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ABSTRACTS

Oral Presentations

O1 PEDIATRIC COLUMNAR LINED ESOPHAGUS (CLO) VS BARRETT'S ESOPHAGUS: IS IT THE TIME FOR A CONSENSUS DEFINITION?

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Aim We describe the clinical, endoscopic and histological features of all cases of Barrett's esophagus (BE) diagnosed at our institution between 2000 and 2007 following the criteria of the British Society of Gastroenterology. This defines BE as a segment of *columnar metaplasia (CLO)* (*whether intestinalized or not*) of any length, visible endoscopically above the gastro-esophageal junction and confirmed histologically. Our diagnosis was reviewed using the criteria of BE defined by the American College of Gastroenterology (ACG).

Material and methods: Information was collected with respect to age, symptoms, treatment, endoscopic and histological features. The diagnosis was challenged after immunostaining for Cdx2 (marker of intestinal differentiation)

Results: Twelve children (10 males and 2 females) with a median age of 11.7 (2 to 17) years had been diagnosed with CLO-BE. Histology confirmed BE in 31/38 endoscopies. The initial diagnosis was reviewed according to Cdx2 results in 10/12 patients: Cdx2 strongly expressed in 4 cases with intestinal metaplasia (the diagnosis of BE was maintained); was negative in 4 other patients with "CLO" mucosa (reviewed diagnosis was that of expansion of the gastric cardia into the distal esophagus); 2 patients had occasional Cdx2 positive cells showing cardia- type mucosa with goblet cells (early BE ?).

Conclusion: The estimated prevalence of CLO-BE in the pediatric population of South Yorkshire (England) is 0.0024%, 0.8% in children referred for endoscopy and 5.5% in the children with reflux esophagitis. Characterization of the BE and confirmation of intestinal differentiation may have prognostic implications that can impact the surveillance program. Our results confirm that Cdx2 is a marker of established intestinal differentiation (either metaplastic or not) as was only reactive in those cases depicting identifiable goblet cells. This suggests that: goblet cells are the key marker of intestinal metaplasia and that the sole finding of CLO does not indicate intestinal differentiation (1/3 of our cases with CLO-BE did not have goblet cells and were Cdx2 negative).

The different criteria used by the ACG and the BSG to diagnose BE creates confusion and discrepancies when calculating the incidence, prevalence and malignant potential of this condition. A unified or consensus classification of BE would solve this conflict.

O2 INTRACTABLE DIARRHEA OF INFANCY WITH INTESTINAL EPITHELIAL DYSPLASIA (TUFTING ENTEROPATHY): IS THERE A CLINICAL AND PATHOLOGICAL CORRELATION?

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Background: Intestinal epithelial dysplasia (IED) is a congenital intestinal mucosa developmental disease characterised by a severe intestinal insufficiency leading to dependence on parenteral nutrition (PN) and in some cases to small bowel transplantation. In rare cases, a favourable evolution leading to wean children from PN has been reported.

Aim: The aim of this study was to evaluate the correlation between intensity of histological lesions on duodenal biopsies and clinical outcome in children with IED treated in our institution

Methods: Between 1993 and 2003, seven children were diagnosed with IED on the basis of the following criteria: 1) intractable diarrhea of neonatal onset with prolonged dependence on PN 2) histological lesions of intestinal mucosa: villus atrophy, epithelial dysplasia with enterocyte dedifferentiation and enterocyte disorganization with rounding of the apical plasma membrane giving a "tufting" appearance of the surface epithelium, abnormal glands (dilatation, branching).

Children followed less than 3 years and children with immunological intractable diarrhea or constitutional enteropathy (microvillus inclusion disease, syndromic enteropathies) were excluded from this study.

Histological lesions were semi-quantified and were compared according to the evolution over time and according to dependence on PN.

Results: Seven children, all from consanguineous parents, were followed for a median duration of 6.5 years. Three were definitively weaned from PN at the age of 3, 4 and 12 years respectively and experienced a normal growth without nutritional assistance.

These three children had severe histological lesion on the initial biopsies before suppression of PN: subtotal villus atrophy associated with partial villus atrophy (2/3), numerous and diffuse enterocyte dedifferentiation with tufting (2/3), hypocellular lamina propria (2/3), abnormal glands (3/3), < 10% intraepithelial lymphocytosis (3/3).

Progressive suppression of PN in some children with IED is possible. In our experience, this favourable outcome could not be predicted from the intensity of histological lesions.
In the future, identification of new biomarkers should best identify these lesions and their evolution.

O3 ISSUES IN SUBTYPING OF RHABDOMYOSARCOMA AT THE PARATESTICULAR SITE.

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AIMS OF STUDY: To review the UK Paratesticular Rhabdomyosarcoma (RMS), registered in MMT 95, with a aim to subtype RMS in this site

BACKGROUND: RMS is the most common sarcoma in children under the age of 15 years. Paratesticular RMS accounts for about 7% of all RMS and this localization is regarded as a favorable prognostic presentation.

MATERIAL AND METHODS: 53 cases of paratesticular rhabdomyosarcoma (RMS) have been reviewed by four pathologists and categorized using standard morphological criteria according to the current World Health organization (WHO) classification of Soft tissue and Bone Tumor.

When available, the patient's age, clinical presentation, diagnostic procedures, treatments methods and outcome were recorded.

In all cases the following histological features were analyzed: microscopic nodularity, percentage of alveolar and embryonal component, perivascular lymphocytic infiltrate and indian filing. Anaplasia (Pleomorphism) was also analyzed in each case.

A large and exhaustive panel of Immunohistochemistry markers were carried out and most specifically for markers such as Desmin, Myogenin, Myod1, EGFR and AP2 beta.

Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) for the ARMS associated PAX3/FKHR and PAX7/FKHR fusion genes and dual colour break apart Fluorescent in Situ Hybridization (FISH) probe for FKHR gene were carried out either in the referring hospital or as part of the review.

Subclassification used for the study was as follows:

Classic Embryonal RMS, Spindle cell Embryonal RMS, Classic Alveolar RMS, Solid alveolar RMS, Microalveolar RMS and Mixed Embryonal/ Alveolar RMS.

RESULTS: Out of 53 cases, histological and immunohistochemical features showed 22 ERMS (of which 20 Classic Embryonal RMS, 2 Spindle cell embryonal RMS), 11 ARMS (of which 10 classic alveolar RMS, 1 solid Alveolar RMS), 7 microalveolar RMS and 13 Mixed Embryonal/ Alveolar RMS.

Molecular analysis was carried out as follows:

14 of 22 ERMS, 6 of 11 ARMS, 1 of 7 of Microalveolar RMS, 11 of 13 of Mixed Embryonal/ Alveolar RMS

In 4 of the ARMS cases (6) RT PCR showed positivity for PAX3/FKHR fusion gene with 100% concordance of RT-PCR and FISH. All cases tested of ERMS, Microalveolar RMS and both ERMS and ARMS components of the Mixed histological subtype were negative for FKHR rearrangements, a finding confirmed by RT-PCR analysis.

Interestingly, Ap2beta antibody showed a strong nuclear positivity in the ARMS cases positive for translocation, indicating AP2 beta could be useful as a new marker for RMS subgroup classification.

CONCLUSION: 20 out of the 53 cases did not fit with the classic International classification with 7 having a Microalveolar pattern and 13 with Mixed Embryonal/ Alveolar pattern.

Molecular diagnostics were not helpful in these cases.

These results will be fully discussed.

O4 hTERT EXPRESSION IN MALIGNANT PERIPHERAL NERVE SHEATH TUMORS (MPNST) OF PEDIATRIC AGE: CORRELATION WITH TUMOR GRADE AND PROGNOSIS.

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Telomerase is a complex ribonucleoprotein enzyme that extends telomeric repeats on the ends of chromosomes, preventing the progressive shortening in each cell division that would lead to replicative senescence of cells. hTERT is the catalytic subunit that provides the function to replicate the ends of chromosomes. In epithelial neoplasms hTERT is frequently increased, but in sarcomas it is less well characterized. We have investigated the expression of hTERT in a series of pediatric MPNST and its correlation with grading and prognosis

Methods and results: 19 MPNST enrolled in the Italian protocol for soft tissue tumors (RMS 88, RMS 96) were

reviewed and graded according to the French FNCLCC system. Immunohistochemical staining for hTERT was performed, and the results were scored as follows: 0, negative; +1, weak positivity in rare cells; +2, strong and diffuse positivity.

The age range of patients was 1-17 yrs; 7 suffered from NF1, 8 did not show any syndrome; for 4 patients the status was unknown. The mean follow-up was 4.8 yrs (range 1-9 yrs). 8 patients died (1 for toxicity), 1 had local relapse, 1 is alive with disease.

hTERT expression was detected in 12 cases (63%), with +1 in 6 and +2 in other 6 tumors. NF1-associated MPNST were positive in 4/7, with +2 in only one case; conversely, 7/8 non NF1-associated MPNST were positive, with +2 in 4 cases; MPNST with unknown NF1 status were positive in 1/4 cases.

The relationship of tumor grade and hTERT expression was the following: G1: hTERT 0 in 1/5, +1 in 3/5 and +2 in 1/5; G2: hTERT 0 in 2/4, +1 in 1/4 and +2 in 1/4; G3: hTERT 0 in 4/10, +1 in 2/10 and +2 in 4/10.

Death occurred in 1/6 patients with hTERT 0, in 3/6 with hTERT +1 and in 4/6 with hTERT +2; follow-up was not available for 2 patients (1 hTERT 0 and 1 hTERT +2).

Conclusions: Pediatric MPNST express hTERT in 63% of the cases, with strong immunoreactivity in 31.5% of cases, and +2 positivity is more frequent in tumors not associated with NF1. In addition expression of hTERT seems to be related to an unfavorable prognosis.

O5 SUBTOTAL CHEMOTHERAPY-INDUCED NECROSIS IN LOCALIZED NON-ANAPLASTIC WILMS' TUMOURS IS AN INDICATOR OF EXCELLENT PROGNOSIS – THE SIOP 93 01 RESULTS

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Pre-operative chemotherapy has been used in the SIOP Nephroblastoma Trials in order to reduce the risk of tumour rupture during surgery, induce a favourable stage distribution with more patients in lower stages requiring less post-operative therapy, and to identify "good responders" in stage IV patients. Previous studies have shown that complete necrosis induced by preoperative chemotherapy in Wilms tumour (WT) is an indicator of low risk, and the histological response to chemotherapy has been used for treatment stratifications in other tumours such as osteosarcoma and Ewing's sarcoma.

The aim of this study was to evaluate whether subtotal tumour necrosis is associated with a comparably good outcome as seen in completely necrotic WTs.

Materials and Methods. The cases were identified from the SIOP 93 01 Nephroblastoma Trial and Study which run from 1993 to 2001. The criteria for inclusions were: cases reviewed by the SIOP Panel of Pathologists; non-anaplastic and non-metastatic WTs; and follow-up of at least 36 months. The subtotal chemotherapy-induced necrosis was defined as the presence of >90% of non-viable tumour.

Results. There were 50 WTs showing complete necrosis including 23 (46%) stage I, 13 (26%) stage II, and 14 (28%) stage III. Out of 164 WTs with subtotal necrosis, 71 (43%) were stage I, 64 (39%) stage II, and 29 (18%) stage III. Event-free survival per stage between the two groups was as follows: stage I - 96% (22/23) vs. 94% (67/71); stage II - 92% (12/13) vs. 92% (59/64); and stage III - 100% (14/14) vs. 97% (28/29) for completely necrotic and sub-totally necrotic WTs, respectively. Overall survival was as follows: stage I - 96% vs. 100%; stage II - 92% vs. 95%; and stage III - 100% vs. 97%, respectively. For all I-III stages taken together, EFS was 96% vs. 94%, and OS was 98% vs. 98%, respectively.

Conclusion. Sub-total chemotherapy-induced necrosis (>90%) in non-anaplastic and non-metastatic WTs is associated with excellent prognosis which is virtually identical to the excellent prognosis of completely necrotic WTs and, therefore, reduction of treatment seems justified as it is already done for completely necrotic tumours.

O6 INTRAUTERINE LASER PHOTOCOAGULATION FOR CONGENITAL EXPANDING PULMONARY LESIONS: LATE HISTOPATHOLOGIC EFFECTS OF A NOVEL THERAPEUTIC INTERVENTION

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Aim: To describe the chronic histopathologic effects on the lungs, following intrauterine percutaneous laser photocoagulation (PLP), a novel therapeutic modality applied for the treatment of congenital expanding pulmonary lesions.

Patients and Method: We describe the laser-induced histopathological effects in two infants successfully treated in utero. Intrauterine PLP was used to photocoagulate the feeding vessels of a congenital cystic adenomatoid malformation in the first case and of a pulmonary sequestration in the second. The pulmonary lesions were surgically resected postnatally, 18 and 5 months after the intrauterine laser intervention respectively.

Results: Chronic laser injury in the resected specimens was mainly characterized by vascular injury, resulting in hemorrhage and necrosis, repair procedures with diffuse stromal fibrosis, secondary structural alterations, atelectasis, and mild inflammation.

Conclusion: These late effects of laser injury to the lungs raise concern for possible long term clinical consequences of laser irradiation. We suggest that the option of elective postnatal surgical resection should be considered in any infant exposed to laser energy during fetal life. More interestingly, in view of the dramatic increase of evolving laser applications, awareness is raised for the potential of laser energy as a source of human injury.

O7 CONGENITAL GLUTAMINE SYNTHASE DEFICIENCY : FIRST NEUROPATHOLOGICAL REPORT

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Aim of study : Human glutamine synthetase (GS) deficiency with systemic deficiency of glutamine was first described in 2005 (1). It results in a congenital syndrome with early fatal course and with brain involvement as a leading sign (2). We report here the first neuropathological description of GS deficiency.

Materials: Patient was the second child of consanguineous Turkish parents. An elder 2^{1/2} years sister was healthy but mother had two miscarriages and a terminated pregnancy at 34 weeks two years before because of the US prenatal detection of multiple malformations including cerebral ventricular dilatation and gyration defects. The proband was a boy born spontaneously at 35₋ weeks after a pregnancy marked by US detection at 29 weeks of polyhydramnios, micromelia, cerebral ventricular dilatation and a paraventricular frontal cyst. Chromosome analysis was normal 46, XY. Birth weight, length and OFC were respectively 10th - 3rd - 10th and 75th - 90th percentiles). At birth he was resuscitated and transferred to the neonatal intensive care unit. He had a very poor neurological condition and heart insufficiency with low blood pressure and died at 2 days of life. EEG showed nearly no cerebral activity, but generalized seizures. Skeletal X rays showed micromelia, brain MRI showed enlarged lateral ventricles and complete agyria except for a few undulations at the fronto-parietal junction, paraventricular cysts, abnormal white matter , thin corpus callosum and small and smooth cerebellum. Biochemical investigation revealed absence of glutamine (serum 2 µmol/l; urine not detected; CSF 11 µmol/l).

Results: Post-mortem examination showed no visceral malformations. On neuropathological examination the brain was small, weighting 202 g (expected weight for gestational age = 335 g), and pachygyric with only a few primary fissures. The cerebellum was small and had a compact foliation. On sections, the white matter displayed the most marked lesions , both at the supra and infra-tentorial level , with multiple cavitations including bilateral and large paraventricular cysts and a diffuse greyish and gelatinous appearance. At histological examination lesions consisted on spongiosis, gliosis and diffuse glial apoptosis. By contrast, the grey matter appeared relatively spared with only intraneuronal calcifications in the thalami, but no anomalies of the cerebral cortex whose lamination was in keeping with the gestational age. There were multifocal necrosis lesions in the olivary nuclei and loss of neurons in cranial nerve nuclei. The lesions observed could be interpreted as clastic. However, they display a marked involvement of the white matter, arguing for a putative disorder of amino-acid metabolism.

Conclusion: The lesions observed in our patient mainly involve the cerebral glial cells according to the reported high concentrations of GS in human brain, and its location into astrocytes cytoplasm. GS catalyzes the conversion of glutamate and ammonia to glutamine. The lesions mechanisms could result either from glutamine deficiency either from deficient ammonia detoxification. Indeed, GS deficiency is lethal in early mouse embryogenesis (3) , interestingly, it is associated with miscarriage in our family. Hyperammonemia is highly toxic for the developing brain and induced both glial and neuronal death (4). From a neuropathological point of view, congenital GS deficiency is a metabolic disorder that presents with clastic features, probably leading to misdiagnoses and impaired genetic counselling.

O8 NEUROPATHOLOGICAL PHENOTYPE OF A NEW TYPE OF LISSENCEPHALY ASSOCIATED WITH *TUBA1A* MUTATIONS

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BACKGROUND: In 2007, Keays et al identified in an ENU-induced mutant mouse, a mutation in *Tuba1a*, a gene coding for alpha 1 tubulin protein, associated with behavioral disorders and a disturbance of the cortical cytoarchitecture. Subsequently, mutations of *TUBA1A* were found in children with mental retardation and lissencephaly with abnormalities of the corpus callosum and cerebellum, on MRI. Recently, mutations of *TUBA1A* were found in 4 fetuses, with a prenatal diagnosis of cerebral dysgenesis leading to a medical termination of pregnancy according to French laws.

OBJECTIVE: To report neuropathological data from these fetuses, for delineating the neuropathological fetal phenotype associated with *TUBA1A* mutations, and compare it with other lissencephalies with known gene mutations (*LISI*, *DCX*, *ARX*, and *RELN*)

DESIGN: These fetuses were studied at 23, 25, 26 and 35 gestational weeks respectively. All were found negative for mutations of *LISI*, *DCX* and *ARX*. Both parents of these fetuses were studied (except in 1 case) None of the identified changes was found in the parents suggesting a *de novo* occurrence of these mutations.

RESULTS: The neuropathological study demonstrated a phenotype including abnormalities affecting constantly the neocortex, hippocampus, corpus callosum, cerebellum and brainstem, and inconstantly, basal ganglia, olfactory bulbs and subventricular germinal zones. The combined anomalies of the 4 cases suggest a disturbance of migration, neuronal differentiation and axonal guidance, although these abnormalities were not identical in each case. This phenotype was different from that of *LISI*, *DCX*, *ARX* lissencephalies, and in agreement with the pattern of expression of *Tuba1A* studied in the mouse embryo.

CONCLUSION: We describe the neuropathological phenotype of a recently identified type of lissencephaly associated with *TUBA1A* mutations. Compared with children mutated for *TUBA1A*, fetal cases are located at the most severe end of the spectrum, suggesting that prenatally diagnosed cases are probably the most severe forms of *TUBA1A* lissencephaly. We would like to emphasize the paramount importance of neuropathological examination for a precise description and identification of the *TUBA1A* phenotype and, more generally, for directing the molecular studies towards an accurate diagnosis.

09 HYPERPLASTIC CARDIOMYOPATHY – A LETHAL FAMILIAL DILATED CARDIOMYOPATHY CHARACTERISED BY MYOCYTE HYPERPLASIA AND PROLIFERATION

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Aim of Study: This is a retrospective review of autopsies of five infants dying in early infancy of a rare form of dilated cardiomyopathy characterized by a distinctive histology of myocyte hyperplasia with marked proliferative activity.

Materials and Methods: We reported five cases of this rare form of hyperplastic cardiomyopathy in the Pathology Division of the Hospital for Sick Children over a 15-year period. Autopsy reports and glass slides including relevant immunohistochemical stains were reviewed. The five infants were all females, and included two pairs of siblings. Death occurred in early infancy (range 22 to 67 days, mean 42 days). No specific birth or early neonatal problems were recorded in all five cases. Clinical presentation was with general lethargy (n=5), decreased feeding (n=4), respiratory distress (n=3), and cyanosis (n=2).

Results: Autopsy revealed findings of congestive cardiac failure in all five infants, with serous pericardial, pleural and peritoneal effusions present in all five cases. The hearts were enlarged and heavy in comparison to age-specific reference values. Chamber dilatation was present in all five cases, with ventricular dilatation more pronounced than atrial dilatation. Mild to moderate endocardial fibroelastosis was present in all cases. The myocardial histological features were distinctive and identical in all five cases: there was prominent hypertrophic changes of myofibres, featuring elongated nuclei with enlarged and hyperchromatic nuclei. Mitotic activity was markedly increased, with mitoses numbering up to 4 per single high-power field. Scattered atypical mitotic figures were noted. This contrasted with age-matched control myocardium in which mitoses were very rare or absent. Immunohistochemical staining for MIB-1 showed a markedly increased proliferative index of up to 20%, which contrasted with age-matched normal myocardium with a proliferative index of less than 1%. Ancillary investigations did not reveal a primary cause for the cardiomyopathy.

Conclusion: We describe five cases of a rare form of dilated cardiomyopathy characterised by distinctive histological features of myocyte hyperplasia and marked mitotic activity. This condition is lethal in early infancy. Its occurrence in two pairs of siblings suggests familial inheritance. To our knowledge, only one previous case of this distinctive entity has been described in the literature (Zerbini C, Weinberg DS, Perez-Atayde AR. DNA ploidy analysis of myocardial hyperplasia. Hum Pathol 1992; 23: 1427-1430). It is important to recognize this distinctive

entity at autopsy for purposes of genetic counseling. Further investigation into the molecular pathogenesis of this condition is warranted.

O10 ASSOCIATION OF NONCOMPACTION OF LEFT VENTRICULAR MYOCARDIUM WITH EBSTEIN'S ANOMALY – A MALFORMATION OR A DEVELOPMENTAL ARREST ?

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Noncompaction of the myocardium (NCVM) is a rare congenital cardiomyopathy characterized by numerous excessively prominent trabeculations and deep intertrabecular recesses. NCVM is most often an isolated cardiac malformation presenting as a sporadic disease. Associated cardiac anomalies are present in some cases. We report a case of noncompaction of heart associated with Ebstein's anomaly presented as fetal hydrops.

This was a second pregnancy in a 34 year old woman with previous miscarriage at 12 gw. The US scan at 20 wks had shown asymmetry on the four chamber view of the heart. The repeat scan at 22 gw showed bright tricuspid valves displaced into the right ventricle. There was fetal arrhythmia and serous cavity effusions. Diagnosis of Ebstein's anomaly with fetal hydrops was made. Parents decided to continue with the pregnancy. There was IUD at 31 gw.

The autopsy showed a macerated, non dysmorphic, hydropic female fetus with linear measurements below 3rd centile and body weight above 10th centile. Examination of heart confirmed Ebstein's anomaly and also revealed noncompaction of left ventricle and possible coronary artery fistula.

This is a fourth case in the English literature including a family with two cases. NCVM is thought to be caused by arrest of normal process of endomyocardial morphogenesis and Ebstein's anomaly is a result of a non liberation of the tricuspid valve from the right ventricular myocardium. Co-existence of these two anomalies further supports the developmental arrest as a mechanism of these anomalies. Ebstein's anomaly rarely presents with early onset hydrops. Co-existent non compaction of ventricle and arrhythmia may explain early hydrops in this case.

O11 SUDDEN DEATH DUE TO ADENOVIRUS TYPE 3 MYOCARDITIS.

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An 11 year old boy collapsed at home. He had attended his general practitioner one day prior with tonsillitis. Cardiopulmonary resuscitation was unsuccessful. He had no past medical history of note and there was no family history of cardiac illness or sudden death.

At post-mortem examination his heart was enlarged (weight 214.2g, expected 124g) and on sectioning the myocardium appeared diffusely abnormal with areas of petechiae and pallor. There was no evidence of myocardial hypertrophy. Histologically there was a severe myocardial infiltrate diffusely present composed of lymphocytes, histiocytes, plasma cells with occasional eosinophils and neutrophils. There were admixed areas of necrosis and haemorrhage. There was no evidence of fibrosis or myofibre hypertrophy.

Adenovirus type 3 DNA was obtained from sections of the myocardium by polymerase chain reaction (PCR) using degenerate hexon gene-specific primers and subsequent nucleotide sequencing. Adenovirus DNA was also detected in the serum by quantitative PCR (mean 6,049 copies/ml) and the adenoviral loads detected in the myocardium tissue (83,910 viral genomes per g of tissue) are at a level which is indicative of infection rather than contamination or latent infection.

Myocarditis is a rare cause of sudden death in childhood. Aetiological agents which cause myocarditis include a wide range of pathogens. Viral myocarditis due to enteroviruses has been reported in up to 50% cases, however PCR for enterovirus was negative on all specimens tested from this child. Various serotypes of adenovirus have been implicated in autopsy series but death due to adenovirus type 3 myocarditis has not previously been reported. Isolation of viruses from myocardial tissue at postmortem is problematic, however the advent of highly sensitive and specific molecular techniques has important diagnostic implications.

O12 LETHAL URINARY TRACT MALFORMATIONS AT THE WIGGLESWORTH PERINATAL-PAEDIATRIC PATHOLOGY SERVICE/IMPERIAL COLLEGE HEALTHCARE NHS TRUST

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Aim of Study: What was the breakdown of lethal urinary tract malformations at the Wigglesworth Perinatal-Paediatric Pathology Service/Imperial College Healthcare NHS Trust? How often was lower urinary tract obstruction due to urethral atresia?

Materials and Methods: Over a 2_ year period, lethal urinary tract malformations were sought in all 584 perinatal post-mortems performed by the Wigglesworth Perinatal-Paediatric Pathology Service/Imperial College Healthcare NHS Trust. When lower urinary tract obstruction was suspected, the pubic bones were separated anteriorly and the urethra was dissected out without mutilating the external genitalia, serially cross-sectioned, and submitted *in toto* for microscopic examination.

Results: Over the 2_ year period, lethal urinary tract malformations were found in 29 perinatal post-mortems (5% of the 584 perinatal post-mortems). The breakdown was:

LETHAL URINARY TRACT MALFORMATIONS

RENAL AGENESIS	3
RENAL AGENESIS [FRASER SYNDROME IN BROTHERS]	2
RENAL AGENESIS [LEFT] AND MULTICYSTIC/DYSPLASTIC KIDNEY [RIGHT]	1
MULTICYSTIC/DYSPLASTIC KIDNEYS	4
MULTICYSTIC/DYSPLASTIC KIDNEYS [MECKEL-GRUBER SYNDROME]	4
URINARY BLADDER EXTROPHY	1
LOWER URINARY TRACT OBSTRUCTION	
URETHRAL ATRESIA	9
POSTERIOR URETRHAL VALVES	3
URETHRAL DYSFUNCTION [SHORT FILUM TERMINALE]	1
HYDROMETROCOLPOS [MCKUSICK-KAUFMAN SYNDROME]	1

[Except for the brothers with Fraser Syndrome (tracheal atresia with voluminous lungs), most had profound lung hypoplasia.]

Conclusions: At the Wigglesworth Perinatal-Paediatric Pathology Service/Imperial College Healthcare NHS Trust, the most common lethal urinary tract malformation was lower urinary tract obstruction due to urethral atresia.

O13 WARFARIN EMBRYOPATHY IN CAPE TOWN

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Aim of Study: to investigate the range of malformations in a postmortem series of 13 fetuses with Warfarin embryopathy

Materials & Methods : the autopsy reports and babygrams of fetuses exposed to Warfarin during pregnancy were retrieved from our archives and reviewed.

Results : Gestational age ranged from 17-37 weeks. Eight mothers had mechanical heart valves and were aged 17-36 years.

On external examination eleven fetuses had a nasal abnormality; the remaining two had normal noses. The characteristic deep grooves of the alar nasi were present in only one case.

Radiographs revealed widespread epiphyseal stippling in two fetuses; a third had dot calcification. Three had 11 pairs of ribs, one had a short sternum, and one had delayed bone maturation. One foetus had dystrophic toes, while five had no radiologic abnormality.

A striking abnormality was cerebral haemorrhage in 8 cases. Two of these had haemorrhaged prior to 20 weeks gestation, 4 developed haemorrhage between 21-30 weeks and two between 31-40 weeks. The haemorrhage was present in multiple sites within the brain in 5 of the 8 fetuses.

Two fetuses had hydrocephalus. White matter necrosis was present in two cases with associated dystrophic calcification in one case.

Other malformations included pelvi-ureteric junction obstruction, premature closure of the ductus arteriosus, optic nerve neuroma, macroglossia and Leydig cell hyperplasia in the testis. Three of the fetuses with congenital malformations also had cerebral haemorrhage.

Conclusion: Warfarin has severe adverse effects in the foetus. However Warfarin offers the mother the greatest protection from thrombosis.

O14 TRISOMY 21 COMPLICATED BY MYELOPROLIFERATIVE DISORDER IN THE PERINATAL PERIOD

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Aim of Study: After two Trisomy 21 stillbirths due to myeloproliferative disorder (MPD), we wondered how often Trisomy 21 was complicated by MPD in the perinatal period.

Materials and Methods: Over a 10 year period, 18 Trisomy 21 (29+ weeks gestation) post-mortems were performed by the Wigglesworth Perinatal-Paediatric Pathology Service and were checked for myeloproliferative disorder (MPD).

Results: Over the 10 year period, 4 of the 18 (22%) Trisomy 21 (29+ weeks gestation) post-mortems had myeloproliferative disorder (MPD). The mean maternal age was 31 years (range: 25-38 years). MPD was not diagnosed antenatally. The mean gestational age was 31 weeks (range: 29-34 weeks). Three were stillborn (2 boys and 1 girl) and one was a liveborn girl (31 weeks gestation) who lived for 9 hours. In the 3 unlimited post-mortems, 2 had hepatomegaly and all 3 had splenomegaly. Despite maceration/autolysis, the liver and spleen were often rubbery due to fibrosis. The liver and spleen were packed with blasts. In the stillborn girl, the massive spleen had ruptured *in utero* with blasts infiltrating the diaphragm and the walls of the stomach and abdomen. In the liveborn girl, blasts distended vessels of her lungs, heart, kidneys, and brain. In the limited post-mortem, back-to-back blasts distended and obstructed the entire lengths of the umbilical cord vessels as well as many placental vessels (fetal plate and chorionic villi).

Conclusions: In our perinatal post-mortem population, myeloproliferative disorder (MPD) complicated 22% of the Trisomy 21 (29+ weeks gestation) post-mortems. Thus, MPD is a continuum that can adversely affect Trisomy 21 babies before birth as well as after birth. In macerated/autolysed Trisomy 21 stillborns, the better-preserved placenta can often provide crucial clues to the diagnosis of MPD.

O15 COULD THE PLACENTA OF THE MATERNAL HYPERINSULINEMIA INTRAUTERINE GROWTH RESTRICTION (IUGR) RAT BE A MODEL FOR HUMAN GROWTH RESTRICTION?

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Background: Maternal hyperinsulinemia is associated with pregnancy-induced hypertension. In our model, which is characterized by perturbation of the NOS system, the growth restricted (GR) offspring develop adult hypertension similar to humans. The hemochorial rat placenta, featuring deep implantation similar to humans, is widely used as a model. We studied the morphologic and molecular aspects of the placenta in our model to evaluate its similarity to the human placenta in GR.

M&M: Placentas of hyperinsulinemic dams (HD) and normal controls (ND) were dissected on day 21 of gestation. Some of the placentas were weighed and submitted for histopathology and molecular studies. Other placentas were dissected with the uterine wall to include the mesometrial triangle and were submitted for histopathology. Immunohistochemistry was performed for the proliferation marker Cdc47, pancytokeratin and α actin. For visualization of uterine NK cells (uNK) P.A.S. stain following diastase treatment was performed. eNOS expression was measured by northern blotting. Image analysis was used to study proliferation rate in the placenta and the interstitial trophoblast (IT)-to-uNK ratio in the mesometrial triangle.

Results: The placentas of the HD were significantly smaller than those of ND ($p < 0.05$) and their proliferation rate was markedly higher both in the labyrinth ($p < 0.001$) and in the junctional ($p < 0.0002$) zones. IT/uNK ratio was significantly lower in the placentas of HD vs. controls ($p < 0.004$). eNOS expression was significantly lower in the placentas of HD than in those of ND ($p < 0.01$). Other morphological changes in the placentas of HD were smaller mesometrial lymphoid aggregates (mLAP) of pregnancy and prominence of intravascular trophoblasts in the region of the mLAP.

Comment and conclusion: With progression of rat gestation the number of IT in the mesometrial triangle increase and the number of uNK decrease. Our findings suggest a delay in the normal process of implantation in our model of PIH and IUGR. Although data regarding eNOS expression in the placenta is conflicting, the lower eNOS expression in our model goes along with lower eNOS expression in human IUGR. The increased proliferation of trophoblastic cells of the HD placentas is concordant with the proliferation of cytotrophoblasts and of immature intermediate trophoblast in the placenta in pre-eclampsia. Further investigation of the processes occurring during implantation resulting in fetal GR in our model is required.

O16 AN UNUSUAL VILLOUS VASCULAR MALFORMATION OF THE PLACENTA ASSOCIATED WITH FETAL HYDROPS AND INTRAUTERINE DEATH - A CASE REPORT.

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Abstract: We report the case of an intrauterine fetal death diagnosed at 30 weeks gestation. The normally formed male fetus was hydropic, growth restricted (4th centile) and severely anaemic. The placenta was markedly enlarged and hydropic and showed a strikingly abnormal villous vasculature associated with an unusual dense, hyaline stroma. This anomalous villous morphology is, to the best of our knowledge, previously undescribed. We postulate that this lesion, possibly a rare variant of placental mesenchymal dysplasia, was the cause of the fetal anemia, hydrops and growth restriction.

Case Report: The male fetus was born to non-consanguineous Caucasian parents with 3 previous healthy children born at term. There was no other relevant past medical, family or obstetric history. Intrauterine fetal death was diagnosed at 30 weeks gestation in an otherwise uneventful pregnancy.

At autopsy the male fetus showed growth restriction (weight on 4th centile (customised)). The baby was very pale and showed mild skin and scalp oedema and small bilateral pleural and pericardial effusions. There were no congenital malformations, no internal haemorrhage and no evidence of viral infection.

The placenta weighed 973g (90th centile 384g) with macroscopically oedematous parenchyma and an oedematous umbilical cord. Histology showed striking enlargement of more than 50% of the villi, many of which contained abundant branching, ectatic, thin-walled vessels. The stroma of the enlarged villi was generally hyalinised and contained dense bands of brightly eosinophilic collagen. The remaining villi were oedematous and poorly vascularised, consistent with placental hydrops.

A Kleihauer test had not been performed at the referring hospital and cytogenetic tests were unsuccessful.

Discussion: The placentomegaly and the histological features seen in the villi are, in part reminiscent of placental mesenchymal dysplasia (PMD); and could conceivably be part of the same phenotypic spectrum. However, to our knowledge, this pattern of vascular malformation has not previously been reported in PMD.

We postulate that fetal anaemia and hydrops was due either to repeated fetomaternal haemorrhage, as occurs in diffuse placental chorangiomas or in-situ choriocarcinoma or to microangiopathic haemolytic anaemia induced by mechanical destruction of red cells traversing these abnormal vessels. Unfortunately, a maternal Kleihauer test was not performed. The transfer function of these abnormal villi would have been extremely poor, resulting in intrauterine growth restriction, chronic hypoxia and ultimately fetal death.

O17 PLACENTA HISTOLOGY AS PREDICTOR FOR SHORT AND LONG TERM OUTCOME AFTER EARLY INTRAUTERINE GROWTH RESTRICTION

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Objectives To examine the relative importance of placental histology and other antenatal and perinatal variables on short and long term outcome of preterm growth restricted fetuses with umbilical artery Doppler abnormalities.

Methods Cohort study of 180 neonates with birth weight <10th percentile, gestational age (GA) <34 weeks and abnormal Doppler ultrasound examination of the umbilical artery (UA). Placenta and various antenatal and perinatal variables were studied in relation to short and long term outcome.

Results Neonatal mortality was significantly associated with GA at delivery, absent/reversed UA Doppler flow and abnormal ductus venosus examination. Both infant and overall death were significantly associated with birth weight, abnormal ductus venosus examination and placental villitis. GA was the only parameter that was significantly associated with both intraventricular hemorrhage and retinopathy of prematurity and placental villitis was the only parameter that was significantly associated with necrotizing enterocolitis. GA, birth weight, male sex and absent/reverse UA Doppler flow showed significant associations with respiratory distress syndrome. Abnormal neurodevelopmental outcome at 2 years of age was associated with birth weight, UA pH<7.00 and placental villitis.

Conclusion The present study confirms that GA and Doppler findings are important predictors for short term outcome in growth restricted foetuses. In addition, presence of placental villitis may aid neonatologists in early identification of infants at increased risk of necrotizing enterocolitis, death and abnormal neurodevelopment at 2 years of age. Abnormal neurodevelopment was also related to weight and acidosis at birth indicating that the severity of malnutrition and fetal acidosis affect long term outcome.

O18 ACUTE AND CHRONIC PLACENTAL MEMBRANE HYPOXIC LESIONS

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Aim of Study: Lamellar necrosis (LN) and microscopic chorionic pseudocysts (MCP) are the two histological placental membrane hypoxic lesions. This study retrospectively compares the clinical and placental associations of LN and MCP.

Materials and Methods: All placentas featuring either membrane LN (Group 1) or MCP (Group 2) were identified in the database of consecutively signed by me 4853 placentae (18-42 weeks gestation). 50 cases that showed both LN and MCP were excluded from the analysis. Frequencies or averages of several clinical conditions and gross and microscopic placental features were compared between Groups 1 and 2 (Chi-square at one degree of freedom or ANOVA, where appropriate).

Results: Although proportions of such clinical conditions as abnormal foetal heart tracings or IUGR or other placental hypoxic lesions such as global placental hypoxia or infarction were higher in each group than in the general placental population (not presented), they did not differ statistically significantly between Groups 1 and 2 ($p > 0.05$). The table compares the clinical and placental parameters for which statistically significant differences ($p \leq 0.05$) have been found between Groups 1 and 2.

Factors	Group 1 (479 placentas with LN)	Group 2 (220 placentas with MCP)
Average gestational age (weeks)	34	35
Preeclampsia	20%	27%
Diabetes mellitus	3.5%	10%
Stillbirths	12%	3%
Caesarean sections	32%	47%
Average placental weight (grams)	365	423
Maternal chorioamnionitis	22%	9%
Foetal chorioamnionitis	3%	9%
Meconium deep in decidua	13%	4.5%
Marginate placenta	12%	6%
Excessive amount of extravillous trophoblasts	4%	13%

Conclusion: LN, a watershed membrane infarction, appears to be an acute membrane hypoxic lesion, while MCP is a chronic hypoxic lesion most likely resulting from degeneration of a more widespread accumulation of extravillous trophoblasts in the placental disc and membranes. The substantial overlap of clinical and placental conditions between Groups 1 and 2 may be explained by the tendency of acute in-utero hypoxia to occur more frequently in conditions complicated by preexisting chronic placental insufficiency. That is most probably why LN occurs more frequently in smaller placentas and why both lesions may be seen together in same placentas.

O19 PERINATAL MORTALITY ANALYSIS IN A UNIVERSITY HOSPITAL IN TURKEY

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Aim of study: Perinatal mortality is one of the most important measures of health care in a country and covers antenatal, intrapartum and early postnatal deaths. Accurate and detailed classifications are necessary for better understanding the etiology of perinatal mortality and to improve it. We aimed to analyze and classify the etiological factors of perinatal mortality in our center.

Materials and Methods: Fetal deaths after 22nd week of gestation and early neonatal deaths were included in the prospective study between 2001 and 2006. All cases were evaluated and classified according to Wigglesworth and a more recent fundamental classification of perinatal death by the Perinatal Mortality Study Group of Hacettepe University Faculty of Medicine including Pathology, Neonatology, Genetic and Cardiology Units of Department of Pediatrics, Perinatology Unit of Department of Obstetrics and Gynecology and Department of Pediatric Surgery.

Results: The total number of births in this period was 9990 and total number of perinatal deaths was 353 (35.3%). Perinatal deaths included stillbirths (21.9%) (intrauterine death, intrapartum death and pregnancy terminations), and early neonatal deaths (13.7%). Analysis of subgroups revealed overall relative frequencies as follows: neonatal death 38%, intrauterine death 28.3%, termination of pregnancy 26.3% and intrapartum death 7.4%. Analysis of data revealed a relative increase in pregnancy terminations, leading to an increase in overall perinatal mortality rate from 35.6% in 2001 to 46.1% in 2006. Wigglesworth classification of data revealed relative frequencies of malformations (35.4%), prematurity (25.2%), asphyxia (12.5%), unclassified (special) etiologies (15.9%) and stillbirths (10.8%). Fundamental classification of data included lethal congenital malformations (36.3%), prematurity (25.2%), placenta/cord pathology (19.0%), unclassified (13.0%), maternal immune system pathology (3.1%), infections (2.8%) and trauma (0.6%). The overall autopsy rate was 61.2%.

Conclusion: Malformations and prematurity constitute the two most common etiological factors responsible from perinatal mortality. Neonatal deaths constitute the largest subgroup; however, since Hacettepe University is a referral center, termination of pregnancy as a result of advances in prenatal diagnosis is also an important subgroup.

O20 DIAGNOSTIC CONTRIBUTION OF BACTERIOLOGY AND VIROLOGY IN 121 CASES OF SUDI. AN APPRAISAL OF THE SOUTH YORKSHIRE INTER-AGENCY PROTOCOL.

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Background: Sudden Unexpected Death in Infancy (Sudi) applies to any death that occurs “suddenly” and “unexpectedly” in children. Sudi can occur in apparently completely well and healthy children, in infants and children who were considered to be mildly unwell but in whom death is unexpected and in others with a known serious but stable condition who suddenly die. The common link among all these situations is the occurrence of a rapid deterioration than culminates in death. Sudden infant death Syndrome (SIDS), the largest single category of death in babies over one month old, is only one type of Sudi.

The Kennedy Report (2004) formed the basis of the local South Yorkshire Inter-agency Protocol which was designed to standardise the approach to cases of Sudi in children younger than 2 years of age in our institution.

Objectives: Assessment of the bacteriology and microbiology results in the post mortem investigations conducted in 121 Sudi cases performed in our institution between January 2004 and December 2007. Our aim was to better define the relevance of these ancillary investigations in Sudi and to investigate the implications of the different post mortem intervals.

Methods: Restrospective investigation of the 121 post mortem reports regarding demographic information, post mortem interval, bacteriology and virology results. The clinico-pathological relevance of these latter were discussed in each case.

Results: The mean age of the patients was 6.6 months (mode: 3 months). Bacteriology and virology were not performed in 5 (4.1%) cases. In the remaining 116 cases the most frequent samples were from the blood, cerebrospinal fluid, middle ears and “other”. Overall the results were considered significant in 52/116 (44.8%) and not significant in 64 (55.2%). These two groups showed no significant difference in age. A blood culture (BC) was done in 105/116cases. This showed a positive result in 57 (55%) but was found to be significant in 17 (16%) and to be post mortem flora in 40 (38%). The average post mortem interval was 1.9 (mode: 1) days independently of the BC result. The cerebrospinal fluid was cultured in 79/116 (68%). This obtained a positive result in 10 (13%) cases but was relevant in 5 and was post mortem flora in other 5 cases. Samples from the middle ears were taken in 31 (27%) children, with 15 (48%) obtaining a significant result while non result was obtained in the remaining 9 patients. Other 115 samples were performed from different sites of the body. These obtained 40 (35%) other significant positive results.

Conclusion: The finding of a clinically significant result in 52/116 (44.8%) of our cases, although no necessarily the cause of death, confirms the relevance of performing multi site microbiology and virology investigations in all cases of Sudden Unexpected Death in Infancy.

O21 VALUE OF COMPLETE AUTOPSY IN FOETUS LESS THAN 500GRAMS – SEQUENTIAL REVIEW OF 100 CASES

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Aim: To review the diagnostic efficacy of post mortem examination in the foetus less than five hundred grams using recorded data from one hundred consecutive post mortem examinations.

Materials and Methods: One hundred consecutive cases from 2005 to 2007 were obtained from the Institution’s post mortem database. Post mortem reports and placenta histology reports were reviewed. Gestational age, birth weight, placental diagnosis, histology findings, cytogenetic results and cause of death were documented.

Results: The weight range of the foetuses was 1.69 to 499grams. Gestational age was 12 to 30 weeks. The incidence of causes of death were as follows: malformations (17%, 11/17 cases had documented aneuploidy); infection (35%); retroplacental haemorrhage (12%); umbilical cord accidents (14%); other (5%) and unexplained (17%). Histology findings were present in 78 cases; myocardial contraction bands (28 cases); intra-alveolar neutrophils (22 cases); presence of neutrophils in lumen of gastrointestinal tract (18 cases); growth arrests in ribs (31 cases); two-tone fatty change in liver (17 cases); stress effects in thymus (21 cases); central nervous system haemorrhage (4 cases). Oil Red O stain of the adrenal glands showed a range of abnormalities; fatty change of inner foetal cortex (26 cases); diffuse fatty change (5 cases); mild fatty change (3 cases); pseudoacinar change of adult cortex (9 cases); coarse fatty change (5 cases). Maceration was documented in 68% of cases.

Conclusions: The combined placental diagnoses provided the cause of death in 63% of cases. The remainder comprised malformations (17%), unexplained (17%) and others (3%-rhesus isoimmunization and cervical incompetence in 2 cases). While the latter causes may seem somewhat mundane, e.g.retroplacental haemorrhage, the use of histology of individual organs can usefully demonstrate a cause and effect profile. These histological results were obtained despite the expected presence of maceration in 68% of cases. The diagnostic yield for this scope of

examinations is significant in leaving only 17% of cases unexplained. This compares favourably with reported series in larger foetuses.

O22 BACTERIOLOGICAL SAMPLING IN SUDI – BLOOD AND GUTS?

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Introduction: It has been suggested that bacteriological sampling in cases of sudden unexpected death in infancy should include a spleen swab instead of, or as well as, blood culture. Putative reasons include a lower incidence of non-significant isolates and an increased chance of identifying significant organisms. In recent years, the author's practise has been to do both investigations. The purpose of this study is to evaluate this approach.

Materials and Methods: All autopsies performed on cases of sudden unexpected death in infancy by the author since 1st June 2000 were identified from departmental records. Only those cases in which both blood and spleen swabs were taken were included in the study. Spleen swabs were obtained by cleaning the surface with isopropyl alcohol and incising with a sterile scalpel blade. Blood samples were obtained from the superior sagittal sinus (or occasionally the heart) with a sterile syringe after cleaning with isopropyl alcohol. Blood culture bottles were not used.

Results: 74 autopsies were carried out on cases of sudden infant death between 1st June 2000 and 31st May 2008. In 62 cases, both blood and spleen samples were obtained and these cases were included in the survey. Blood and spleen swabs were both reported as showing "no growth" in 48 cases. Bacteria were isolated from blood only in 9 cases, and spleen only in 1 case. Both swabs yielded bacterial growth in 4 cases. All isolates were regarded as non-significant. The bacteria isolated from blood were coagulase negative staphylococci (6 cases), other single isolates (4), mixed organisms (2) and unspecified contaminants (1). The spleen yielded coagulase negative staphylococci (4 cases) and unspecified contaminants (1 case). When both swabs were positive, the organism was the same in one case and different in two cases. In five cases, the cause of death was a specific infective lesion (4 pneumonia, 1 acute on chronic pyelonephritis). Blood and spleen swabs were negative in all these cases, except for one isolate of coagulase negative staphylococci from a blood swab in a baby with pneumonia.

Conclusions: The results of this study suggest that spleen swabs in cases of sudden infant death may be less likely than blood swabs to yield non-significant bacterial isolates. This may be of value in assessing the significance of organisms grown from other sites. However, it cannot be concluded that spleen swabs should replace blood swabs, as this study provides no data on the sensitivity for identification of significant infective organisms.

ABSTRACTS

Poster Presentations

P1 SEPTAL AGENESIS : AN UNUSUAL MANIFESTATION OF VALPROATE EMBRYOPATHY

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BACKGROUND: Sodium Valproate (VPA) is the most popular antiepileptic drug because of its broad range of anticonvulsivant effects and relative freedom from sedative and behavioural effects. About 0.5 percent of pregnant women are affected by epilepsy. VPA is also prescribed in psychiatric disorders such as bipolar disorders affecting young women, which probably increases the rate of exposed women. The teratogenicity of Valproate has been demonstrated with the development of Antiepileptic Drug Pregnancy Registries in different countries. Prenatal exposure to VPA results in a constellation of malformations referred to as the Fetal Valproate Syndrome or Valproate Embryopathy. This congenital syndrome includes a characteristic facial phenotype, intra uterine growth retardation, different visceral and skeletal malformations and central nervous system dysfunction. Central nervous system involvement results in developmental deficits/mental retardation and malformations that are nearly constantly neural tube defects.

OBJECTIVE: We report unusual neuropathological findings in a fetus exposed to Valproate that probably expands the spectrum of anomalies associated with VPA prenatal exposure.

DESIGN: In a primigravida 19 year old epileptic woman, ultra sonography showed, at 23 weeks of gestation, “a ventriculomegaly and a large single ventricle suggesting a holoprosencephaly”. She suffered her first seizure at age 16 and took VPA, 4 g/day since 3 years and throughout the pregnancy. After medical termination of pregnancy, at 25 weeks of gestation, an autopsy was carried out and we performed a neuropathological examination.

RESULTS: The female fetus showed bifid ureter, macrocrania and characteristic dysmorphic facial features, associating high forehead, hypertelorism, short nose with broad nasal bridge, flat philtrum, thin upper lip and micrognathia. Neuropathological examination disclosed a moderate ventriculomegaly, an absence of septum pellucidum, a fusion of septal areas and hypoplastic hippocampi. All the other cerebral structures were normal, particularly optic pathways. Only one case of Septo-optic Dysplasia diagnosed after birth, on MRI, has been reported in the literature (McMahon et al 2001).

CONCLUSION: We report the first neuropathological study of isolated agenesis of the septum pellucidum, in a fetus exposed to VPA. This observation expands the phenotype of the Fetal Valproate Syndrome.

P2 MEDULLARY COMPRESSION CAUSING SCHWANNOSIS AND REFLEX ANOXIC SEIZURES.

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A 7 year old boy with a history of VACTERL Syndrome (Vertebral anomalies, Anal atresia, Cardiovascular anomalies, Tracheoesophageal fistula, Oesophageal atresia, Renal/Radial anomalies, Preaxial limb anomalies) was found collapsed in bed. Cardiopulmonary resuscitation was unsuccessful. At age 5 years an MRI had shown basilar invagination of the skull base and narrowing of the foramen magnum. Angulation, swelling and abnormal high signal at the cervicomedullary junction and a syrinx in the cervical cord were felt to be secondary to compression of the medulla. Surgical decompression resulted in initial symptomatic improvement. Later reflex anoxic seizures developed and required several admissions.

Post mortem examination showed bronchopneumonia. The medulla appeared slightly enlarged on sectioning.

Microscopy showed bilateral replacement of the medullary tegmentum by an irregularly circumscribed cellular lesion which encroached on the gracile and cuneate nuclei and which was composed of elongated cells with spindled nuclei showing minimal atypia. Cells were immunopositive for GFAP and S100 but not neurofilament. Wallerian degeneration of the crossed and uncrossed cervical corticospinal tracts was present. The pathologic findings were interpreted as intramedullary schwannosis with mass effect.

Schwannosis, whilst rare is typically observed in traumatised spinal cords where its presence is viewed by some as attempted, albeit aberrant, repair by inwardly migrating Schwann cells of peripheral origin. Involvement of brain stem is exceptional. In our view the compressive effect of the basilar invagination on this boy’s medulla was of sufficient magnitude to have caused tumoral medullary schwannosis with resultant intermittent respiratory compromise leading to reflex anoxic seizures.

P3 RELEASE OF ERYTHROBLASTS TO THE PERIPHERAL BLOOD SUGGESTS HIGHER EXPOSURE TO HYPOXIA IN CASES OF SUDI WITH CO-SLEEPING COMPARED TO SUDI NON-CO-SLEEPING.

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Background: Sudden unexpected death in infancy (SUDI) refers to the sudden death of an infant which is initially unexplained. In some cases the death may be explained after the post-mortem (PM). SUDI includes sudden infant death syndrome (Sids). Co-sleeping is regarded as a major risk factor for SUDI/Sids. Risk increases with multiple bed sharers and usage of drugs/alcohol by the bedsharer(s). The release of nucleated red cells (nRBCs, erythroblasts) to the peripheral blood has been described to occur in cases with a probably hypoxic mode of death.

Aim: To assess the significance of the release of erythroblast to peripheral blood in cases of SUDI occurring during co-sleeping

Material and methods: The presence of nRBCs was investigated in samples of blood collected in EDTA at the PM of 28 cases of SUDI < 2 years of age and in 6 other cases > 2 years. The data was analysed with SPSS version 13 for Windows using ANOVA One-Way and Post Hoc Tests.

Results: The cases were retrospectively assigned to one of the following categories: I) SUDI with no co-sleeping (9 cases, mean age: 29 months); II) SUDI while co-sleeping (15 cases; mean age: 2.6 months); III) COD in obvious hypoxic circumstances (3 hangings, 2 cardiac malformations, 1 meningitis 1 intoxication: mean age 4.3 years) and IV) Sids in the cot (3 cases, mean age: 3.1 months). NRBCs were present in 5/9 cases of group 1 (range: 0-2% Mean NBRBCs: 0.5%); 10/15 cases of Group 2 (range: 0.5-8%; Mean: 1.87%); 7/7 cases of Group 3 (range: 0.5-6; Mean: 3.78%) and 0/3 cases of Group 4 (mean: 0). Anova One-Way test obtained a value of $F=5.786$ and showed a significance of .003 amongst the 4 groups.

The presence of diffuse intra-alveolar haemorrhage was associated to higher release of nRBCs (Mean % nRBC: 3.1; range: 0-8) than focal haemorrhage (Mean % nRBCs: 0.6; range: 0-3).

Conclusion: The higher mean of % nRBCs seen in the co-sleeping SUDI cases compared to the non-co-sleeping cases suggests a higher exposure to hypoxia in the co-sleeping group which may have led to the increase in % nRBCs. More cases need to be analysed to confirm this hypothesis.

P4 COMPARISON OF CYTOKERATIN EXPRESSION IN LIVER BIOPSY SPECIMENS IN PATIENTS WITH BILIARY ATRESIA OF POOR AND GOOD PROGNOSIS

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Aim of the study was to compare intrahepatic cytokeratin expression in patients with biliary atresia of poor and good prognosis.

Material and Methods: In order to compare intrahepatic histological changes in patients with biliary atresia of poor and good prognosis, we have examined retrospectively 29 liver biopsy specimens taken during hepatoporoenterostomy modo Kasai. We divided the material into two groups: 12 biopsy specimens were qualified to the first - failure group because patients died or needed liver transplantation within 2 years after Kasai procedure and 17 biopsy specimens were qualified to the second - favorable group because children have survived over 5 years with no complications. All specimens were formalin fixed, paraffin embedded and evaluated for CK 7, 8, 18, 19 using an Envision kit (Dako)

Results: Liver fibrosis was assessed as follows: grade 1 mild fibrosis: expansion of fibrous tissue in the portal tract; grade 2 moderate fibrosis with portal to portal bridging; grade 3 severe fibrosis with portal to portal bridging; grade 4 cirrhosis with a reconstruction of hepatic lobules. The following categories of lesions were investigated: cholangitis, cholangiolitis, Ductal Plate Malformation, ductopenia, ductular proliferation, bile duct dilatation. Results: CK 7 expression was absent in bile duct cells with ductal plate malformation and was lower in patients with biliary atresia of poor prognosis. Expression of Ck 8, 18, 19 was similar in both groups. Ductular proliferation, reported by some authors as predictor of poor prognosis was observed in our material in both two groups and was rather associated with high grade fibrosis and cholestasis. In one case it was absent, but grade of fibrosis and cholestasis was also low. Proliferation was more intensive when ductal plate malformation was present.

Conclusion: CK 7 is a maturation marker in bile duct cells.

P5 NEONATAL HEMOCHROMATOSIS: A CONGENITAL ALLOIMMUNE HEPATITIS, REPORT OF 3 CASES WITH DIFFERENT PRESENTATIONS

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Neonatal haemochromatosis (NH) is a rare, severe neonatal liver disease associated with extrahepatic iron deposition. Increasing evidence suggests that the disease begins in utero as an alloimmune hepatitis in many cases

and fetal liver injury is a dominant feature. We herein describe three cases with NH presenting different clinical pictures.

Case 1 was a 4-month-old girl who was admitted to hospital with difficulty in feeding, vomiting and diarrhea. She had been hospitalized in another medical center for the first two months of life, due to hepatic failure and had been discharged when her clinical condition and laboratory findings had improved. On admission to our hospital she had dehydration, growth retardation, and hepatic and renal failure. She died of liver failure and sepsis on the 15th day of hospitalization. Autopsy revealed iron storage in the liver, pancreas and thyroid. Liver histology showed bridging fibrosis, pseudoacinar transformation, hemosiderosis and cholestasis.

Case 2 was a 22-day-old girl born with cesarean section following a 39 weeks of pregnancy and was admitted to our center with bleeding diathesis and jaundice compatible with hepatic failure. She was treated with presumptive diagnosis of congenital hepatitis and sepsis. She died of liver failure on 8th day of admission. Autopsy revealed heavy iron deposition in pancreas and less in adrenals, liver, myocardium and kidney. No hepatocytes but pronounced fibrosis and histiocytic infiltration were detected in the liver.

Case 3 was a 24-day-old boy who presented with massive ascites and jaundice in the first weeks of life. There was first cousin consanguinity. Past history revealed a sibling death with similar findings in another hospital. The patient was diagnosed as primary hemaphagocytic syndrome since he had bicytopenia, sibling death, parents' consanguinity and diffuse haemophagocytosis in bone marrow aspirate. Despite immunosuppressive treatment he died of acute renal and hepatic failure on the 16th day of admission. Autopsy revealed iron deposition in pancreas, Brunner glands, adrenal cortex, liver, myocardium and kidney. Liver showed cirrhosis, cholestasis and bile duct proliferation. Slides and paraffin blocks from the autopsy of the sibling were requested, reviewed and similar findings were found. All cases had hyperferritinemia, high serum AFP concentration and disproportionately low transaminase levels for the degree of hepatic injury.

Although neonatal haemochromatosis usually results in death in utero or in the first month of life, rare cases can survive for months. Since the risk of recurrence in subsequent offspring is high in affected woman and gestational use of IVIG has been shown to be effective to prevent recurrent severe NH, it is of vital importance to diagnose NH through a proper investigation including a complete autopsy.

P6 FISH ON EXTRACTED NUCLEI FROM FORMALIN FIXED AND PARAFFIN EMBEDDED TISSUES FOR THE DIAGNOSIS OF CHROMOSOMAL ANEUPLOIDIES IN MALFORMED FETUSES

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Introduction: The most frequent chromosomal anomalies in human pathology are aneuploidies especially the trisomy 13, 18 and 21 and the monosomy X since they are compatible with a postnatal life. These anomalies generally produce severe malformations that could terminate the pregnancy without any prenatal Karyotype. The use of fluorescent in situ hybridization (FISH) to detect and characterize these chromosomal anomalies is largely applied in lymphocytes and amniocytes but its use on formalin- fixed and paraffin-embedded tissues is not routinely made. The aim of this study is to detect above mentioned anomalies using FISH technique.

Material and Methods: 20 fetuses have been screened for the specific malformations of these chromosomal aneuploidies. Nuclei have been extracted from kidney and liver formalin- fixed and paraffin embedded tissues. FISH then was tested on the extracted nuclei by a combination of a contig of probes from chromosome 21, 13 on one hand and centromeric probes of chromosomes X and 18 on the other hand.

Results: Trisomy 21 was detected in one case, trisomy 18 was confirmed in 4 cases, trisomy 13 in 4 cases and monosomy X in 2 cases.

Conclusion: The application of FISH on fetal tissues is very useful in detecting chromosomal anomalies in embryofetopathology. FISH can so, straighten (strengthen may be better to use confirm) the diagnosis what constitutes a help to the genetic counselling for the related couples or in the cases where a differential diagnosis exists.

P7 HEM/GREENBERG SKELETAL DYSPLASIA: DIAGNOSTIC HISTOPATHOLOGICAL FINDINGS AT 13 WEEKS OF GESTATION

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Background Greenberg skeletal dysplasia is a very rare autosomal recessive, in utero lethal osteochondrodysplasia for which only eight index cases of diverse ethnic origin have been reported so far. The defect is associated with a defect in cholesterol biosynthesis and due to mutations in the gene encoding the lamin B receptor.

Methods A familial case of three fetuses of a consanguineous Greek couple is presented including prenatal, physical, radiographic, histopathologic and molecular genetic findings.

Results The tentative diagnosis of Greenberg skeletal dysplasia based on pathological findings was confirmed by the identification of a homozygous N547D amino acid substitution in the LBR gene in the third affected fetus.

Conclusion The present case represents the ninth described case of Greenberg dysplasia and the second case of Greek origin. The characteristic “moth-eaten” radiographic appearance is already seen at 13 weeks gestational age, while histopathology of cartilage and bone provides diagnostic findings.

P8 THANATOPHORIC DYSPLASIA AND TEMPORAL LOBE DYSPLASIA

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Aim of the study To compare ultrasound and post-mortem findings in 24 fetuses with Thanatophoric dysplasia (TD) and to register and describe the morphological findings in temporal lobe dysplasia (TLD).

Materials and Methods Included were fetuses with an ultrasound examination at the National Center for Fetal Medicine (NCFM) and an autopsy performed during the period 1985 to 2007. The ultrasound scan included a survey of the fetal anatomy and the post-mortem examination was performed according to a standardized autopsy protocol.

Results Thanatophoric dysplasia constituted 2.4 % of all cases of developmental anomalies registered at the Department of Pathology and Medical Genetics, St. Olavs Hospital, Trondheim, Norway from 1985 to 2007. There was an ultrasound diagnosis of skeletal dysplasia in all cases, but the diagnosis of thanatophoric dysplasia was not always specified and in one case the suspected ultrasound diagnosis was achondrogenesis. In the last 6 cases from 2004 to 2007 TD was visualized by ultrasound and confirmed by autopsy. In these cases the biparietal diameter (BPD) compared to mean abdominal diameter (MAD) was increased as a sign of megalencephaly.

At autopsy 20 cases were diagnosed as TD type I, four were type II, two of the type II cases were siblings, both of these had hydrops and cystic hygroma. In none of the cases diagnosed before 1998 was the diagnosis of TLD mentioned. In these cases the description of the brain was unremarkable, though in several the brain was either macerated or traumatized and therefore difficult to examine. After 1998 all cases except two were combined with TLD. In one of these cases the brain was described as normal, and in the other it was specifically mentioned that TLD was not present.

Conclusions The present comparison of ultrasonographic diagnoses with post-mortem findings demonstrate good accordance between the two methods. TLD was present in 79 % of the cases with TD autopsied during the last ten years. TD is caused by mutations of the fibroblast growth factor receptor 3 gene (FGFR3) and there is evidence for direct implications on brain development. It is tempting to postulate that all cases of TD are accompanied by TLD necessitating a specific search for this anomaly, thereby confirming the diagnosis of TD.

P9 TWO AUTOPSY CASES OF SECOND TRIMESTER TRIPLOID FOETUS ASSOCIATED WITH PARTIAL HYDATIDIFORM MOLE

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Aim: To present two autopsy cases of second trimester triploid foetus associated with partial hydatidiform mole.

Case 1: A 37 year old woman’s antenatal ultrasound scan at 17 weeks gestation demonstrated absence of foetal heart action. Delivery of a phenotypically male foetus weighing 20 grams followed. At autopsy several anomalies including syndactyly, atrial septal defect and soft palate defect were present. Placental histology showed features consistent with partial hydatidiform mole. Triploidy, 69XXY was diagnosed on placental cytogenetics. Post-miscarriage Human Chorionic Gonadotrophin (HCG) was negative.

Case 2: A 28 year old primigravida had antenatal ultrasound scan at 17 weeks gestation showing a foetus with ventriculomegaly, nuchal thickening, narrow thorax and exomphalos. The placenta was enlarged. Triploid pregnancy was diagnosed on amniocentesis at 18 weeks gestation. Days later the mother developed symptoms of pre-eclamptic toxemia presenting to hospital with blood pressure of 159/101mmHg. Intra-uterine death was diagnosed on ultrasound scan. Delivery of a phenotypically female foetus weighing 340g followed. At autopsy several anomalies

including cystic hygroma, syndactyly, exomphalos, atrial septal defect and hypoplastic lungs were present. Occasional clear vesicles ranging in size from 0.5 – 1 cm were seen on gross examination of the placenta and histologic features of a partial hydatidiform mole. Cytogenetic studies on foetal skin culture and placenta confirmed triploidy (69XXX karyotype). Post natal scan showed bilateral large ovarian theca lutein cysts. Post-miscarriage HCG remained elevated and decreased from 22,600U/L to 7U/L over 17 weeks. Theca lutein cysts also resolved slowly on scan in association with decreasing HCG levels over the course of 20 weeks post natal follow-up.

Conclusion: Partial hydatidiform mole results from diandric triploidy. Triploidy is rare in second trimester with a previous study identifying a rate of 0.37 in 10,000 fetuses (Huang et al.). The majority of partial moles abort spontaneously in the first trimester, whereas only rare cases reach the second trimester. We present two second trimester cases with congenital anomalies associated with triploidy and cytogenetic and histologic evidence of partial hydatidiform mole. One case was associated with pre-eclampsia and large bilateral theca lutein cysts, features which are infrequently associated with partial molar pregnancy.

P10 ISOLATED OLIGOMEGANEPHRONIC HYPOPLASIA OF KIDNEY: A RARE CAUSE OF FETAL ANAMNIOS. A CASE REPORT

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Introduction: Oligomeganephronic hypoplasia of the kidney is a rare condition, mostly leading to anamnios in fetus, characterized by a reduced number of glomeruli with hypertrophy, seen in both kidneys.

Patient and method: We report the first case diagnosed in our department.

It was a 28 week female fetus.

The pregnancy was terminated for anamnios and fetal growth retardation identified in ultrasonography examination.

External fetal examination showed a diffuse cutaneous oedema with deformative sequence caused by the anamnios.

At the visceral examination, the kidneys were hypoplastic weighting 2gs together.

The histological study compared to a control specimens confirms the hypoplastic feature of the kidneys with reduced number of the nephrons, which were hypertrophic.

These changes support the diagnosis of the oligomeganephronic hypoplasia of the kidney.

Conclusion: Oligomeganephronic hypoplasia of the kidney is mostly genetically determined, and associated to many malformative syndromes, however vascular placental anomalies and intra uterine growth retardation could be the causes.

P11 SPONGIFORM/NONCOMPACTED HEARTS AND PERINATAL DEATHS

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Aim of Study: In a perinatal pathology population, how often is death associated with a spongiform/noncompacted heart?

Materials and Methods: Over a 2_ year period, spongiform/noncompacted hearts were sought in all 584 perinatal post-mortems performed by the Wigglesworth Perinatal-Paediatric Pathology Service. Spongiform/noncompacted hearts were most easily documented by cutting cross sections of the apex of the heart without jeopardizing the heart base harboring the valves and the connections to the systemic and pulmonary circulations.

Results: Over the 2_ year period, spongiform/noncompacted hearts were found in 6 perinatal post-mortems (1% of the 584 perinatal post-mortems). Maternal age ranged from 24 to 36 years (mean: 30 years with 67% being 30+ years). Four (67%) were girls and 2 (33%) were boys. Only one of the boys was diagnosed antenatally with termination of the pregnancy at 24 weeks gestation. Four (3 girls and 1 boy) died spontaneously in utero (range: 13 to 18 weeks gestation with mean: 16 weeks gestation). One, a liveborn 40 weeks gestation girl who had a brother diagnosed with “cot death”, died suddenly at 17 days of age during Sunday lunch. The liveborn girl also had a small membranous ventricular septal defect and multiple, mineralized infarcts in her right papillary muscles. All 6 had well-formed left anterior descending coronary arteries. An absent left hypogastric artery with 2-vessel umbilical cord was found in one female fetus. In all 5 fetal deaths, there was asymmetric growth retardation with brain sparing (brain weight/liver weight range: 4/1 to 16/1 with mean: 6/1). All 6 died in congestive heart failure.

Conclusions: In our perinatal post-mortem population, 6 deaths (1%) were associated with spongiform/noncompacted hearts (“spongiform cardiomyopathy” or “noncompaction of ventricular myocardium”) that can be associated with poor ventricular function and arrhythmias. At post-mortem examination, spongiform/noncompacted hearts were most easily documented by cutting cross sections of the apex of the heart.

P12 CHORIOAMNIONITIS

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Introduction: Chorioamnionitis is around the entire world a common cause of prematurity, abortions and stillbirths. With this communication we present the appearance of the disease in the north region of Sweden with the intention to stimulate the interest for the disease and its prevention.

Material and methods: A retrospective follow-up of morphologically examined abortions and perinatal deaths at the Department of Pathology, University Hospital, Umeå, Sweden, during the years 2000-2007 was analysed what regards chorioamnionitis: gestational age and sex, maternal age, grade of inflammation, inflammatory answer from mother and/or baby, bacteriological findings.

Result: The result of the analysis are presented and compared with similar reports. Chorioamnionitis was the cause of abortion or perinatal deaths in 20 % , and half of those was first diagnosed at the pathological department, many occurred in children e.g. from gestational week 28 up to term or after delivery. A short general discussion of the disease is performed.

Conclusion: Too many otherwise healthy fetuses and children are lost due to this disease, and a break-through in early diagnosis and prevention is highly wanted.

P13 A UNIQUE PLACENTAL TUMOR

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Introduction: Chorangiocarcinoma is the name designated to a chorangioma (CA) manifesting increased trophoblastic proliferative activity. Only 3 such cases have been published. Other studies challenged this entity, by demonstrating that proliferation of the trophoblast around CA is a common phenomenon.

Case history: A hyperechogenic placental mass was observed during a routine ultrasound examination on the 30th week of gestation. A term delivery followed an otherwise normal pregnancy. The newborn weighed 2610gr with Apgar scores 9/9 and normal physical examination.

Pathological examination revealed a well demarcated subchorionic placental mass measuring 8x8x5 cm, displaying a variegated appearance. A chorangioma containing multiple nodules of malignant epithelial tumor with central necrosis were seen on microscopic examination. The nuclei were pleomorphic, mostly mononuclear with focal multinucleation and displayed a high mitotic rate.

Results: immunohistochemical stains for pancytokeratin and bhCG were strongly positive and Mib-1 index was >90% in viable cells. The epithelial nodules were well delineated by basement membrane, as demonstrated by laminin immunostaining. An electron microscopic study verified the trophoblastic nature of the pleomorphic cells. Followup: Maternal serum _HCG levels dropped to negative values one month after delivery. Whole body computed tomography (CT) scan of the mother was normal. The fetal brain and abdominal ultrasound and chest x-ray were negative for metastatic lesions.

Conclusion: Our case differs from the previous reports of chorangiocarcinoma by a few characteristics which support its true malignant nature. Similar to the usual choriocarcinoma it displays significant necrosis. Also, it has a more complex structure, not merely surrounding the villous vascular lesion, but rather forming an intricate structure within the CA. Being limited to the CA without invasion beyond the basement membrane or into the surrounding placenta it should be considered in the spectrum choriocarcinoma in situ.

P14 PLACENTAL CHARACTERISTICS OF MONOCHORIONIC DIAMNIOTIC TWIN PREGNANCIES IN RELATION TO PERINATAL OUTCOME.

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Introduction Perinatal mortality and morbidity is higher in monochorionic diamniotic (MC) twin pregnancies than in dichorionic (DC) twin pregnancies. Vascular anastomoses between both sides of placenta can cause inter-fetal transfusion and twin-to-twin transfusion syndrome (TTTS), which develops in 10-15% of all MC twin pregnancies. However, intrauterine demise and neurological damage as a consequence of ischemia caused by changes in blood pressure due to inter-fetal transfusion may also occur in MC pregnancies without antenatal signs of TTTS. Placental

vascular anastomoses, unequal placental sharing and abnormalities in umbilical cord insertions are associated with fetal growth and birth weight discordancy.

Aim of the study We studied the relation between placental characteristics and perinatal outcome in monochorionic diamniotic (MCDA) twin pregnancies, including neonatal morbidity.

Methods Between January 1998 and January 2007 150 pairs of MCDA twins were delivered in the University Medical Centre, Utrecht, The Netherlands. Mortality, neonatal morbidity and birth weight discordancy were studied in relation to type of anastomoses, type and distance between cord insertions and placental sharing.

Results There were 45 (15.0%) perinatal deaths. There was a trend towards a higher foetal mortality of one or both infants in the presence of VV-anastomoses (20.0%) compared to pregnancies with AA-anastomoses (18.2%). Pregnancies with a death of both children were more likely to have AA-anastomoses and pregnancies complicated by single death were more likely to have a VV-anastomosis. Perinatal mortality was significantly increased in the presence of velamentous cord insertion (OR 3.65, 95% CI 1.83-7.28) and occurred more often in twins with a small distance between cord insertions. Data concerning neonatal morbidity were similar. TTTS occurred predominantly in the presence of AV-anastomoses without compensating superficial AA-anastomoses ($p=0.005$) and occurred more frequently in the presence of velamentous cord insertion (OR 1.79, 95% CI 0.94-3.44). Twins with unequal shared placentas had significantly more often severe birth weight discordancy, though only in the presence of AA-anastomoses (OR 4.09, 95% CI 1.74-9.63). In unequally shared placentas without AA-anastomoses, there was no relation with severe birth weight discordancy (OR 1.06, 95% CI 0.08-13.52).

Conclusion In MCDA twins, placental characteristics determine perinatal outcome, TTTS and fetal growth. Prenatal identification of these characteristics by ultrasound may alter counselling and intensity of pregnancy surveillance.

P15 ANAPLASTIC SARCOMA OF KIDNEY. A CASE REPORT

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Introduction Anaplastic sarcoma of kidney is a recently described renal neoplasm. A series of 20 cases was reported in 2007, by Vujanic and Beckwith, et al. They have re-reviewed the cases with unusual anaplastic features. All tumors have showed a spindle cell component with anaplastic changes. Chondroid differentiation, foci of osteoid and osteoclast-like cells have been seen in varying numbers of cases. We report another case of anaplastic sarcoma of kidney in a 3-and-a-half-year old boy.

Case: A 3-and-a-half-year-old boy was admitted with a left-sided abdominal mass. An open biopsy has been performed in another hospital, and then he was referred to our center. A computed tomography revealed a large left renal mass. The mass was resected together with the surrounding omentum.

Findings: The tumor weighed 780 g and the largest diameter was 15 cm. The capsule was perforated and was covered by omentum. The cut surface of the tumor was solid, fleshy, and yellow-tan in color. Histologically it was composed of spindle cells arranged in a fascicular pattern. Rather primitive round to oval cells and myxoid stroma were seen in places. Anaplastic changes with bizarre pleomorphic cells containing irregular hyperchromatic nuclei were scattered throughout the tumor. Chondroid differentiation was present, whereas osteoclast-like like giant cells were also found. The tumor had an infiltrating margin with entrapment of renal tubules. Small cysts lined by hobnail epithelium and areas of necrosis were present. No nephrogenic rest was observed in kidney. The omentum was also infiltrated. Immunohistochemistry revealed diffuse vimentin positivity. Areas of CD34 and S100 were also detected. Some tumor cells were positive for PGP9.5, CD56 and smooth-muscle-actin. Cytokeratin was positive only in entrapped tubules. Desmin was found to be negative.

After surgery the child was given chemotherapy. He is free of tumor after two years of follow up.

Conclusion: In our Pediatric Pathology Department we have nearly 500 cases of renal tumors and this is the first anaplastic sarcoma of kidney. It fits all the histological criteria mentioned in the cited paper and it shows additional immunohistochemical findings. Since it is a newly identified renal neoplasm, it is worth to review some of the archival cases, particularly with prominent spindle cell component and anaplastic features, and still staying as a question mark in mind.

P16 KAPOSIFORM HAEMANGIOENDOTHELIOMA (KHE) PRESENTING AS A LEFT-SIDED OVARIAN MASS.

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AIM: To describe a case of a newborn baby girl with Kaposiform Haemangioendothelioma presenting as left sided abdominal mass. Diagnostic considerations and clinical management of this locally aggressive vascular tumour arising in a hitherto undescribed site are discussed.

CASE DESCRIPTION: A 14-day old girl presented as an emergency with bilious vomiting. A left-sided abdominal mass was noted which on ultrasound was cystic and arising from the left pelvis. Small bowel obstruction was confirmed on contrast study. At laparoscopy a large cyst arising from the left ovary was found and further scattered small dark red nodules on the surface of bowel loops and parietal peritoneum. On follow up at 10 wks there was only a single residual peritoneal nodule.

Macroscopic examination showed a nodular haemorrhagic and focally necrotic mass (max 6 cm, 58g). Microscopically, multiple unencapsulated nodules with angiomatoid and intervening spindle cell areas were noted. Angiomatoid areas were of tightly packed capillary blood vessels. In spindle cell areas vascular channels were less well formed. Only minimal nuclear atypia and rare mitosis were present. CD34 and CD31 immunohistochemical staining were strongly positive, D2-40 and GLUT-1 negative. Peritoneal nodules (at diagnosis and on follow up) showed similar histological appearances.

DISCUSSION: KHE is a rare vascular tumour of early childhood usually arising in deep soft tissues or retroperitoneum. The outcome of KHE largely depends on the site and extent of disease, surgical resection being the main treatment option, and the presence of a consumptive coagulopathy. Peritoneal and visceral involvement unassociated with retroperitoneal or soft tissue involvement has not, to our knowledge, been described. The lesion showed an infiltrative growth pattern with angiomatoid and more cellular spindle cell (Kaposi sarcoma like) areas, characteristic of KHE. Necrosis, however is an unusual finding, and may be secondary to vascular compromise or torsion. Complete macroscopic excision of the principal mass was achieved in our patient. Interestingly, second look surgery in our patient, suggested regression of a majority of small peritoneal deposits.

CONCLUSION: Kaposiform haemangioendothelioma is to be added to the differential diagnosis of abdominal/ovarian masses in early childhood. Its clinical presentation may mimic postnatal ovarian torsion or small bowel obstruction. Surgery is considered the treatment of choice.

P17 KEARN SAYRE SYNDROME: THE IMPORTANCE OF CYTOCHROME OXIDASE STAINING FOR THE DIAGNOSIS OF CHILDHOOD MITOCHONDRIAL DISEASES

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AIM: Kearns-Sayre syndrome is mitochondrial disease that characterized by a triad of features including onset in persons younger than 20 years, chronic progressive external ophthalmoplegia and pigmentary degeneration of the retina. It may affect many organ systems. Patients with Kearns- Sayre syndrome may develop a wide range of complications. Cardiac conduction defects play an important role in the clinical condition of these patients, that is, heart block is a significant and preventable cause of mortality. A better understanding of Kearns-Sayre syndrome will help in the design of improved therapeutic strategies, such as gene therapy.

CASE REPORT: We present a 13-year-old boy with Kearns-Sayre syndrome. His complaints were short stature, ptosis and weakness. Clinical findings consisted of failure to thrive, external ophthalmoplegia, bilateral ptosis, mild hypotonia, retinitis pigmentosa and complete heart block. Cerebrospinal fluid protein and lactate levels were increased. Cranial magnetic resonance imaging showed bilateral symmetric hyper intensities in basal ganglia, midbrain, and brainstem. Electrocardiogram and Holter monitoring revealed complete heart block and occasional unifocal ventricular premature complexes. Echocardiogram showed trivial mitral insufficiency. The ragged- red fibers were not shown by modified Gomori's trichrome staining. But SDH (succinate dehydrogenase) and COX (cytochrome oxidase) combined enzyme staining was demonstrated the correlation of COX negative fibers with SDH-positive ones. In addition increased number of mitochondria especially in subsarcolemmal location on electron microscopic examination of the skeletal muscle was determined. No mutations were found in the DNA from blood samples.

CONCLUSION: Muscle mitochondrial DNA analysis has shown that 80 percent of patients with Kearns-Sayre syndrome have deleted mitochondrial DNA. However, mutations could not been demonstrated in blood samples. Electron microscopy is also limited use in the diagnosis of mitochondrial disease. Because ragged red accumulate with aging and it's critical to know the percentage of abnormal fibers. On the other hand the subsarcolemmal mitochondrial masses are particularly prominent in the muscle of children. Contrary ragged red fibers were not being noticeable with the Modified Gomori's trichrome staining in muscle biopsy of infants with the mitochondrial

myopathies. In conclusion; enzyme activity reveal on muscle biopsy was important of the diagnosis in mitochondrial diseases especially in early childhood.

P18 INTERSTITIAL LUNG DISEASE AND ABCA3 MUTATIONS IN TWO SIBLINGS

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ABCA3 protein is a transmembrane protein localised in the membrane of lamellar bodies and involved in lipid transport and surfactant metabolism. ABCA3 mutations were recently reported in neonate with severe respiratory distress and in older children with chronic interstitial lung disease.

We report two cases of interstitial lung disease associated with ABCA3 deficiency in the same consanguineous family

The first child, a female neonate presented with an unexplained respiratory failure few hours after birth which resolved after resuscitation (extubated after 10 days). Interstitial lung opacities were observed on X ray. At 2 months of age, a new episode of unexplained respiratory distress occurred leading to a surgical biopsy at the age of 5 months. In spite of ventilation and steroid therapy death occurred at the age of 7 months due to refractory hypoxemia.

The fourth child of the family, a male neonate presented at 4 hours of life a progressive respiratory failure (extubated after 10 days). Alveolo-interstitial opacities were observed on X ray, suggesting a surfactant deficiency. Because of persistent polypnea and growth retardation, surgical biopsy was performed at the age of 4 months. In spite of steroid therapy, the child was oxygen-dependant until the age of 7 years

The two lung biopsies showed interstitial fibrosis with few inflammatory cells, alveolar type II cells hyperplasia, increased alveolar macrophages. No alveolar proteinosis was observed. These lesions are consistent with a chronic interstitial lung disease of childhood.

Western blot analysis on BAL showed accumulation of pro SP-B and pro SP-C with normal range Sp-B and SP-C protein level.

In the second case, unreported compound heterozygote mutations of ABCA3 gene were identified (D115E and D253H).

These new ABCA3 mutations in this family are associated with severe neonatal distress leading to death in the first child at the age of 4 months and to chronic steroid sensitive hypoxemia in the now 7 year old sibling. Histologically, these lesions are characterized by a chronic interstitial lung disease without alveolar proteinosis on wedge biopsies of both children.

P19 PRIMARY HYDATID CYST OF THE THYMUS IN A CHILD: A CASE REPORT

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Cystic lesions of the mediastinum are one-fourth of all mediastinal masses and usually identified incidentally. However hydatid cysts are very rarely presented in the thymus. A 13 years-old boy was admitted to our hospital because of chest pain during deep inspiration. Chest X-ray and chest computed tomography (CT) examination showed a homogeneous cystic lesion with a size of 7,5 x 7 cm at the anterior mediastinum. Thymectomy was performed following left thoracotomy in order to complete pericystectomy. Histological diagnosis was hydatid cyst. To the best of our knowledge, this is the first case in the English literature of a primary hydatid cyst of the thymus in a pediatric age.

P20 INCREASED NUMBER OF EOSINOPHILS IN THE LIVER BIOPSY IS A USEFUL FEATURE OF DISSEMINATED BCG INFECTION IN PATIENTS WITH AN UNDERLYING IMMUNODEFICIENCY.

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Introduction: Disseminated Bacillus Calmette-Guerin (BCG) infection is a rare but severe complication of BCG vaccination. It is usually associated with an underlying immunodeficiency. As patients with disseminated BCG infection usually present with non-specific symptoms, pathologists may receive biopsies from various sites including skin, liver, lymph nodes or bone marrow. These biopsies are likely to show non-specific features, especially if the patient has an underlying immunodeficiency. We present two cases of disseminated BCG infection that showed similar peculiar features that included the presence of numerous eosinophils in the liver .

Case 1: 5 months old male presented with fever, rash and hepatosplenomegaly. The differential diagnosis included sepsis, Langerhans cell histiocytosis and storage disorders. A bone marrow trephine showed a reactive marrow with

increased number of eosinophils. CD1a and S100 were negative. A liver biopsy showed expansion of the portal tracts with numerous eosinophils and neutrophils. Numerous eosinophils were also present in the sinusoids. Few vague aggregates of histiocytes were noted but no granulomas were seen. A subsequent skin biopsy showed a dermal infiltrate composed of histiocytes, lymphocytes, neutrophils and eosinophils. No granulomas were present. A ZN stain showed Acid Fast bacilli in the histiocytes. A ZN on the liver biopsy showed similar findings. A diagnosis of disseminated BCG on a background of immunodeficiency was made.

Case 2: 9 week old male presented with fever, poor feeding and a rash. On examination, he had jaundice, axillary lymphadenopathy and hepatosplenomegaly. The differential diagnosis included infection, TB, Langerhans cell histiocytosis and storage disorders. He was treated with antibiotics and anti-TB treatment but he deteriorated and died. Post mortem examination showed a generalized lymphadenopathy, maculopapular rash and an indurated BCG vaccination site. The liver contained numerous eosinophils in the portal tracts. The bone marrow showed increased number of eosinophils. The BCG site showed several vague granulomas with giant cells. ZN stain showed Acid Fast bacilli in the skin, liver, lungs and lymph nodes.

Conclusion: The differential diagnosis of increased number of eosinophils in the liver includes drug reactions and parasitic infections. Our cases indicate that disseminated BCG infection should be added to the diagnostic list when presenting on a background of immunodeficiency. One possible mechanism is increased production of Interleukin-5 by lymphocytes. Alternatively, increased eosinophil production may be the only immune response the body is able to mount in cases of immunodeficiency.

P21 DESCENDING NECROTIZING MEDIASTITIS – A RARE BUT DREADED COMPLICATION OF CHICKENPOX IN CHILDREN

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ABSTRACT Descending necrotising mediastinitis (DNM) is a rare but severe condition with poor clinical outcome (mortality rate 25-40%).

CASE We report a case of sudden unexpected death in a 4- year-old girl who presented with multiple scabbed lesions over the trunk and face conforming to the lesions of chicken pox. She also complained of sore throat, pain and difficulty in breathing.

The salient autopsy findings included bilateral pleural effusions and purulent mediastinitis involving the pericardium. The upper respiratory tract showed tracheal ulceration and the lower lobes of both lungs were collapsed. The thymus was small and atrophic and mild cervical lymphadenopathy was noted.

Histological examination showed necrotising tonsillitis, peri-tonsillar soft tissue necrosis, inflammation of the deep neck space and extensive necrotising ulcerations in the trachea. The necrotising inflammation extended anteriorly from the trachea between the muscle plane and the thyroid gland. The serosal surface of trachea showed necrotising inflammation tracking all along its length. The mediastinum showed extensive necrotising inflammation involving the pleura, pericardium, diaphragm, oesophagus, trachea and connective tissue. The lungs showed atelectasis with bacterial colonies in the pulmonary vessels but no acute pneumonia was present. The blood vessels of all organs showed bacterial colonies without significant acute inflammatory response. Both blood and CSF cultures were positive for *Streptococcus pyogenes* (Group A) and the PCR confirmed the diagnosis of chicken pox.

COMMENT The varicella infection made her prone for Group A *Streptococcus* infection which resulted in necrotising tonsillitis with subsequent spread into the peri-tonsillar and deep neck space and caused DNM. In children, varicella infection is a well recognized predisposing condition for invasive Group A *Streptococcus* infection with well-documented sequel like necrotising fasciitis. However, DNM is a rare complication in children with chickenpox and this is only the second reported case in English literature