment.

10 Diffuse Pulmonary Alveolar Hemorrhage in Myelodysplastic Syndrome

A Edgecombe, I Teo, H Sekhon, BF Burns. University of Ottawa, Ottawa, ON, Canada; The Ottawa Hospital, Ottawa, ON, Canada.
Background: Diffuse alveolar hemorrhage (DAH) is a rare and frequently fatal condition characterized by widespread alveolar hemorrhage. The aetiologies are diverse and include vasculitides, connective tissue disorders, drugs, infections, diffuse alveolar damage and malignancies. Associated haematological neoplasms include leukemias and multiple myeloma. DAH as a manifestation of myelodysplastic syndrome (MDS) is a rare finding.
Design: A 79-year-old male with coronary artery disease and type II diabetes mellitus presented with petechiae. He had a history of viral-like symptoms three weeks previous to presentation. He was severely thrombocytopenic (platelets 4 x 10^9/L) and immune thrombocytopenic purpura (ITP) was initially diagnosed. However, he was refractory to treatment with immunoglobulin, corticosteroids and cyclokapron. Hemoptysis developed and persisted, requiring multiple transfusions. While in hospital, the patient had a non-ST segment elevation myocardial infarction, acute renal failure, leukocytosis (24.0 x 10^9/L) and fever, leading to broad spectrum antibiotic treatment. Cultures and rheumatologic work-up were negative. A bone marrow biopsy revealed MDS with multilineage dysplasia and excess blasts. His pulmonary hemorrhage precipitated hypoxemic respiratory failure and cardiac arrest.
Results: At autopsy, petechiae were documented. Bilateral massive pulmonary hemorrhage was evident with right and left lungs weighing 1460g and 1640g respectively. Microscopically, there was extensive intra-alveolar hemorrhage with diffuse alveolar damage, without evidence of vasculitis. Bacterial and fungal stains were negative. Severe dysplasia of the erythroid and megakaryocytic lineages was confirmed. The heart had a recent transmural and circumferential myocardial infarction involving the left ventricle.
Conclusions: Pulmonary hemorrhage is a rare and fatal complication in patients with MDS. Our case is novel in documenting fatal DAH as an initial presentation of MDS.

11 Sudden Death in Splenic Artery Segmental Mediolytic Arteriopathy

A Edgecombe, I Teo, M Marinescu, C Milroy. University of Ottawa, Ottawa, ON, Canada; The Ottawa Hospital, Ottawa, ON, Canada.
Background: Segmental mediolytic arteriopathy (SMA), a variant of fibromuscular dysplasia, is a rare non-inflammatory vascular disease. Mediolysis of the arterial media may be associated with aneurysm, dissection and stenosis. Visceral SMA primarily involves the branches of the celiac and superior mesenteric arteries and the middle-aged to elderly are typically afflicted. Potential complications include organ infarction and catastrophic intra-abdominal hemorrhage.
Design: A 20-year-old male had a nine-year history of type I diabetes, without diabetic complications. After retiring to bed one night, he suddenly cried out and collapsed. On arrival to hospital, vital signs were absent and resuscitation was unsuccessful. There was no evidence of illicit drug or alcohol abuse. His diabetes was well controlled with a recent haemoglobin A1c of 6.3%. A medico-legal autopsy was ordered.
Results: At autopsy, hemoperitoneum with 3000 ml of blood and clot was evident. The splenic artery was found to be ruptured 13 cm from the celiac artery origin. No other vascular anomalies were identified. Microscopically, there was segmental transmural mediolysis of the splenic artery media with extensive loss of the external elastica. Intima and internal elastica were focally absent. Extravasated erythrocytes were focally prominent within the media. Peri-adventitial inflammation was noted. The adjacent splenic artery had fibromuscular dysplasia. Neither vasculitis nor atherosclerosis was identified. Other vessels were normal.
Conclusions: Visceral SMA is a rare cause of fatal intra-abdominal hemorrhage. Isolated splenic artery SMA is exceedingly uncommon. The aetiology remains unknown. To our knowledge, we describe the youngest patient with visceral artery aneurysm and rupture associated with SMA. SMA of visceral arteries, therefore, must be included in the differential diagnosis of spontaneous intra-abdominal bleeding in all age groups.

12 Sudden Death from Superior Mesenteric Artery Thrombosis in a Cocaine User

A Edgecombe, C Milroy. University of Ottawa, Ottawa, ON, Canada; The Ottawa Hospital, Ottawa, ON, Canada.
Background: Cocaine-mediated tissue injury is well established; particularly myocardial ischemia and infarction. Gastrointestinal complications, including mesenteric ischemia, ischemic colitis and intestinal perforation, occur less frequently. Several mechanisms have been postulated including vasoconstriction and vasospasm. Cocaine-induced visceral arterial thrombosis is a rare finding.
Design: A 49-year-old male presented with a 24-hour history of severe abdominal pain, anorexia, nausea and vomiting. Physical examination documented tachycardia and a soft, non-rigid abdomen with voluntary guarding. Abdominal X-ray did not show evidence of peritoneal free air or bowel obstruction. Laboratory investigations revealed elevated white blood cells (33.8 x 10^9/L) and a high anion gap (33 mmol/L); a blood gas was not done. Three hours after initial presentation, the patient had a cardiac arrest. Resuscitation was unsuccessful. Neither computed tomography nor angiogram was performed. His past medical history was significant for cocaine, methadone and ethanol use and smoking. Even though he was diagnosed with type II diabetes, his random blood glucose measured 9.5 mmol/L and his haemoglobin A1c was 6.5%, despite Metformin non-compliance. A medico-legal autopsy was ordered.
Results: At autopsy, the jejunum was ischemic, without obvious infarction. The superior mesenteric artery (SMA) was occluded near its origin by moderate atherosclerosis with superimposed thrombus that extended for 3 cm. The myocardium had old fibrosis, without acute infarction. Severe triple coronary artery atherosclerosis was noted. Toxicological blood analysis confirmed cocaine and methadone use.
Conclusions: SMA thrombosis has been described as a rare complication of chronic cocaine use; sudden death has not been reported. While accelerated atherosclerosis has been documented in the coronary arteries of cocaine users, SMA atheroma is a novel finding. This report emphasizes the need to consider chronic stimulant drug abuse in accelerated atheroma and thrombosis.

13 Documentation of the Esophageal Atresias: A Single Institution Experience in Turkey within 8 Years [35 Cases]

D Etit, U Bayol, D Altinel, F Aktas, I Gokcol Erdogan, N Sen Korkmaz, A Tan. Tepecik Training and Research Hospital, Izmir, Turkey.
Background: Esophageal atresia (EA) is a rather common neonatal anomaly frequently associated with other congenital anomalies such as cardiac, genitourinary, and anorectal malformations and chromosomal disorders. The incidence of oesophageal atresia is 1:3000-3500 of live-born infants. Associated anomalies occur in 50% of patients.
Design: Retrospective study of neonatal autopsies of EA between 1998 - 2005 in Izmir Tepecik Training and Research Hospital. Out of 163 cases which had gastrointestinal system abnormalities, a total of 35 cases with EA were analyzed in terms of associated system disorders and causes of death.
Results: According to our series; there were 21 males and 14 females with a mean age of 9 days. Out 35 EA cases, 4 (11%) were associated with cardiac anomalies including heart and large vessel disorders, 8/35 (22%) cases had genitourinary system abnormalities, while 7/35 (20%) had hepatobiliary and 8/35 (22%) had central nervous system malformations. Most of our cases died of superinfections.
Conclusions: In our institutional experience EA (21%) was a significant gastrointestinal tract abnormality among the perinatal autopsy series. As expected; EAs were accompanied with cardiac, genitourinary, hepatobiliary and central nervous system malformations. Most common causes of death were infections.

14 Effectiveness of Superficial Perinatal Post-Mortem Examinations in the Rotunda Hospital from 2000 – 2007

TJ Fitzgerald, JE Gillan. St Vincent's University Hospital, Dublin, Co Dublin, Ireland; Rotunda Hospital, Dublin, Co Dublin, Ireland.
Background: Recent years have seen a decline in the perinatal autopsy rate. Reasons for this include reluctance of clinicians to gain consent for post-mortem examinations and refusal of consent by parents. This may be due to the perceived invasive nature of the standard post-mortem. Perinatal post-mortem examinations however, can provide important information both for families and for maintaining standards of care. The superficial post-mortem examination circumvents many parents' major objection to a standard post-mortem. In addition to assessment of gestational age and identification of dysmorphic features, many other characteristics can be evaluated. These include nutritional status, degree of autolysis, pallor, petechiae, traumatic and other iatrogenic lesions. Photographs can be taken for review by a clinical geneticist at a later date. Examination of the placenta can also provide important information, such as evidence of ascending or haematogenous infection. Fibroblasts prepared from placental tissue can be used for cytogenetic investigations.
Design: During the period of the study, superficial examinations were carried out on all perinatal deaths where consent for a full autopsy was refused. The examinations were carried out in a standardised fashion with external measurements entered on a standard form. The placentas were also examined grossly and microscopically with sampling of the fresh placenta for microbiology and cytogenetic studies in selected cases. Post mortem radiology was routinely performed in all cases. Data on these examinations were accumulated from annual clinical reports published by the hospital.
Results: Over the eight-year study period superficial post-mortem examination reached a diagnosis in 130 of 153 cases (85%) in normally formed infants weighing 500g or more, in 188 of 357 cases (53%) less than 500g and in 60 of 66 cases (91%) in infants weighing 500g or more with major malformations. This is in contrast to full post-mortem examinations where a diagnosis was achieved in 217 of 239 cases (91%) 500g or more and 224 of 296 cases (76%) less than 500g.

Diagnostic Rate (%)

	Full	Superficial	Superficial - malformation
≥500g	91	85	91
<500g	76	53	-

Conclusions: The superficial autopsy is a useful alternative to the standard autopsy when consent for a full examination cannot be obtained. It is most useful in birth weights of greater than 500g. It has limitations however, and should not be seen as a replacement for the standard autopsy.

15 Occult Cardiac Amyloidosis: A Rare Contributor of Postoperative Demise Following Cardiac Surgery

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Background: Cardiac amyloidosis is an uncommon disorder that occurs when fibrillar proteins are deposited in the myocardium and/or coronary artery walls and leads to abnormalities in contraction and conduction. Patients with cardiac amyloidosis can present with angina, symptoms of myocardial infarction, or sudden death. We present two patients who underwent cardiac surgery whose postoperative courses were complicated by poor cardiac output and eventual death. Autopsies showed previously undiagnosed severe cardiac amyloidosis.

Design: Patient#1: 52 year old man admitted for triple CABG following coronary in-stent restenosis. Postoperative course was complicated by low cardiac output requiring inotropes and an intra-aortic balloon pump. Further complications included atrial fibrillation, sepsis, and hepatic and renal insufficiency. On postoperative day 26 the patient suffered a fatal cardiac arrest. **Patient#2:** 86 year old man admitted for aortic valve replacement and CABG. His post-operative course was complicated by right ventricular failure, sinus ventricular tachycardia and left ventricular dysfunction for which he required prolonged inotropic support. He developed bilateral pleural effusions and a mediastinal soft tissue abscess. On postoperative day 32 the patient went into asystole and died.

Results: Patient#1: Heart weight was 575g and all coronary artery bypass grafts were intact and uncomplicated. There was extensive myocardial involvement by amyloid. Amyloid depostis were also observed within the walls of epicardial arterioles and in the vein grafts. Moderate deposition of amyloid was detected systemically. The amyloid was AL type and an underlying plasma cell dyscrasia was identified. **Patient#2:** Heart weight was 550g and the aortic valve prosthesis was uncomplicated. Coronary artery bypass grafts were intact and patent. There was moderate to severe amyloid involvement in the myocardium of all chambers. Amyloid also involved the visceral vessels (pulmonary arteries and veins) and was the senile type.

Conclusions: Occult cardiac amyloidosis is an infrequently described entity that can contribute significantly to postoperative morbidity and mortality. There are no specific clinical signs or symptoms that are associated with this disorder. Prior cardiac surgery can cloud the clinical picture because many of the observed signs and symptoms can be attributed to postoperative sequelae. These cases demonstrate a rare but potentially fatal condition that can be considered in postoperative cardiac surgery patients who are doing poorly.

16 Diaphragm Pathology at Autopsy: A Survey

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Background: Diaphragm pathology includes congenital, environmental, metabolic, inflammatory, degenerative diseases and (mal)adaptive states due to underlying cardiorespiratory disease and iatrogenic manipulations (mechanically assisted ventilation). However, the diaphragm may be not fully examined at autopsy. This study reviews the incidence of recorded diaphragmatic pathology at autopsy.

Design: A natural language search for the word diaphragm against autopsy reports was performed. This search identified autopsy reports indicating that section(s) of diaphragm were submitted for histology. For each identified case, the final report was reviewed. Diaphragmatic pathology was classified into congenital, metabolic, inflammatory, immune, neoplastic, degenerative, adaptive and environmental.

Results: 512 total autopsies were in the AP-LIS for 2003-2009. 34 cases documented diaphragm sections (fetal to 80 years). Eight cases were from patients less than one year of age. The spectrum of disease in these patients included reactive changes to bronchopulmonary dysplasia (2), congenital defects (one Pentalogy of Cantrell), inflammatory disease due to peritonitis/necrotizing enterocolitis (1), and diaphragmatic eventration due to neurogenic atrophy/phrenic nerve palsy (1). Three cases took diaphragm sections as part of routine microscopy. In the older age group metastatic malignancy was frequently represented (8 cases - 2 metastatic sarcoma and remainder ovarian, gastric and breast primary). Degenerative disease (1 Charcot Marie Tooth, 1 phrenic nerve palsy), reactive inflammatory disease (5), immune disease (1 scleroderma/dermatomyositis, 1 SLE), environmental disease(3 pleural plaques), congenital disease (1 diaphragmatic hernia), and one metabolic disease (unclassified mitochondrial disorder) were all represented in these cases. The remainder were cases of routine sections or patients with COPD and or mechanical ventilation.

Conclusions: The diaphragm may be involved in a wide array of disease states either primarily or as part of a systemic process. This muscle is not frequently studied at post-mortem examination (6.6% of cases with histologic examination). Pathologists need to be aware of the spectrum of diseases involving the diaphragm, routinely record normal variations of the muscle as well as any pathology. We now are modifying our routine autopsy reports to include an area for recording diaphragm measurements as well as any pathologic findings.

17 Grown-Up Congenital Heart Disease and Sudden Death in a Medical Examiner's Population

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Background: Advances in the management of congenital heart disease (CHD) have allowed many children born with heart defects to survive into adulthood, and in the United States there are now more adults than children living with CHD. Even with surgical correction, however, this population is at increased risk of sudden death. There are also adults with undiagnosed CHD who first present with sudden death. A retrospective review of cases from a large medical examiner's office was conducted to examine the spectrum of CHD presenting as sudden death in adults.

Design: The case files from 1991 to 2007 of the Miami-Dade County Medical Examiner Department were reviewed in this retrospective descriptive study. Adults (individuals >16 years of age) whose cause of death was attributed to the primary or secondary effects (medical/surgical complications) of CHD were included. The following data was collected and stored in a Microsoft Access database: age, sex, race, cause and manner of death, circumstances of death, relevant clinical history, whether autopsy was performed, and autopsy findings related to cardiac and other congenital anomalies. Basic statistics were used to analyze the data.

Results: Of 51,228 adult cases investigated between 1991 and 2007, 80 cases (0.2%) were attributed to CHD. The age range was 17 to 90 years; 65% were male and 35% female. The autopsy rate was 81%. The cardiac malformations described at autopsy were:

Obstructive lesions: bicuspid AV	24 (36.9%*)
Obstructive lesions: other than bicuspid AV	5 (7.7%)
Flow lesions (eg. TOF, ASD, VSD, PDA)	14 (21.5%)
Complex (HLHS, DORV, single ventricle)	1 (1.5%)
Mixed (combination of flow and obstructive lesions)	3 (4.6%)
Anomalous coronary anomalies	17 (26.2%)
Unclassifiable	1 (1.5%)

* % of autopsied cases with CHD

Two females died in the peripartum period. Eleven cases had a history of cardiac surgery, of which two had surgery within 2 weeks of death.

Conclusions: CHD is a rare but important cause of sudden cardiac death in adults. In a large medical examiner's population, bicuspid aortic valves and anomalous coronary arteries are the most commonly recognized entities. However a wide spectrum of simple to complex malformations may be seen, with or without prior surgery, and in a wide age group. Once a solely pediatric entity, CHD is now grown up, and in the future will likely be seen with increased frequency in forensic pathology settings.

18 Fatalities of Novel H1N1 Influenza Virus Display Diffuse Alveolar Damage, Peripheral Pulmonary Thrombosis, and Cytophagocytosis

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Background: A novel pandemic strain of H1N1 influenza A virus emerged in the spring of 2009. The histopathologic features of severe infection with novel H1N1 influenza virus have not been described.

Design: We retrospectively reviewed medical records and autopsy findings from four patients who died from novel H1N1 influenza virus infection. H1N1 influenza virus was confirmed by PCR conducted on ante mortem and/or autopsy specimens. All patients were managed with extracorporeal membrane oxygenation (ECMO). We also reviewed autopsies from 8 age and sex-matched control patients without H1N1 infection who were managed with ECMO.

Results: All patients were men, age 28–57 years (mean 44.8 ± 12.6 years). Disease course varied from 16 to 38 days. One patient had culture-proven respiratory bacterial superinfection during hospitalization. Diffuse alveolar damage (DAD) affected all influenza patients, compared to 50% of the control group. Concomitant acute bronchopneumonia was present in two influenza patients, including one with bacterial superinfection. Thrombosis of peripheral pulmonary vasculature occurred in three influenza patients, with infarcts in one. Peripheral thrombosis was also seen in three controls. Cytophagocytosis, a feature of hemophagocytic syndrome, was present in bone marrow, spleen, and lymph node in four, one and one influenza patients, respectively. The extent of involvement was variable. The diagnosis of hemophagocytic syndrome could not be established with certainty on the clinical and laboratory data available after death; however, all of the patients met 3-4 clinical criteria. Cytophagocytic cells were seen in two of the control cases, including one patient who died of a possible viral pneumonia.

Conclusions: Lung involvement in severe novel H1N1 infection is characterized by thrombosis, hemorrhage and DAD. Hemophagocytic syndrome, which has been associated with other viral illnesses including influenza, may contribute to the severe infection seen in a subset of patients. Careful clinical evaluation to assess for the presence of hemophagocytic syndrome is recommended.

19 Pathology Opinions about Autopsy Cost, Referral, and Centralization

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Background: One of the reasons cited for the decline in hospital autopsy rates is the disinterest of pathologists themselves in performing a difficult and non-remunerative procedure. Autopsies desired by families outside of the hospital system can be a particular problem, especially for small pathology practices. Regionalized large autopsy centers have been proposed as a potential solution. Advantages would include the use of experienced providers, potentially education of trainees, and standardization of autopsy procedures.

Design: A one page ten question survey was distributed by electronic mail to all members of the state Pathologists Association including academic pathologists, pathologists in private practice small groups (5 or less) larger groups (greater than 5), and pathologists in private hospitals. Questions included demographic information, queries regarding attitudes about autopsy in general, cost versus benefit of autopsy, whether there is a clear system for referral for private autopsies and interest in a regional autopsy center.
Results: 42 (21%) of physicians responded to the survey. 50% of respondents perform less than 25 autopsies per year in their practices. In spite of reportedly low numbers, 71% strongly agree or agree that autopsy can provide findings relevant to clinical practice and 52% disagreed that modern diagnosis is so accurate that autopsy is not necessary. However, 52% report that autopsy creates more cost than benefit to their practices with 24% neutral on this question. Pathologists in private hospitals and small practice groups responded proportionately more frequently in the "strongly agree" category for this question. A clear overall majority (74%) disagree that there is a clear system for referrals of private autopsies, and 47% of respondents agree that they are interested in referring autopsies to a regional center, with private hospital and small practice group pathologists agreeing proportionately more frequently.
Conclusions: The pathologists surveyed appear to value the autopsy as a tool in clinical medicine; however, the performance of autopsy outside of a hospital setting is considered a burden in many practice environments. Currently, family requested autopsies in our state are referred to individual independent providers through the state Pathologists Association, though the survey results show that this fact may not be widely known. Implementation of a centralized referral center or system must include details such as cost and payment, but interest does seem sufficient for exploration of such a system in our state.

20 Utilization of Notch1 and Prion Markers to Detecting Pluripotent Pancreatic Cells: An Autopsy Study

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Background: The normal form of cellular prior protein (PrP) is a GPI anchored membrane protein, and are expressed in many cell types. The over-expression of PrP has been identified in many tumor cells, including gastric, breast and pancreatic cancers. We also found that PrP expression in precursor cells in fetal pancreas but not in adult pancreas. These precursor cells have similar morphology to the centroacinar cells which can differentiate to endocrine cells, ductal cells and acinar cells. Multiple cell types of the pancreas appear asynchronously during embryogenesis, which requires that pancreatic progenitor cell potential changes over time. Notch signaling pathway plays an important role in the process of pancreatic embryogenesis. So it is interesting to know the developmental expression patterns of Notch1 and PrP in fetal and adult pancreas.
Design: Forty-three autopsy cases between years 2002-2009, from gestational age 14 weeks to 18 years after birth, were retrieved. Normal pancreatic tissue resected for non-pancreatic neoplasms in 20 patients, ranging from 25 to 77 years old, were obtained as well. Immunohistochemical study was performed using monoclonal antibodies specific for PrP, Notch1, AE1/AE3, and a panel of neuroendocrine markers.
Results: The expressions of PrP are identified in endocrine cells and centroacinar cells of the pancreas, from fetal to adult; while notch 1 expression identified in acinar cells and centroacinar cells. Neither PrP and Notch 1 expression are detected in developed ducts in any pancreas. Abundant centroacinar cells expressing both PrP and Notch 1, which carries both acinar and endocrine lineage markers, identified in pancreas from gestational age 14 weeks to 3 months after birth. After that period, the centroacinar cells expressing both PrP and Notch1 decreased dramatically.
Conclusions: In different developmental stages of pancreas, PrP expression present only in mature and precursor cells of neuroendocrine lineage; while notch 1 expression present in mature and precursor cells of acinar cells. In fetal and young pancreas, centroacinar cells have both PrP and Notch 1 expression. The data suggest that utilization of co-expression of PrP and Notch 1 could identified pluripotent cells in pancreas, which may shed light on pancreatic carcinoma stem cell and/or diabetes mellitus research.

21 Medical Complications in Lung Transplant Patients – Autopsy Data from a Single Center

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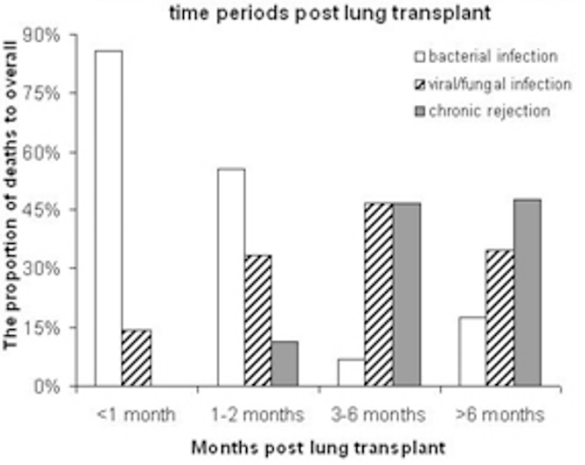
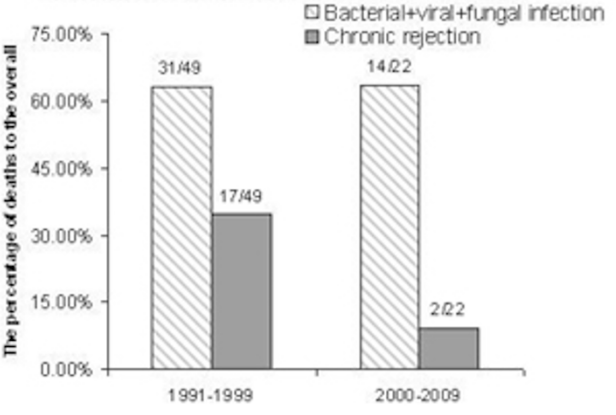
Background: Although lung transplantion (tx) has become an established treatment for end stage lung disease, and patient survival continues to improve, deaths from medical complications post lung tx are still relatively high.
Design: To better understand the role of rejection and infection in the mortality of lung tx patients, we reviewed the autopsy findings over 17 years from a single lung tx center. We grouped the patients into 2 cohorts depending on the date of death: 1991-99, and 2000-09. We compared the incidence of infection versus rejection in the 2 groups.
Results: Autopsy findings from 71 lung tx patients [27 females (38%), 44 males (62%)] were analyzed. The pre-tx diseases included: α1 antitrypsin deficiency/chronic obstructive pulmonary disease (41%), cystic fibrosis (21%), idiopathic pulmonary fibrosis (23%). Post lung tx, the main cause of death within <1 month was bacterial infection, during >1 month to <3 months was viral/fungal infection, and threreafter (>3 mo.) chronic rejection.

Figure 1 Deaths by three major causes at different time periods post lung transplant



The predominant bacterial pathogens were Enterococci and Pseudomonas spp. (n=19, 86%). The main viral pathogen was CMV (n=16, 80%), and fungal pathogens were Candida (n=10, 50%) and Aspergillus (n=8, 40%). Deaths from infection/sepsis continued to remain high in the 2000s, with the same %-age as in the 1990s.

Figure 2 Percentage of deaths caused by infection and rejection in the past two decades



However, the timing of death from infection post-tx shifted. While in the 90s, 71% of deaths from infection occurred in <6 months, in the 2000s only 21% occurred during that time. In the most recent decade, in the patient population studied, deaths from chronic rejection have been diagnosed at autopsy less frequently ($p<0.05$).
Conclusions: Infections continue to be the main cause of death in lung tx recipients. The reduction in the incidence of diagnosis of chronic rejection at autopsy may be related to the shift in long-term post-tx care (from tertiary to primary) and a reduced rate of autopsy in these patients.

22 Patterns of C4d Immunohistochemical Staining in Non-Transplant Myocardial Ischemia: Implications for Interpretation of Post-Transplant Endomyocardial Biopsies

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Background: C4d immunohistochemical staining is a marker of recent classical pathway complement activation that is useful for evaluation of antibody-mediated rejection in transplant biopsies. C4d also stains areas of ischemic myocyte necrosis. We describe the pattern and intensity of myocyte, interstitial, and microvascular staining at different stages of ischemic injury/infarction in the non-transplant setting.
Design: Thirty autopsies with ischemic injury were reviewed. Nine acute myocardial infarction, 3 contraction band necrosis, 9 subendocardial ischemic, and 9 chronic ischemic injury cases were stained with polyclonal antibody for C4d.
Results: Acute myocardial infarction cases showed strong staining of necrotic myocytes; larger infarcts showed more intense peripheral versus central staining. Subendocardial ischemic injury stained homogeneously and was easier to quantify versus H&E staining. Necrosis with contraction bands was strongly highlighted in individual myocytes. One case of "contraction band necrosis" noted on H&E was negative and subsequently reclassified as artifactual. Two of 9 cases of scarring/chronic ischemic injury showed rare positive cells. C4d was noted to highlight cardiac amyloid in 4 cases. Microvascular staining was noted in only 2 cases. This staining was faint and not associated with injured areas. Both of these patients were septic; therefore this may be artifactual staining. Autolysis had no effect on staining.
Conclusions: C4d is a useful diagnostic tool to highlight necrotic myocytes, especially in the absence of large areas of obvious necrosis. It is useful for quantitating the degree of subendocardial ischemia, as well as differentiating true from artifactual contraction band injury, and it can be used on autolyzed material. It can be used to outline edges of a large infarct and to define acute extension of an old infarct. Microvascular staining

is not seen around areas of infarction. This finding may help in the interpretation of perioperative ischemic injury versus humoral rejection in heart transplants, wherein microvascular staining in post-implantation biopsies should prompt additional clinical investigations to rule out humoral rejection. Finally, C4d highlights amyloid deposition in the myocardium, a finding of interest that should be further investigated.

23 Immunoexpression of CD117 and CD34 in Human Fetal and Neonatal Lungs Focusing on Alveolar Capillary Dysplasia

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Background: Alveolar capillary dysplasia(ACD) is a rare lethal pulmonary disorder. Many infants with ACD have additional malformations, such as intestinal malrotation, duodenal atresia, imperforate anus, aganglionosis/hypoganglionosis of colon, absent gallbladder(GB), tracheoesophageal fistula with esophageal atresia, asplenia, arteriovenous malformation(AVM) of liver and trisomy 21. Recently, there are few manuscripts that 16q24.1 microdelition is associated with VATER, ACD and CD117 immunostaining is helpful to diagnose ACD.

Design: We selected several cases of autopsied fetal and infant lung tissue with variable malformations ; duodenal atresia(DA) with cardiac anomaly and single umbilical artery(2 cases), DA with Down syndrome(3 cases), VATER with/without DA(10 cases), absent GB(2 cases), asplenia(2 cases), CCAM(3 cases), Single umbilical artery(SUA,1 case), AVM of liver(1 case), neonatal ACD(2 cases) and normal control tissue(9 cases). Immunostaining of CD117 and CD34 are performed to evaluate the expression pattern, semiquantitatively.

Results: In two cases of ACD, there is uniform CD117 immunonegativity in the septal interstitial cells and decreased densities of CD34 positive capillaries. Relatively decreased densities of CD34 positive capillaries and markedly decreased numbers of CD117 positive septal interstitial cells are found in following cases ; DA with cardiac anomaly and SUA(2 cases), DA with Down syndrome(2 cases), VATER with DA(2 cases), each one case of VATER with asplenia, VATER, asplenia and CCAM. Remaining cases do not reveal any remarkable different expression patterns comparing with control cases.

Conclusions: DA with other malformation and asplenia are disorders that we may search for coexisting ACD in cases of persistent pulmonary hypertension in newborn.

24 Sudden Demise in a 37-Week-Old Male Infant Due to D-Transposition of Great Vessels with a Closed Foramen Ovale

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Background: Congenital heart defects cause significant morbidity and mortality in the pediatric population. D- transposition of the great arteries (D-TGA) accounts for about 6% of all congenital heart diseases. By definition, the aorta originates from the right ventricle (RV) and the pulmonary artery (PA) arises from the left ventricle (LV). The systemic and pulmonic circulations run in parallel requiring atrial or ventricular communication in order for mixing of the blood. D-TGA is compatible with fetal life but may be life threatening after birth when the physiologic shunts (foramen ovale, ductus arteriosus) close. We report a case of D-TGA with an intact ventricular septum and a closed foramen ovale, presenting as cardiorespiratory failure shortly after birth.

Design: This male infant was born at 37 weeks gestation to a 31-year-old Caucasian female (G6 P4 A1) by elective Cesarean section. The prenatal history was unremarkable and a mid-trimester ultrasound failed to detect structural abnormalities. The infant initially cried, however APGAR was 2 at 5 minutes. The heart rate was below 100 and the baby was not pink. All attempts at resuscitation were unsuccessful. A chest x-ray showed complete opacity of the lungs. The baby was pronounced dead and permission was granted for a full autopsy.

Results: At autopsy the body weight and measurements were appropriate for gestational age and there were no dysmorphic features. The larynx and trachea were unobstructed. The lungs (91 grams) demonstrated diffuse pulmonary hemorrhage. Examination of the heart (26.12 grams) revealed that the aorta arose anterior and to the right of the PA. There was normal atrial situs and systemic venous return. The atrial septum showed a closed foramen ovale with ballooning of the septum into the left atrium. The unremarkable RV gave rise to the aorta via a muscular outflow tract. The coronary arteries arose in the usual anatomy. The pulmonary venous return was into the left atrium. The unremarkable LV gave rise to the PA through a membranous outflow tract. The ductus arteriosus was narrowly patent (2mm). All valves were normal appearing. Microscopic exam was unremarkable. Cytogenetics studies revealed a normal karyotype.

Conclusions: We present a case of D-TGA with an intact ventricular septum and closed foramen ovale, which is exceedingly rare with only three case reports identified in the literature. This is a lethal combination, and should be considered, among other congenital abnormalities in any sudden demise after birth.

25 Occult Component of Hepatocellular Carcinoma Presenting as Metastatic Neuroendocrine Carcinoma of Unknown Primary: An Autopsy Case

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Background: Hepatocellular carcinoma (HCC) is one of the common causes of cancer-related deaths worldwide. HCC commonly exhibits histologic polymorphism with rare cases described to have tumor cells with neuroendocrine features. The origin of these cells is unknown. It has been speculated that they either represent a histological component of the original HCC or differentiation under certain circumstances. The prognosis and treatment of HCC with neuroendocrine differentiation is uncertain; however, the few existing reports show this tumor to have higher proliferative activity and malignant potential than ordinary HCC. We report an unusual case of HCC with neuroendocrine component with metastases, some of which composed entirely of the neuroendocrine component.

Design: Formalin fixed, paraffin embedded tissue was stained with H&E. Immunohistochemical stains with HepPar1, alpha-fetoprotein (AFP), thyroid transcription factor (TTF-1), synaptophysin (SYN), and chromogranin (CHR) were performed by using Ventana System and kits.

Results: The patient was a 54-year-old female with history of hepatitis C who underwent a liver transplant in 2008. Evaluation of the explanted liver showed a 1.0 cm moderately differentiated HCC with angiolymphatic invasion. The clinical course of the patient was complicated with retroperitoneal lymphadenopathy, biopsy of which showed high grade neuroendocrine carcinoma. The patient underwent chemotherapy, complicated with angioinvasive fungal infection. At the time of autopsy retroperitoneal lymphadenopathy and a lung nodule were noted. No possible primary site of malignancy was found. Lymph nodes retained metastatic neuroendocrine carcinoma. Examination of the lung nodule showed metastatic HCC with features identical to the primary liver tumor. Review of the surgically resected liver tumor revealed a population of small cells with neuroendocrine features, dispersed among ordinary HCC. These cells were negative for HepPar1, AFP&TTF-1 and positive for SYN&CHR.

Conclusions: We report an unusual case of HCC admixed with neuroendocrine carcinoma with multiple metastases, characterized by two distinct phenotypes- one, similar to the primary HCC lesion and second, composed entirely by the high grade neuroendocrine component. An occult neuroendocrine component of hepatocellular carcinoma may present as metastatic neuroendocrine carcinoma with an occult primary site.

26 Aspiration Pneumonia and Tracheoesophageal Fistula Secondary to a Swallowed Button Battery

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Background: Button batteries are swallowed by over 2,100 people per year, however, most of these incidents resolve uneventfully. In rare instances, particularly when the swallowed battery is of larger diameter (20 to 23 mm), the battery can become lodged in the esophagus necessitating medical attention. Only 19 cases of severe esophageal damage secondary to the ingestion of button batteries have been reported in the English literature. Fatal cases have been reported only twice in the literature, and our literature search revealed none in the past 30 years. We report a case of acute bronchopneumonia and tracheoesophageal (TE) fistula caused by a swallowed button battery in a 3-year-old girl.

Design: The decedent came with clinical history of being 3 weeks status post tonsillectomy and adenoidectomy and refusing to eat solid food after the surgery. She stopped eating completely 10 days later. The patient was, subsequently, brought to the emergency department with vomiting and acute respiratory distress. She experienced cardiopulmonary arrest in the intensive care unit and could not be resuscitated. A full autopsy was performed.

Results: Postmortem examination revealed a longitudinal fistula (measuring 1 cm) between the posterior trachea and anterior esophagus, with surrounding fibrosis and hyperemia. Lodged above the carina, a 20mm battery coin in the vertical position was identified. The lung parenchyma was diffusely congested. Microscopic examination revealed bronchopneumonia and blood-filled alveolar spaces, with evidence of a TE fistula. The cause of death was documented as severe acute bronchopneumonia and massive blood aspiration due to a TE fistula secondary to a button battery lodged in the esophagus.

Conclusions: As indicated in the unfortunate outcome of this unique case, it is important for pediatricians to have a heightened index of suspicion in the clinical setting of a toddler with dysphagia and anorexia. Although there is no consensus in management, most research suggests an initial X-ray to document the location of the object. While all foreign bodies impacted in the esophagus should be removed expeditiously due to their risk of serious complications, management of most other ingestion cases with watchful waiting is acceptable. Proactive education on the dangers of battery ingestion, inclusion of such dangers in childproofing guidelines, and manufacturing child-resistant battery compartments are also deemed effective in minimizing the incidence of swallowed button batteries and its potential, though rare, fatality.

27 Expression of Yes-Associated Protein Increases in Pancreatic Tumors with High Tumor Burden, a Study Utilizing Rapid Autopsy Technique

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Background: The Hippo signaling pathway is a highly conserved potent regulator of mammalian cell growth, division, and apoptosis. Yes-associated protein (YAP) is the nuclear effector of the Hippo pathway. We and others have reported that, in humans, there is amplification of the chromosome region containing the YAP gene (11q22), and that over-expression exists in several human tumor types. Utilizing a unique resource involving rapid autopsy technique, we investigated YAP expression in pancreatic cancers from patients with varying tumor burdens.

Design: Tissue microarrays containing pancreatic tumors (n= 140), harvested via rapid autopsies from 36 patients, were stained with YAP by immunohistochemistry. Autopsy cases were stratified by extent of tumor burden as follows: Primary Only (metastatic burden=0), Low (1-10 metatastases), Extensive (11-99), and Widespread (100-1000's). The YAP expression intensity and distribution were evaluated in these tissues with non-neoplastic pancreatic epithelium as controls (n=10). For each patient, the nuclear and cytoplasmic YAP expression intensity was scored on a four-point scale in multiple samples and averaged to yield a positive or negative result.

Results: Control tissues of non-neoplastic pancreatic epithelium showed 80% nuclear (Nuc) reactivity with YAP and 30% cytoplasmic (Cyt). Pancreatic tumors with primary

only showed 83% Nuc and 17% Cyt; low burden showed 71% Nuc and 43% Cyt; extensive burden showed 86% Nuc and 43% Cyt; widespread burden showed 100% Nuc and 56% Cyt.

YAP Staining in Pancreatic Ductal Adenocarcinomas

Tissue	Nuclear Staining	Cytoplasmic Staining
Non-neoplastic Ductal Epithelium (Control)	80% (8/10)	30% (3/10)
Primary Only (Metastatic Burden = 0)	83% (5/6)	17% (1/6)
Low Metastatic Burden (≤10)	71% (5/7)	43% (3/7)
Extensive Metastatic Burden (10-99)	86% (6/7)	43% (3/7)
Widespread Metastatic Burden (100-1000's)	100% (16/16)	56% (9/16)

Conclusions: Pancreatic carcinomas demonstrating widespread tumor burden show increased nuclear expression of YAP compared to non-neoplastic tissues ($p< 0.7$) and low metastatic burden tumors ($p<0.8$). Our findings are limited by the number of rapid autopsies available for analysis. However, our findings suggest that activation of the Hippo signaling pathway may occur through YAP as part of normal pancreatic epithelial homeostasis and has increased expression in tumors with widespread metastatic behavior.

28 Single Umbilical Artery with Congenital Anomalies. A Study of Perinatal Autopsies and Placentas

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Background: Single umbilical artery(SUA) is a common umbilical cord malformation recognized as a marker for searching other fetal malformations. The aim of this study is to determine the frequency of SUA and survey malformations with SUA and reevaluate the significance of SUA.

Design: A retrospective study was performed based on the medical records and karyotype studies from 1996 to 2009 of patients that underwent perinatal autopsy and pathologically examined placentas submitted at the department of pathology, Asan Medical Center, Seoul, Korea.

Results: During the length of the study, 1,048 perinatal autopsies and 9,313 placenta cases were submitted and analyzed. The average gestational age is 22 + 6/7 weeks. There were 222/10,361 cases (2.1%) of SUA. The number of SUA with anomalies was 148/222 cases (66.7%). The highest association of SUA with malformation was found for cardiovascular malformations. Regarding the individual types of malformation, SUA was most commonly associated with ventricular septal defect, atrial septal defect, tetralogy of Fallot, hypoplastic left ventricle, imperforate anus, omphalocele, pulmonary abnormalities (hypoplasia, abnormal lobation and agenesis), renal cystic dysplasia or agenesis, scoliosis, limb malformation. Karyotypic analysis was performed only in 51/75 autopsy proven cases of SUA with anomalies. There are 15/51 cases (29.4%) of karyotypic abnormality ; four cases (26.6%) were trisomy 18, three cases (20%) were trisomy 13 and 8 cases (53.4%) were other chromosomal aberrations (3 cases of 46XY, inv(9)(p12q13), each one case of 46XX, add(16)(p13.3), 47XX, t(8;9)(p21.3;q31) mat, 46X, der(X;14)(q10;q10)+i(X)(q10), 47XX,+der(12)t(11;22)(q23.3;q11.2)mat, 46 del (6)(q26)).

Conclusions: SUA is a common malformation that we may call attention to the possibility of associated anomalies. Relatively high incidence of chromosomal aberration in this survey could be a supportive data to recommend to perform karyotyping in cases of SUA with anomalies.

29 Infections of the Central Nervous System in Colombia: Analysis of 512 Non-Perinatal Autopsies

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Background: Central Nervous System (CNS) infections are caused by a diverse group of organisms. Correlation with gross examination, histopathologic evaluation and laboratory data typically yields a definite diagnosis.

Design: This prospective study analyzes neuropathologic findings in all academic autopsies performed between January 2004 and march 2009 at the Hospital Universitario de Santader in Bucaramanga, Colombia. Perinatal cases were excluded.

Results: Evidence of CNS infection was foun in 56 out of 512 non-perinatal autopsies. The mean age was 36.2 years with a male:female ratio of 1:1. In only 15 cases (26.7%) a correct premortem diagnosis was documented. Thirty one patients (55.35%) were HIV-positive. The final diagnoses included: Cerebral toxoplasmosis *(*17 cases – 30.4%), pyogenic meningitis (16 cases – 28.6%), Mycobacterium tuberculosis-associated meningoencephalitis (six cases - 10.7%), *Cryptococcus neoformans* meningoencephalitis (five cases – 9%), lymphocytic viral encephalitis (three cases – 5.4%), herpetic meningoencephalitis (two cases – 3.6%), rabies encephalitis (two cases – 3.6%), Chagas disease encephalitis (one case – 1.8%), *Plasmodium falciparum* meningoencephalitis (one case – 1.8%), cerebral mucormycosis (one case – 1.8%), meningoencephalitis due to P*aracoccidioides brasiliensis* (one case – 1.8%), and neurocysticercosis (one case – 1.8%). In several cases HIV infection modified the "classical" histopathologic findings.

Conclusions: A significant number of lethal CNS infections are diagnosed only after postmortem examination. Microbiological and histologic evaluation identify the etiologic agent in virtually all of the cases. Finally, HIV infection frequently modifies the "typical" gross and microscopic features of specific CNS infections.

30 Chagas Disease in Postmortem Examination. Analysis of 11 Autopsies in Bucaramanga, Colombia

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Background: Chagas disease (CD) is an important cause of morbidity and mortality in South America. Involvement of heart, esophagus and colon has been typically found in Tripanosoma cruzi infection.

Design: A prospective descriptive study was conducted in autopsies performed at the Hospital Universitario de Santander in Bucaramanga, Colombia, from January 2002 to May 2009.

Results: Out of 682 non-perinatal autopsies performed, 11 cases of CD (1.8%) were identified. The mean age was 29 years; the study included nine men and two women. In only one of them (9.1%), a correct premortem diagnosis of CD was rendered. The erroneous/inaccurate clinical pre-mortem diagnosis included: Hantavirus infection (2), exogenous intoxication (2), cytomegalovirus infection in kidney transplant recipient (1), pneumonia (1), central nervous system (CNS) tumor (1), cerebral toxoplasmosis in AIDS (1), infective endocarditis (1), and heart failure, not otherwise specified (1). In all the cases the presence of trypanosomiasis was documented histologically. All eleven cases showed evidence of cardiac involvement. Esophageal involvement was found in a single case, and CNS involvement was found also in one case. In every case the cause of death was ultimately related to CD. The presumed route of transmission included: Oral transmission (five cases), triatominae bite (four cases), reactivation of chronic CD due to AIDS-related immunosuppresion (one case), and reactivation after immunosuppressive therapy for renal transplantation (one case).

Conclusions: Despite the fact that CD is endemic in some regions of South America, a correct premortem diagnosis of CD is only rendered in a minority of cases. Cardiac involvement remains the most common -and frequently the only- manifestation of T. cruzi infection. Reactivation after immunosuppresion should be considered in endemic and non-endemic geographic regions.

31 Cutaneous Manifestations of Staphylococcus aureus Sepsis: An Autopsy-Based Study

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Background: *Staphylococcus aureus* is a well known cause of severe infections. Recognition of cutaneous manifestations may help in the clinical diagnosis.

Design: S. aureus septic shock as a cause of death was searched in the 285 academic autopsies performed at Hospital Universitario de Santander, Bucaramanga, Colombia, between january 1, 2008 to december 31, 2008.

Results: Nine patients died of *S. aureus* septic shock (3.1% of the total number of postmortem examinations). The mean age was 15.88 years (range: 2 to 47 years). There were 7 males (78%) and 2 females (22%). The infection was considered community-acquired in all these patients. The clinical course lasted between 4 and 6 days. A correct premortem diagnosis was made in only 3 patients (33%). A primary cutaneous focus was identified in 7 patients (78%); in 2 cases the primary focus was localized in the osteoarticular system (22%). Macroscopic cutaneous manifestations included generalized pustules (56%), generalized petechial erythema with subcutaneous edema (22%) and a chicken pox-like rash with pustules and vesicles (22%). Microscopically, septic vasculitis was recognized in the 7 cases with pustular lesions (78%). Septic vasculitis was characterized by vascular wall infiltration by numerous polymorphonuclear cells, bacterial colonies and fibrin thrombi in capillaries; there were also variable degrees of dermal-epidermal detachment with accumulation of polymorphonuclear cells. In the cases with generalized erythema (2 patients - 22%), there was a superficial perivascular mononuclear infiltrate and edema.

Conclusions: Recognition of cutaneous manifestations in *S. aureus* sepsis may be helpful in early diagnosis of this severe infection.

32 What Is Diabetic Dermopathy? A Histopathologic Study of 14 Necropsies

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Background: Diabetic dermopathy is a common, however, nebulous and poorly understood entity seen as round, pigmented macules located on the anterior surface of the lower legs of diabetic patients. The clinical features have - in the past - been attributed to localized stasis dermatitis, arteriolosclerosis, and capillaritis.

Design: Skin biopsies of lesions of diabetic dermopathy were taken from 14 autopsies and examined histologically. Their diabetic status was determined from chart review. They were examined for histologic features, hemosiderin deposition, melanin deposition, and intimal thickening of the small vessels. Each were graded on a three tier system: mild, moderate, and severe. PAS and Fontana stains were done to evaluate for intimal thickening and melanin deposition, respectively. Comparison of the degree of intimal thickening was done between vessels in the skin and those in the kidneys.

Results: All patients had significant arteriolonephrosclerosis, however - surprisingly - only 2 cases exhibited intimal cutaneous arteriolar thickening in PAS stain. Iron deposition was noted in 9 cases. Ten samples were positive for mild to moderate positivity with Masson-Fontana stain. Nine cases were positive for melanin and iron. Five cases demonstrated the same dermal deposit with positivity for both melanin and iron stains. Only two cases had histologic features of stasis dermatitis.

Conclusions: The results suggest that microangiopathy does not play a significant role in the pathogenesis of diabetic dermopathy. Deposition of material which stained with both melanin and iron stains was a common finding. This histologic finding is

characteristic of ingestion of certain medications which raises the possibility of this disorder being related to medication ingestion.

33 Suspected H1N1 Cases: Clinical Presentations and Autopsy Findings in Cases of Early Death

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Background: H1N1 or Human Swine influenza is a pandemic. A respiratory illness similar to seasonal flu, the morbidity and mortality are higher in some age groups. In cases with no laboratory confirmation, it is essential to rapidly confirm the diagnosis for the public health services(PHS). We were ordered to perform 4 such suspected H1N1 autopsies(April to Sept 09) and present the findings to highlight the clinical spectrum of respiratory disease that can mimic H1N1 and the need for an organized approach to the autopsy.

Design: The 4 autopsy cases with clinical suspicion of H1N1 infection were reviewed. Patient's age, sex, recent travel history, presenting symptoms were recorded. All the autopsy material was studied in detail by light and electron microscopy as well as immunohistochemistry. Appropriate tissues were sent to the public health lab for H1N1 other virus and bacterial testing.

Results: The ages ranged from 32 to 67 years, with three male and one female patient. Two had a history of recent travel(Mexico & China). The presenting symptoms were cough, fever and shortness of breath in all cases, for 1 to 8 days. The tissues in one of the cases were positive for HINI on PCR and DNA sequencing of H genes. The lungs in this case showed bilateral diffuse alveolar damage involving all lobes with edema and patchy hemorrhage. There was also evidence of bilateral bronchopneumonia with gram positive cocci. The lungs in other cases showed confluent bronchopneumonia, pulmonary hemorrhages and diffuse alveolar damage.Death in one of the cases was attributed to septic shock secondary to an unsuspected acute appendicitis.

Conclusions: The major changes in the positive case, were in the lungs and were by themselves not differentiable from any other cause of DAD eg SARS. There was superimposed bacterial bronchopneumonia. Cultures from other cases were negative for H1N1 and seasonal flu.The autopsy provided a rapid answer(under 24 hours) making it possible for the PHS to take further steps as necessary. Cases with a clinical suspicion of H1N1 should have an autopsy and all cultures obtained. All the cases had significant changes in the lung. At this time H1N1 cases appear to have a nonspecific pathology, not independently predictive of H1N1. Reliance on molecular studies, for a definitive answer, is therefore essential.

34 Leptomeningeal Dissemination in Diffuse Intrinsic Pontine Gliomas, a Comparison between Magnetic Resonance Imaging and Autopsy Findings

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Background: Diffuse intrinsic pontine gliomas (DIPG) constitute 60-75 % of tumors found within the pediatric brainstem. These malignant tumors are often rapidly progressive and the median survival is less then 12 months with leptomeningeal dissemination often being the harbinger of disease progression. We report a case series of DIPG and compare the clinical and post-mortem findings.

Design: We reviewed the ante-mortem clinical course and magnetic resonance imaging (MRI) and compared the autopsy results from 4 recent cases of DIPG. The autopsies were restricted to the central nervous system.

Results: Average age ranged from 5 to 11 years with a mean of 7.25 years. The genders were equally represented (2 males and 2 females). All 4 patients presented with cranial nerve and/or cerebellar dysfunction. 2 patients were biopsied and 2 were diagnosed via MRI. All 4 patients were treated with radiation and chemotherapy. Time to progression (clinical worsening with documented MRI progression) ranged from 22 days to 365 days with an average of 210 days. The average time from last imaging and death was 40 days and ranged from 4 days to 75days. The average survival, from initial diagnosis was 315 days, ranging from 120 to 455 days. The average time from progression to death was 90 days. At autopsy, all 4 patients had disease which had spread to the midbrain and medulla and 2 had disease in the cerebellum. The average size of the pontine tumor was 4.4 centimeters (cm) and ranged in size from 3 to 6.5 cm. 3 of 4 patients had hydrocephalus and 2 patients had ventricular shunts. 1 case had bilateral uncal herniation. These findings were consistent with the ante-mortem MRI findings. Microscopically, all cases were diagnosed as glioblastoma, WHO, grade IV. 3 of 4 cases had leptomeningeal dissemination at autopsy. 2 of these patients were not diagnosed prior to death. In both cases of autopsy diagnosed leptomeningeal dissemination MRI imaging was performed ante-mortem and in close proximity to the time of death; the time interval between imaging and post-mortem analysis were 4 and 60 days.

Conclusions: DIPG is a devastating malignant tumor with few post-mortem analyses. MRI is often utilized to monitor and predict disease progression, however, leptomeningeal dissemination is not always diagnosed on ante-mortem imaging studies, as seen in this review, and thus MRI is not always predictive of leptomeningeal dissemination or disease progression.

35 Postmortem Diagnosis of Hodgkin Lymphoma: An Issue Regarding to Fine Needle Aspiration Biopsy

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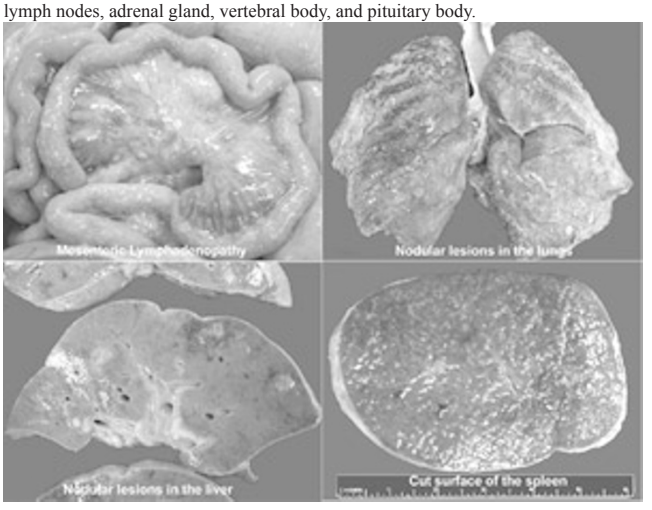
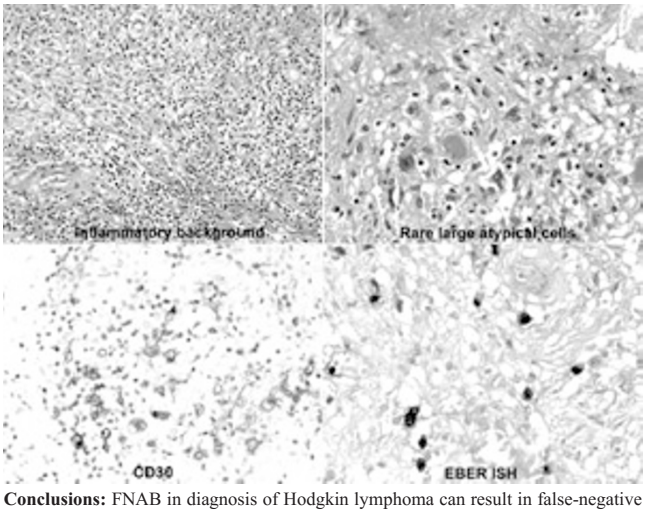
Background: Fine needle aspiration biopsies (FNAB) are increasingly being used in diagnosis of lymphoma. These procedures are rapid, minimally invasive, well tolerated, and cost effective. The accuracy of diagnosing Hodgkin lymphoma by FNAB varies widely but has improved over time. We here describe a case of systemic Hodgkin lymphoma with repeated inconclusive premortem FNAB.

Design: A 75-year-old male presented with anemia and splenomegaly. CT scan revealed multiple mass lesions in the lung and liver, mediastinal hilar lymphadenopathy, and splenomegaly. A systemic metastatic tumor was suspected. Repeated FNAB of the liver masses showed prominent necrosis and inflammatory reaction. Rare atypical cells were noted, but immunostains failed to prove the nature of these cells. The patient died several months later.

Results: Grossly (Figure 1), prominent lymphadenopathy was noted in the mesentery and pulmonary hilar regions. Multiple mass lesions were present in the lungs and liver. The spleen was enlarged (495 grams) with a nodular cut surface. Microscopically (Figure 2), the masses in the lung and liver revealed prominent necrosis and inflammatory reaction. Occasional large atypical cells were noted with one or multiple irregular nuclei and large red nucleoli. These atypical cells were positive for CD79a, PAX5 and CD30, weakly positive for CD15, but negative for CD3 and ALK1. These tumor cells were also positive for EBER in situ hybridization. The tumor also involved spleen, multiple lymph nodes, adrenal gland, vertebral body, and pituitary body.





Conclusions: FNAB in diagnosis of Hodgkin lymphoma can result in false-negative results, owing to many factors, including extensive fibrosis and necrosis, sparse or absent Reed-Sternberg cells, and misinterpretation of RS cells as reactive atypia. Therefore, in cases with high suspicion for lymphoma or other malignancy, a tissue biopsy may be indicated if FNAB is inconclusive.

36 A State-Mandated, Detailed Autopsy Consent Does Not Impact the Autopsy Rate at an Acedemic Medical Center

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Background: Autopsy rates at our institution have been constant for over a decade and have remained higher than the reported national level. Recent revision of state law required that our autopsy permission form be expanded to include mandatory information to provide informed consent. This included questions regarding restriction of an autopsy, organ and tissue disposition, donation of organs and tissues for research and education. When this form was implemented, concern was expressed that this lengthier, detailed consent would reduce the autopsy rate. The aim of the study is to report on whether a more extensive consent form dissuades families from agreeing to an autopsy.

Design: Autopsy rates from 1996 to 2008 were calculated. Rates before and after implementation of the revised autopsy form were then compared. In addition, 123 autopsy authorization forms, signed between 2007 and 2009 were reviewed. The answers given for each inquiry field were recorded and were used to calculate rates of response.

Results: Autopsy rates over the past 13 years have remained between 19-26%. Of the autopsy consent forms reviewed, families requested an unrestricted autopsy 68% of the time. 32% asked that tissues not processed for histology, should be returned to

the patient's body for disposition. Permission to retain organs in the department for teaching and research was given 60% of the time. 28% of families excluded the patient brain from the autopsy. Of patients' whose brain was included in the autopsy, 23% of families declined donation for research. Special requests were made 30% of the time including: the date the body was to be returned; inspection of specific organs; specifying who to contact with results; plans for open casket viewing; requests for pre-autopsy viewing; requesting autopsy and skeletal x-rays. Permission to test the patient for HIV/Hepatitis B, in the event that a technician was injured, was given 100% of the time, as was permission to photograph the patients' autopsy.

Conclusions: The implementation of a detailed informed consent has not reduced the autopsy rate at our hospital. A third of families agreeing to the procedure chose to limit the autopsy, and less than a third asked for organs to be returned to the patient. A majority of families gave permission for organ and tissue retention for teaching and research. An expanded autopsy consent allows next-of-kin to make fully informed decisions about an autopsy procedure and the disposition of their family member's remains.

37 Importance of Placental Availability When Correlating Clinical and Pathologic Cause of Death in Second and Third Trimester Fetal Deaths

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Background: It is known that the majority of second and third trimester fetal deaths are caused by a single or a combination of placental pathologies. This makes the use of placental examination an essential tool when determining fetal cause of death. However, 15 to 20 percent of stillbirths have no identifiable etiology.

Design: A retrospective study of 224 fetal autopsies performed at our Institution (Boston Medical Center) from 2000 to September 2009. Postmortem and placenta histology reports were reviewed. Gestational age, premortem clinical diagnosis, placental diagnosis, postmortem gross and histology findings, and final anatomic diagnosis were recorded.

Results: A total of 224 fetal autopsies were reviewed, of these, 197 (88%) of cases had placentas available for study, and 27 (12%) did not. One hundred and twenty-six (126) (56%) of cases had a placental cause of death (COD) (70% for 2nd trimester (T) and 30% for 3rd trimester (T) deaths).

Table 1

	Placentas Available	Placental COD	Other COD	No COD
Total (224)	197 (88%)	126 (56%)	42 (19%)	57 (25%)
2nd T (145)	132 (91%)	102 (70%)	23 (16%)	20 (14%)
3rd T (79)	65 (82%)	24 (30%)	19 (24%)	37 (47%)

Major placental causes were acute chorioamnionitis (ACA) with ascending amniotic-fluid infection (65 of 2nd T and 5 of 3rd T), and placental vascular disease/placental abruption (PVD) (30 of 2nd T and 14 of 3rd T). Umbilical cord (UC), twin to twin transfusion (TTT) and congenital malformations (M) (16 of 2nd T and 11 of 3rd T) were also recorded. No cause (NC) of fetal death was found in 20 of 2nd T and 37 of 3rd T cases. Of the 27 (12%) cases with no available placenta for study, 20 (14 of 2nd T and 6 of 3rd T) had a known cause of death due to congenital malformations (12), other causes were amniotic ascending infection (3), and other (5). Seven (7) cases had no postmortem known cause of death.

Table 2

	ACA	PVD	UC	TTT	M	O	NC
2nd T	65	30	2	7	16	5	20
3rd T	5	14	4	1	11	7	37

Conclusions: Placental examination is a key factor in the evaluation of cause of fetal death, however, a complete autopsy report can be generated with sufficient clinical history and histologic evaluation of fetal organs. In our study, placental examination provided the lead diagnosis in the majority (56%) of cases with the support of organ histology. Only 26% (7 of 27) cases with no placenta available for study remained with no postmortem cause of death (2 of 2nd trimester and 5 of 3rd trimester fetal deaths).

38 Adenovirus Pneumonia – An Under-Recognized Cause of Morbidity in Children

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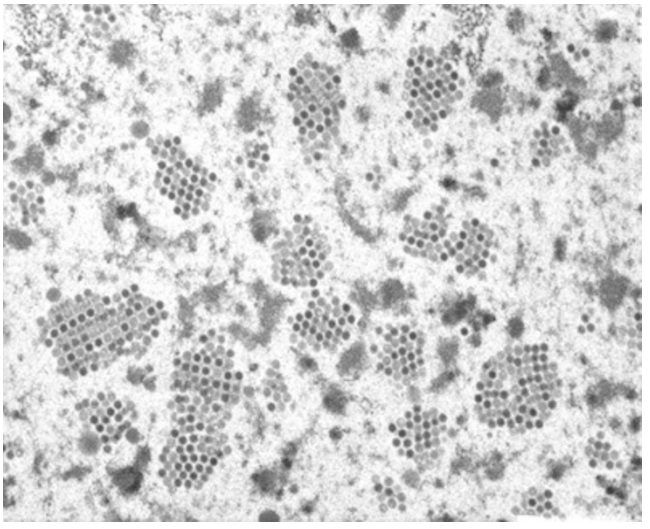
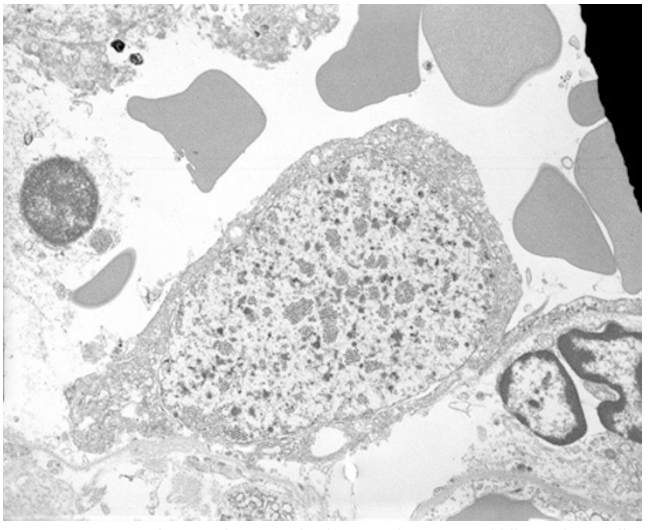
Background: Adenovirus (AV), a ubiquitous non-enveloped, icosahedral double-stranded DNA virus is a common cause of human infections. 52-serotypes of AV have been identified, and these cause morbidities ranging from upper respiratory tract infections (RTI) to gastroenteritis. In immunocompromised patients and young children, AV infections are often much more severe and may include lower RTI and meningoencephalitis. We present an autopsy case performed on a 2-yr old girl who was admitted with respiratory compromise, which progressed to bacterial pneumonia, sepsis, and death 8-days after admission.

Design: The autopsy was performed using the Letulle method. Resected tissue was fixed in 10% buffered formalin and embedded in paraffin. Tissue sections (5µm) were cut and then stained with hematoxylin and eosin. Electron Microscopy (EM): Fragments of formalin-fixed lung tissue were cut into 1-mm cubes. These were then fixed in 4F1G for 4 hours, postfixed in osmium tetroxide, dehydrated in graded alcohols, and embedded in epoxy resin. The sections were stained with uranyl acetate and lead citrate and examined on a JEM 1200 transmission EM.

Results: On autopsy, viral cytopathic effects manifesting primarily as smudgy nuclear chromatin were identified within pneumocytes, while EM studies demonstrated hexagonal 90 nm viral particles containing nucleocapsids in Figure 1 and within pulmonary endothelial cells in Figure 2. Both the light microscopic and EM findings were typical of AV, indicating that the decedents respiratory failure, which initiated the cascade of events that lead to her death, was likely due to AV pneumonia.





Conclusions: ADV is an under-recognized cause of severe morbidity and mortality in children and immunocompromised patients. This case emphasizes the difficulty in clinical diagnosis of ADV pneumonia, the need for clinicians to maintain adenovirus infection in the differential diagnosis, and the importance of autopsy examination in general for case characterization.

39 Effect of Prostacyclin Treatment on Lesions of Pulmonary Arterial Hypertension

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Background: Pulmonary arterial hypertension (PAH) is a rare disease characterized by abnormal remodeling of peripheral vessels. Therapy involves both warfarin and continuous infusion of prostacyclin analogs. In addition to its immediate vasodilatory effects, prostacyclin is speculated to slow the disease process by decreasing inflammation, thrombosis, and smooth muscle proliferation; however, there has been no examination of the long term effects of prostacyclin on the lesions of adult PAH.

Design: We evaluated the morphology of vascular lesions in 22 autopsy cases with clinical diagnoses of PAH, including prostacyclin-treated and untreated patients. We used CD61 staining to determine the presence of platelet thrombi and CD3 and CD68 staining to quantify vascular inflammation.

Results: Patients dying within one year of starting prostacyclin therapy frequently had an underlying diagnosis of scleroderma, and they displayed primarily concentric vascular lesions and pulmonary capillary hemangiomatosis-like (PCH) foci. Four of the six patients who survived for a year or more (1-18 years) following initiation of prostacyclin therapy had idiopathic or anorectic-drug related disease, and in addition to concentric arterial disease they had large plexiform lesions with dilations. The average size of plexiform lesions in treated cases was significantly larger (0.39 mm^2, n=5) than in untreated cases (0.15 mm^2, n=6). Fewer plexiform lesions from treated cases had platelet thrombi (25%) than those from untreated cases (76%). Both groups had a similar number of thrombi in other vessel types, with the exception of cases with angioma-like lesions, which had extensive capillary platelet aggregates despite prostacyclin and warfarin therapy. Quantification of macrophages and T cells revealed no differences in inflammatory infiltrates between treated and untreated cases either in plexiform lesions alone or in abnormal vessels as a whole.

Conclusions: The increased plexiform lesion size in patients treated with prostacyclin may reflect prostacyclin's effect on vascular remodeling or the natural progression of the disease under conditions of prolonged survival. The decrease in platelet thrombi might be

due to prostacyclin or warfarin treatment. Unexpectedly, treatment with prostacyclin did not decrease vascular inflammation. Together these results provide the first description of possible treatment effect on the morphology of end-stage PAH.

40 Post-Mortem Imaging as an Alternative to Autopsy: Development of Techniques for Improving Diagnostic Accuracy

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Background: Increasing public objection to autopsy has led to a search for minimally-invasive alternatives. In the first large validation study of post-mortem imaging in non-forensic autopsies, we identify specific strengths and weaknesses of imaging and, on the basis of this data, refine radiological techniques in order to improve diagnostic accuracy.

Design: Adult deaths reported to the Coroner (n=120) were investigated using whole body CT and MRI, followed by full autopsy. The first 10 cases were used to familiarise radiologists with post-mortem changes, the final 10 for coronary angiography. For the remaining 100 cases, radiologists were blinded to autopsy results. Following reporting, radiology and autopsy findings were reviewed and discrepancies discussed. This was performed in 6 batches of 15-20 cases, in order to increase radiologists' experience.

Results: There was a major discrepancy between radiological and autopsy cause of death in 30% of cases. Radiologists were asked to indicate their level of confidence in the cause of death and whether autopsy would be required if this was a routine service. Confidence levels were definite 45%, probable 27%, possible 18% and unascertained cause 9% of cases. In 46% of cases, the radiologists indicated that autopsy was not required. For this group, the major discrepancy rate was 13%. The commonest source of error on imaging was missed coronary heart disease (CHD). As this is also the most frequent cause of death at Coronial autopsy, improved sensitivity for CHD is required before post-mortem imaging can be recommended for routine practice. In order to improve detection of myocardial lesions, additional oblique MRI sequences were introduced, providing short axis sections of the heart which revealed myocardial infarcts not previously detected on imaging. In order to identify coronary artery lesions that could not be demonstrated on cross-sectional imaging, we developed a novel method of post-mortem CT coronary angiography, validated in the final 10 cases.

Conclusions: Common causes of sudden death are frequently missed on CT and MRI. Defining the specific weaknesses of cross-sectional radiology facilitates the development of imaging techniques that may improve diagnostic accuracy.

41 Demographic, Ethiologic and Pulmonary Histopathological Findings in Patients with Acute Respiratory Failure: An Autopsy Study

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Background: Acute respiratory failure (ARF) has been one of the most important causes of death in intensive care units. Until this moment few studies have showed data about causes of death and certain aspects of pulmonary pathology observed in autopsies of patients with ARF are still unknown. This study considers 4,218 autopsies of patients who died of ARF and describes the demographic data, ethiology, and histological pulmonary findings.

Design: From 1,990 to 2,005, 24,336 pathological reports were reviewed. From these reports were selected 4,218 autopsies (17.33%) from patients age older than 1 year with ARF as cause of death. The following data were obtained: age, sex, and major associated diseases (found at the autopsy). Pulmonary histopathology was categorized as: diffuse alveolar damage (DAD); pulmonary edema (PE); alveolar hemorrhage (AH); and acute interstitial pneumonia (AIP).

Results: The age of the patients ranged from 1 to 99 years (median 51). Three hundred fifthy seven (357) (8.46%) patients were between 1 and 20 years old, 1,712 (40.59%) between 21 and 50 years old and 2,150 (50.97%) older than 50 years. Patients were male in 2,448 (58.04%) and female in 1,770 (41.96%) of the cases. DAD was present in 1,807 (42.84%), PE in 972 (23.04%), AH in 425 (10.08%) and AIP in 194 (4.60%) necropsies. The principal underlying diseases were bronchopneumonia in 1,079 (25.58%) patients, Acquired Immunodeficiency Syndrome in 1,047 (24.82%), sepsis in 508 (12.04%), liver cirrhosis in 494 (11.71%), cancer in 463 (10.98%), pulmonary thromboembolism in 339 (8.04%), acute myocardial infarct in 201 (4.77%), brain stroke in 188 (4.46%), tuberculosis in 156 (3.70%), chronic kidney failure in 100 (2.37%) and leukemia in 53 (1.26%) patients.

Conclusions: ARF has showed as an important cause of death, present in about 17% of autopsies. This report is the first autopsy study to include demographic data, ethiologic diagnosis, and respective histopathological findings in patients with ARF. Further studies are necessary to elucidate the complete pulmonary physiopathological mechanism involved with each associated disease.

42 Death during Dialysis: Findings at Autopsy

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Background: Sudden cardiac death occurring during dialysis has not been extensively studied at autopsy.

Design: A retrospective review of autopsy records from a single calendar year at a state-wide medical examiner's office was performed. Cases of sudden deaths occurring during or within 6 hours after dialysis at outpatient facilities were retained for study. Causes of death and cardiac findings were tabulated. Cardiomegaly was determined based on body height and weight; mild cardiomegaly was defined as <50 grams above the 95% upper limit; moderate 50-99 grams; marked 100-200 grams; and massive >200 grams above the limit, respectively. Severe coronary atherosclerosis was defined as >75% area luminal narrowing.

Results: There were 14 sudden dialysis-related deaths, among a total of 435 autopsies of sudden cardiac death. The mean age was 63 years (range: 34-84 years); there were 8 males (58 ± 12 years), and 6 females (71 ± 8 years). There were 11 African Americans and 3 Caucasians. The mean body mass index (BMI) was 29.3 (range 22-54), with 9 decedents with a BMI > 25 and 5 with BMI > 30. Six patients had a diagnosis of diabetes mellitus (43%) and 11 were hypertensive (79%). Thirteen decedents became unresponsive and arrested during dialysis, and one became short of breath while on dialysis and expired en route to the hospital. The cause of death was natural and cardiac in all 14 autopsies. The mean heart weight was 612 g (range: 350-980g); cardiomegaly was present in 13 (93%), 4 moderate, 4 marked, and 5 massive. There was severe atherosclerosis in 6 cases (43%), involving 1 vessel (n=1), 2 vessels (n=3), and 3 vessels (n=2), including one patient with prior bypass graft surgery and 2 patients with healed transmural infarcts. Biventricular hypertrophy characterized the 13 hearts with cardiomegaly, 5 with left ventricular dilatation > 4 cm; histologically, there was diffuse myocyte hypertrophy and interstitial fibrosis. One patient (7%) had no morphologic arrhythmogenic substrates, and died of cardiac arrhythmia, with no other findings at autopsy.

Conclusions: In sudden death occurring during dialysis, the cause of death is related predominantly to concentric left ventricular hypertrophy, with concomitant coronary atherosclerosis in less than one-half of cases. There appears to be a predilection for African Americans and obesity.

43 Sudden Unexpected Death: Severe Diffuse Involvement of Coronary Arteries in Clinically Silent Aortoarteritis in a Young African-American Male

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Background: Aortoarteritis is a chronic inflammatory disorder of large elastic arteries usually affecting the aorta and its larger branches. Sudden cardiac death as the first manifestation of aortoarteritis with severe involvement of coronary arteries is extremely rare. We therefore report a patient who presented with sudden cardiac death as primary manifestation of aortoarteritis.

Design: Forensic autopsy was performed and the cause of death was established. The heart and aorta were then examined grossly and microscopically.

Results: A 24-year-old, African-American well built and muscular male had no known previous history of cardiac disease. He suddenly collapsed to the ground and displayed generalized seizure-like activity. He died despite extensive resuscitative efforts. Autopsy revealed markedly narrowed coronary arteries. All coronary arteries had predominant concentric intimal thickening and narrowing. The left anterior descending coronary artery had fibrotic intimal thickening with up to 90% stenosis. The right coronary artery, posterior descending coronary artery, left circumflex coronary artery, and the first diagonal coronary artery branch were up to 80-85%, 95-99%, 80%, and 50-60% narrowed respectively. There was wrinkled and cobblestone appearance in the intimal surface of ascending aorta, aortic arch and descending aorta with ostial narrowing of the coronary arteries. Microscopically, concentric fibroproliferative type intimal thickening with an inflammatory cell infiltrate within the adventitia were identified in all coronary arteries. Similar changes were present in the aorta. There were also healed subendocardial myocardial infarct and healed fibrous scar in left ventricle. Spirochete stain was negative. Detailed review of history revealed that the patient has no family history of sudden cardiac death. There was no history of alcohol or drug abuse with negative toxicology test. All above findings supported the diagnosis of healed aortoarteritis.

Conclusions: We report one case of fatal healed aortoarteritis. Based on the patient's young age and the microscopic findings, the etiology is most likely Takayasu aortoarteritis. To our best knowledge, severe diffuse involvement of coronary arteries in aortoarteritis with sudden death as first manifestation in young black male has been rarely reported in the literature.

44 Additional Morphologic and Genetic Data in Alstrom Syndrome

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Background: Alstrom Syndrome (ALMS) is a recessively inherited disorder with a complex and variable clinical spectrum. Cardiac abnormalities are known to occur in more than 60% of these patients but have not been well characterized. ALMS is caused by mutations in ALMS1 (Chr 2p13), a gene ubiquitously expressed with unknown function. ALMS1 has been implicated in ciliary function and intracellular transport, but the link between mutation of ALMS1 and development of disease is poorly understood. We report the clinical, pathological and genetic features in a Caucasian male born of non-consanguineous parents. He developed nystagmus (at 10 months), blindness, hearing loss (at 7 years), type 2 diabetes mellitus (at 7 years), obesity (BMI: 35, at 9 years), acanthosis nigricans, short stature and scoliosis. He had hypothyroidism, hypogonadism, splenomegaly, dyslipidemia, and abnormal liver and renal function tests. At 19 years of age, he presented with acute severe respiratory distress, bilateral pulmonary infiltrates and left ventricular ejection fraction of <10%. He died the following day.

Design: Autopsy was performed according to the standard protocol. Tissue was fixed in formalin and glutaraldehyde for histologic and electron microscopic examination, respectively. Mutational analysis for ALMS1 gene was performed at the Jackson Laboratory, Bar Harbor, Maine.

Results: Autopsy revealed an enlarged (420g) and hypertrophied heart (left and right ventricular free wall thickness 1.7 & 0.9 cm, respectively; and septal thickness of 2.1 cm). Histologic and ultrastructural examination showed signs of disorganized myocyte architecture, including disarray of myofibrils, intertwined hypertrophic myocytes with bizarre-shaped nuclei and moderate interstitial fibrosis. Kidneys showed focal glomerulosclerosis and interstitial fibrosis. There was florid lymphocytic thyroiditis

and testicular atrophy with aspermatogenia (negative OCT3/OCT4 stain). There was evidence of acute multifocal bronchopneumonia and congestive heart failure. He carried two heterozygous mutations in ALMS1: 11316_11319delAGAG; R3772fs in exon 16 and 8164C>T ter; R2722X in exon 10.
Conclusions: This report describes previously undefined cardiac abnormalities in this rare multisystem disorder. Myofibrillar disarray is probably directly linked to ALMS1 mutation, while fibrosis in multiple organs may be a secondary phenomenon to gene alteration. Whether and how intracellular trafficking or related signals lead to cardiac dysfunction is a subject for further research.

45 Sudden Cardiac Death in Young Adults: An Audit of Coronial Autopsy Findings

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Background: Sudden adult cardiac death is in most cases attributable to atheromatous coronary artery disease. Non-atheromatous causes of cardiac death include congenital heart diseases, cardiomyopathies (CM) and valvular heart disease. In recent years the advent of sudden adult cardiac death with a morphologically normal heart (sudden adult death syndrome, SADS) has generated much debate and led to the establishment of registries to investigate these deaths further.
Design: A list of suspected sudden cardiac deaths among young adults (16 – 45 years) was compiled using data from the Central Statistics Office in Ireland from 2004 to 2009. The pathologists and coroners involved in each case were contacted and a copy of the autopsy report requested. The autopsy reports were audited using agreed dataset criteria including demographic factors, toxicology, detailed cardiac parameters, histology and toxicology. The findings were reviewed with regard to cause of death, cardiac pathology and diagnosis of sudden cardiac death.
Results: 90 autopsy reports were received and audited, 16 cases were excluded due to age criteria (≤ 16 years). There were 74 adults, 27 women (36%) and 47 men (64%). The mean age at death was 27.7 years (range 17 – 41 years). The breakdown of the cause of death was as follows: 47 cardiac deaths, 22 non-cardiac deaths, 3 SUDEP and 2 SADS. Coronary artery disease (CAD) was identified in 24 patients (32.4%), however only 26% of these had evidence of IHD. CAD was seen in association with CM in 5 and SADS in 2. Overall, 23 patients (33%) had an enlarged heart (weight > 400g women and 500g men), for which the causes of death included hypertrophic cardiomyopathy (HCM, n=4), dilated cardiomyopathy (DCM, n=3), left ventricular hypertrophy (LVH, n=5), myocarditis (n=1) and valvular disease (n=3) and ischaemic heart disease (IHD, n= 5). Causes of death with a normal heart weight included DCM in 2, ARVD in 1, myocarditis in 2, IHD in 10, and SADS in 8. LVH was seen in that group in 3 cases, but death not attributed to it.
Conclusions: Sudden adult death is a diagnosis of exclusion with important consequences for the living relatives, in the era of molecular diagnosis of genetic cardiomyopathies and channelopathies. Thourough exmination of the heart at autopsy is mandatory in cases of sudden adult death, as SADS is a diagnosis of exclusion, and some cardiomyopathies may present with an apparently normal heart.

46 Recurrent Respiratory Papillomatosis with Malignant Transformation in Lungs: A Retrospective Longitudinal HPV Study

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Background: Recurrent respiratory papillomatosis (RRP) is etiologically associated with vertical transmission during vaginal delivery from an HPV infected mother. Even though cervicovaginal HPV infection is extremely common, RRP occurs in only 4.3 per 100,000 children. Approximately 1-2% of the patients with an early onset of RRP eventually develop laryngeal squamous cell carcinoma (SCC); pulmonary SCC is even rarer. The malignant transformation of RRP to SCC has been linked to various HPV strains and may result from the spontaneous loss of HPV expression. Here we study HPV presence in the early, intermediate and terminal stages of RRP with extensive pulmonary involvement and development of SCC.
Design: Four laryngeal biopsies, obtained at early, intermediate and late stages of disease, as well as autopsy sections were studied by in-situ hybridization with low-risk (types 6/11) and high-risk (types 16/18) HPV DNA probes using Ventana kit on BenchMark XT autostainer with appropriate positive and negative controls. Autopsy was restricted to the chest.
Results: A 13-year-old male underwent 14 excisions of laryngeal papillomas since the age of 2. The lesions caused airway obstruction, frequently complicated by pneumonias and exacerbations of asthma. The patient died from respiratory failure and suppurative bronchopneumonia. Autopsy findings were remarkable for multiple squamous papillomas with viral change and dysplasia in the trachea and both main-stem bronchi. Some papillomas showed in-situ and invasive, focally necrotizing squamous cell carcinoma with vascular invasion and hilar lymph node metastasis. Lung parenchyma uninvolved with tumor demonstrated severe acute bronchopneumonia with microabscess formation. HPV assay showed consistent diffuse strong reaction (>400 viral copies) with low-risk HPV probes in all 4 RRP biopsies, as well as the in-situ and invasive SCC. Low-copy numbers (10-50) of high-risk HPV were detected only in 2 biopsies at the intermediate stage of RRP.
Conclusions: This is a rare instance of early onset RRP with documented progression to dysplastic papillomas, pulmonary SCC in situ and invasive SCC with local metastases. The rarity of RRP, presumed to be acquired during vaginal delivery, is not congruent with the common occurrence of low-risk HPV in the female genital tract, where these viruses are seldom associated with malignant transformation. The HPV typing in this case supports earlier similar reports and suggests an important role of low-risk HPV strains (6/11) in the malignant transformation of RRP in the lower respiratory tract.

47 Comparison of Autopsy Findings of 2009 Pandemic Influenza A (H1N1) with Seasonal Influenza in Four Pediatric Patients

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Background: The swine-origin influenza A (H1N1) virus that emerged in humans in early 2009 has reached pandemic proportions and cause over 120 pediatric deaths nationwide. Studies in animal models have shown that the 2009 H1N1 influenza virus is more pathogenic than seasonal A virus, with more extensive virus replication and shedding occurring the respiratory tract.
Design: We report four cases of influenza A-associated deaths (two pandemic and two seasonal) in persons less than fifteen years of age who had no underlying health issues. Autopsy finding on isolation of virus from various tissue specimen, cocurrent bacterial infection and pathological changes of the respiratory tract were compared between swine-oringin influenza A H1N1 and seasonal influenza infected patients.
Results: The swine-origin influenza A-subtype H1N1 was isolated from post-mortem throat swabs, lung and brain tissue and was confirmed by real time RT-PCR in two cases. Isolates from throat swabs in two other cases were positive for seasonal influenza A virus H1N1 (non-swine) and H3N2, respectively. Evidence of concurrent bacterial infection, S. *aureus* (MRSA), was found in lung and blood specimens in both swine-origin influenza A H1N1 patients. H. *influenzae bacillus* was identified from the throat culture in one of two seasonal flu cases. Examination of the respiratory tract revealed marked hemorrhagic and necrotic changes of upper airway mucosa and hemorrhagic pleural fluid in swine-origin H1N1 patients. Whereas pathology evaluation of postmortem lung specimens showed non-specific edema and congestion in seasonal flu cases, diffuse alveolar damage with prominent hyaline membrane and type II pneumocyte proliferation, hemorrhagic necrosis of bronchiolar walls and neutrophilic infiltration were evident in the lungs of swine-origin H1N1 infected patients.
Conclusions: Our study suggests that bacterial superinfection in lungs and acute respiratory distress syndrome can play a pivotal role in fatal swine-origin influenza A (H1N1) cases.

Bone & Soft Tissue

48 CD1a Immunopositivity in Perivascular Epithelioid Cell Neoplasms (PEComas): True CD1a Expression or Technical Artifact?

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Background: PEComas comprise a family of rare neoplasms composed of morphologically distinctive perivascular epithelioid cells exhibiting a "myomelanocytic" immunophenotype. The distinction of PEComas from other tumors with melanocytic and smooth muscle differentiation can be difficult. A recent study has claimed that PEComas routinely express CD1a, a Langerhans cell-associated transmembrane glycoprotein involved in antigen presentation, and that expression of this marker may be helpful in the distinction of PEComas from various mimics. We evaluated a series of PEComas and potential mimics for CD1a expression.
Design: A total of 54 cases (27 PEComas; 11 leiomyosarcomas; 10 melanomas; 6 clear cell sarcomas) were evaluated in 2 laboratories (Laboratory A: 31 cases, Laboratory B 23 cases). Nine Laboratory B cases were retested at Laboratory A. Laboratory A methods: MTB1 clone (1:20, Novocastra), heat-induced epitope retrieval in EDTA (pH 8.0), Dako Advance detection system (Dako Corp.) with background reducing diluent. Laboratory B methods: MTB1 clone (1:30, CellMarque), heat-induced epitope retrieval in Medium Cell Conditioner #1 (pH 8.0–9.0), streptavidin-biotin detection system with DAB chromogen. Scoring: 1+, 5-25%; 2+, 26-50; 3+, >51%. Langerhans cells served as a positive internal control in all tested cases.
Results: All Laboratory A cases were negative. 16 Laboratory B PEComas (14 renal angiomyolipomas, 1 soft tissue PEComa, 1 pulmonary clear cell "sugar" tumor) showed CD1a immunopositivity (1+: 7 cases; 2+: 7 cases; 3+: 2 cases). All non-PEComas were negative. All positive PEComas showed cytoplasmic staining only, without membranous staining. The 9 Laboratory B positive PEComas were negative when retested at Laboratory A.
Conclusions: We conclude that PEComas do not truly express CD1a in a biologically plausible membranous pattern, but may instead show aberrant cytoplasmic immunopositivity in some laboratories. Close inspection of published photomicrographs of previously reported CD1a-positive PEComas shows an identical pattern of cytoplasmic positivity. This aberrant pattern of immunopositivity likely reflects a technical artifact related to epitope retrieval and detection methods. Alternatively, this staining could represent cross-reactivity with an epitope unique to PEComas, as it was not observed in non-PEComas. Ultimately, however, we do not believe there is a real role for CD1a immunohistochemistry in the differential diagnosis of PEComas.

49 Novel *EWSR1-POU5F1* Fusion in Soft Tissue Myoepithelial Tumors. A Molecular Analysis of 29 Cases, Including Soft Tissue, Bone and Visceral Locations Showing Common Involvement of *EWSR1* Gene Rearrangement

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Background: The diagnosis of myoepithelial tumors (MET) outside salivary glands remains challenging, especially in unusual clinical presentations, such as bone or visceral locations. Few reports have indicated an *EWSR1* gene rearrangement in soft tissue MET, and, in one case each, the fusion partner was identified as being either *PBX1* or *ZNF444*. However, larger studies to investigate if these genetic abnormalities are recurrent or if