P1
Case Report: A Post Mortem Diagnosis of Pulmonary Veno-occlusive Disease

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A 23 year old Albanian male presented to the Emergency Department of our institution with extreme breathlessness. He described feeling like he was drowning and was producing copious amounts of pink frothy sputum. Clinical examination revealed a patient in severe respiratory distress. The patient continued to deteriorate and one hour after arrival was intubated, ventilated and transferred to the intensive care unit. A CT of the thorax showed peri-bronchial ground glass shadowing with consolidation and extensive mediastinal nodes. An echocardiogram showed severe pulmonary hypertension. Despite continued resuscitation efforts, he continued to deteriorate and was dead within 36 hours of admission. This patient had previously presented to two separate accident and emergency departments with symptoms of haemoptysis, chest pain and breathlessness within the four weeks prior to this admission. A diagnosis of sarcoidosis had been suspected and the patient had been discharged on treatment. He had since failed to attend for planned follow up. It was also noted that he was a crack cocaine and heroin smoker.

Post mortem examination revealed evidence of the acute respiratory distress syndrome (ARDS) and right ventricular hypertrophy and dilatation. Post mortem histology revealed focal bronchopneumonia and significant narrowing of the pulmonary vasculature, principally affecting the small to medium sized veins with many vessels showing pinpoint stenosis. These features were highly suggestive of a diagnosis of pulmonary veno-occlusive disease (PVOD).

This case highlights that PVOD is an under-recognised and often misdiagnosed condition. Moreover, it demonstrates the value of post mortem histology in modern medicine: Firstly to provide an accurate cause of death, and secondly to highlight rare diseases such as PVOD, which may otherwise have gone completely unrecognised.

P2
Primary Mitral Valve Sarcoma Causing Sudden Death in a Child: A Case Report

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Primary cardiac sarcomas are rare tumours in adult and paediatric practice. We report a case of primary mitral valve sarcoma causing sudden death in a child. A seven year old girl complained of chest pain, collapsed and died at home. At autopsy the heart was morphologically normal with a closed foramen ovale. A cord-like vegetation was adherent along part of the circumference of the mitral valve with the remainder floating free within the left ventricular outflow tract, extending through the aortic valve. Histological examination of the lesion revealed a mitotically active markedly pleomorphic spindle cell tumour with scattered multinucleate cells. The adjacent mitral valve showed involvement in the area of attachment with associated neovascular reaction. An extensive immunohistochemical panel yielded no positive results, consistent with a diagnosis of undifferentiated sarcoma. The myocardium was normal. In view of the history and autopsy examination, we find it reasonable to assume that the distal tumour occluded one of the coronary ostia leading to myocardial ischaemia and sudden arrhythmic death. This is only the sixth case of primary mitral valve sarcoma in a child, with only one previous case of sudden death due to mitral valve sarcoma (in adults or children) documented in the literature.

P3
Aberrant E-Cadherin Expression in Lobular Breast Carcinomas

Western General Hospital, Edinburgh, United Kingdom

Background: Invasive lobular breast carcinoma is characteristically e-cadherin negative and immunohistochemistry for e-cadherin is often used to differentiate between ductal and lobular carcinomas. However aberrant e-cadherin expression has been described in some lobular carcinomas. This may lead to some lobular carcinomas being labelled ‘ductal carcinoma’, which has implications for patient management and prognosis.

Aim: We aimed to identify and quantify lobular carcinomas which show aberrant expression of e-cadherin, in a cohort of cases from our institution.

Method: We reviewed 169 breast biopsies that were carried out in 2008. This included all cases that had been diagnosed as lobular breast carcinomas and all biopsies which had been stained with e-cadherin using immunohistochemistry. All the cases were reviewed by a single consultant pathologist. The H&E and e-cadherin slides were reviewed. We identified cases of carcinoma which had a lobular morphology on H&E, but which showed aberrant e-cadherin expression.

Results: Of the 169 cases, 106 showed the morphology of invasive lobular carcinoma, of the classical, pleomorphic, solid and alveolar subtypes. 26 (25%) of these cases showed aberrant e-cadherin expression. In the majority of these cases the pattern of staining was unusual, showing weak membranous staining with increased staining at the intracellular margins, compared to the strong membranous staining seen in invasive ductal carcinomas.

Discussion: These results show that e-cadherin expression in invasive breast carcinoma should not rule out the diagnosis of lobular carcinoma.
Is There an Increase in Phyllodes Tumours? An Audit of Biphasic Lesions of the Breast in Edinburgh.

Western General Hospital, Edinburgh, United Kingdom

Phyllodes tumours are rare neoplasms with a reported incidence of between 0.3 and 1% of breast tumours. On the impression of an increase in the rate of diagnosis of phyllodes tumours in our department we audited our reporting of biphasic lesions. The reports of all excised biphasic lesions from 2004 to 2008 were reviewed. From 497 operations on 474 women 545 lesions were excised (45 phyllodes (PT), 500 fibroadenomas (FA)). Of PTs 27 were benign, 17 borderline, 1 malignant. Of FAs 61 (12.2%) were reported as having atypical features (most commonly occasional mitoses and / or mild stromal cellularity).

The histological criteria for diagnosis and sub-categorisation of phyllodes tumours, and for their differentiation from fibroadenomas are poorly defined. There is, in addition, some basic results from the audit and the rates of diagnosis per year and are tabulated:

<table>
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<tr>
<th>Year</th>
<th>PT</th>
<th>FA with atypia</th>
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<tr>
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<td>2005</td>
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<td>2008</td>
<td>119</td>
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An increase in our rate of diagnosis of phyllodes tumours, suggest reasons for this and discuss the difficulties in the diagnosis and classification of biphasic lesions of the breast.

Borderline HER2 Protein Positive Breast Cancers Have Similar Patient Outcome Regardless of HER2 Gene Amplification Status

Nottingham University Hospitals, Nottingham, United Kingdom

HER2 plays an important role in breast cancer progression and provides predictive and prognostic information. However, prognostic information provided by IHC expression categories and prognostic value added by using in-situ hybridisation (ISH) in borderline cases remains unclear. We have assessed HER2 status in a large well-characterised breast cancer series prepared as tissue microarray (n=1858) using IHC (HercepTest, DakoCytomation) and chromogenic ISH (CISH, DuO CISH, DakoCytomation) in order to identify relationships with clinico-pathological variables and patient outcome. None of these cases have received anti-HER2 therapy. There was excellent overall concordance between HercepTest negative (scores 0/1+) and positive (3+) with CISH positive/ negative (defined as HER2/Chr17 copy number ratio of ≥2, p<0.001). Twelve percent of cases were identified as HER2 positive (those with 3+ HercepTest scores or 2+ with gene amplification). Of the 74 borderline HercepTest 2+ cases, 44 cases (59%) showed HER2 gene amplification. We identified that HercepTest 2+ non-amplified cases were not significantly different from those amplified 2+ or 3+ cases with respect to their clinical outcome (BCSS and DFS). The overall concordance between HercepTest and CISH analysis for HER2 status was excellent. All HercepTest 2+ cases identified were observed to have poor outcomes similar to those HercepTest 3+ cases regardless of gene amplification status. In the current clinical environment, cases exhibiting IHC 2+ with non-amplified HER2 gene status are not offered targeted HER2 therapy but do exhibit aggressive clinical behavioural characteristics and therefore optimal treatment strategies for these patients need to be determined.

The Histone H4 K16 Regulatory Axis in Breast Tumours: Modulation by Small Molecule Inhibitors

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Breast tumours display significant phenotypic and molecular heterogeneity. Recent research has attempted to generate improved molecular classifications of breast tumours using gene expression profiling, and tumour microarray immunohistochemistry. We recently reported that global levels of posttranslational modifications (PTMs) in core histones are radically altered in breast tumours, and that these factors show a strong association with tumour phenotype, prognostic factors and patient survival (El-Sheikh et al, 2009). In this study, we focussed on a key histone PTM (acetyl H4K16), and profiled the expression of a range of chromatin modifying enzymes that modulate H4K16 and other histone PTMs in 880 primary breast carcinomas. Our data show significant associations of these PTMs with the expression of HAT and HDAC factors and their regulators. In addition, using a MCF7 model, we show that small molecule inhibitors such as garcinol can modulate the expression levels of chromatin modifiers, and reprogram cancer-associated PTMs, including AcH4K16. This is accompanied by inhibition of proliferation through a blockade of S phase and cell cycle arrest.

An Audit of Node Positivity in Axillary Sentinel Node Biopsy/ Sampling — Would Intra-operative Assessment Improve the Patient Journey?

Western Infirmary, Glasgow, United Kingdom

Purpose of the study
Sentinel node biopsy is the gold standard axillary staging procedure in patients with early invasive breast cancer but lack of intra-operative assessment facilities results in many women undergoing a second operation for completion axillary clearance. Intra-operative assessment may be undertaken by frozen section or by one-step nucleic acid amplification.

The aim of this audit is to determine how many cases in this unit required a second operation, demonstrating the percentage of cases that would benefit from the implementation of intra-operative cytokeratin assay analysis.

Methods
All wide local excision and mastectomy cases with a sentinel lymph node biopsy, dye-directed lymph node biopsy and 4-node sample submitted to the unit in 2009 were included in this audit. The data collected included the number of reported positive nodes, frozen section reports (if performed) and surgical outcome for node positive patients. Summary of results
396 cases were included. A total of 52 cases (13%) with positive lymph nodes underwent a second operation for completion axillary node clearance. In addition, 50 cases had a frozen section performed at the time of initial surgery. 14 of these cases (28%) were reported positive and all these patients underwent completion axillary clearance during the initial operation.

Conclusion
In total, 66 women (17%) with node positive disease (including those with a positive frozen section) underwent completion axillary clearance. In financial terms, the guide unit cost saving in avoiding second surgery is £2,549 per patient. Therefore, the implementation of intra-operative cytokeratin assay analysis could reduce the need for second surgery in 66 cases per year, resulting in a saving of £168,234. This saving needs to be balanced against the purchase and running costs involved in setting up the cytokeratin assay analysis in this hospital.
Expression of the Trefoil Protein TFF3 in Human Breast Cancers

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Trefoil factors are small proteins that are secreted from mucous secreting epithelia. Motogenic actions of trefoil proteins may help tumour cell invasion and metastasis. TFF3 mRNA expression is regulated by oestrogen in breast cancer cell lines. Association between oestrogen receptor and TFF3 mRNA expression has been demonstrated in breast tumours. TFF3 protein has not been analysed previously in human breast cancers. A tissue microarray was constructed from 300 primary breast tumours and 76 metastatic deposits. TFF3 expression was evaluated by immunohistochemistry with an antibody raised against correctly-folded human TFF3. The intensity of immunoreaction in 1,000 tumour cells was evaluated as: absent, weak, moderate or strong. The association of TFF3 expression with clinico-pathological features and with oestrogen receptor expression was tested statistically with SPSS software (p<0.01). TFF3 is expressed in normal and malignant breast epithelial cells and not expressed in stromal, endothelial or immune cells. Expression of TFF3 varied enormously between tumours; 238 cases were positive. TFF3 expression is highest in mucinous and tubular breast carcinomas. It is expressed at higher levels in lobular than in ductal cancers. TFF3 expression is associated strongly with oestrogen and progesterone receptor expression. There is a negative association between TFF3 expression and tumour grade. There is however a positive association between TFF3 expression and presence of vascular invasion and presence of axillary LN metastasis. TFF3 expression is higher in metastatic breast tumour cells than in primary breast tumour cells. The association between TFF3 and oestrogen receptor suggests that TFF3 expression is dependent on oestrogen in breast tumours. The high expression of TFF3 in breast tumours with vascular invasion and in metastatic tumour cells supports the hypothesis that TFF3 predisposes towards breast cancer cell invasion.

A False阳性 Positive (C5) FNAC from a Lymph Node with Benign Vascular Transformation of the Sinuses (VTLNS)

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A 70 year old woman presented with a symmetrical breast lump while part of the breast screening programme. Mammography demonstrated a calcified mass, 30mm diameter and a 9mm, radiologically indeterminate, ipsilateral axillary lymph node. Ultrasoundography of the symptomatic mass was sonographically malignant (US). The axillary tail lymph node had an sonographically indeterminate echogenic centre. Ultrasound guided needle core biopsy showed Grade 2 IDC. The cytology smear from the axillary lymph node was reported as false positive for carcinoma cells (C5). A right mastectomy and axillary node clearance was performed. Histological examination demonstrated a Grade 3 IDC with high grade comedo ductal carcinoma in situ. Pathological node status of the specimen was ascertained from 19 lymph nodes in the tail of the mastectomy specimen (level I nodes), nine in a separate piece of tissue incorporating level II nodes (largest 13mm) and 4 level III nodes in a piece of apical tissue. All 32 lymph nodes examined were free of tumour (pT2, pN0, pMx). However several showed characteristic VTLNS with an intra-sinusoidal proliferation of endothelial cells stainable for VWF accompanied by an intra-sinusoidal fibrous reaction. Pre-operative staging of the axilla using FNAC can triage women with operable breast cancer prior to an initial nodal surgical procedure. VTLNS is an example of a benign process that can simulate metastatic involvement of a lymph node by carcinoma diminishing the accuracy of this test.

Sudden Cardiac Death (SCD) in Individuals with a History of Alcohol Use with or without Antipsychotic Medication and/or Class A-C Drugs.

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Alcohol-related deaths in the UK have steadily increased, rising from 4,023 in 1990 to 9,021 in 2008. Most are non-cardiac. This study aims to highlight cardiac causes particularly within the younger generation. One hundred and sixty-five cases of SCD with a history of alcohol were referred to our specialist cardiac pathology centre from January 1996 to February 2010. Drinking patterns were categorised into 4 groups: alcohol prior to death (n=100), binge drinker (n=32), chronic alcoholism (n=54, of which almost half had fatty liver/cirrhosis and 8 had alcohol withdrawal) and moderate to heavy drinker that could not be classified into binge or chronic (n=21). The majority of cases were young males (n=114, 69%), mean age 35±12.8 years, range 15-76 years. Adolescents (<20 years) made up 10% and 40% were ≤30 years of age. Some also took class A-C drugs to death (n=100), binge drinker (n=32), chronic alcoholism (n=54, of which almost half had fatty liver/cirrhosis and 8 had alcohol withdrawal) and moderate to heavy drinker that could not be classified into binge or chronic (n=21). The majority of cases were young males (n=114, 69%), mean age 35±12.8 years, range 15-76 years. Adolescents (<20 years) made up 10% and 40% were ≤30 years of age. Some also took class A-C drugs (n=47) and/or had mental health problems taking antipsychotic medication (n=24). An important finding is that half died suddenly with a morphologically normal heart at both macroscopic and microscopic level (n=82), strongly suggesting the possibility of channelopathies, e.g. Brugada and long/short QT. Additionally, these SCD may have occurred through a fatal arrhythmia precipitated by alcohol use. Cardiomyopathy was also a dominant cause of death (n=49) followed by coronary artery pathology (n=16). Other important causes were toxic myocarditis (n=11), CHD (n=5), aortic dissection (n=1) and an AV nodal lesion (n=1). This study highlights the importance of SCD linked to a history of alcohol use. Our study also raises awareness of SCD in individuals that had consumed non-toxic levels of alcohol just prior to their death and emphasizes the risk of the pro-arrhythmic effects of alcohol in those who have underlying cardiac conditions.
Cytospin Preparations Provide Better Quality Diagnoses Than Direct Smears in Nodal Needle Aspiration Specimens For Non-Small Cell Carcinoma (NSCLC): A Multicentre Review.

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Background: Diagnostic cytology is undertaken mainly via direct smear (DS) or cytospin (CS) preparations, with usage often dependent on institute and operator preference. The ASTER trial, a prospective randomized trial to compare immediate surgical staging (SS) against endosonography (ES) followed by (SS), was a multicentre (n=4) project that provided an opportunity to prospectively compare the two techniques.

Methods: 119 cases from the SS/ES arm, prepared and diagnosed locally, two using DS (mainly May-Grumwald-Giemsa stained) (n=85) and two CS (mainly Papanicolaou-stained) (n=36) preparations, were subsequently reviewed by a reference pathologist, with number of slides per case/nodal station, % positive cases/stations, time per case, and interobserver (IO) agreement recorded. A further comparison was made from the laboratory of the reference pathologist where practice changed from direct smear (n=52) to cytospin (n=55) in 2006.

Results: For CS versus DS, there was 100% versus 97.5% IO agreement, taking 12.5 versus 27.2 mins/case (av. 4.7/1.3 versus 14.8/5.6 slides per case/station), but with lower positive pick-up rate per case/station (38.5/17.9 versus 60/29.3 %). However, the non-ASTER data set from a single institution (CS vs DS) showed a higher positive pick-up rate with CS than DS (56.4/46.2 vs 38.5/34.9% (case/station); slides per case/station 3.53/2.13 vs 8.38/5.25; inadequacy/poor quality rate (4.6% vs 23.1%).

Conclusions: CS allows quicker diagnosis (less slides/better quality preparations) and has better IO agreement. CS also allows cell pellet preparation for further refinement of diagnosis of NSCLC. The lower positive pick-up rate in the ASTER trial was reversed in the single institution experience, likely reflecting variation in institution practices and patient selection.

Primary Leiomyosarcoma in the Parotid, Tongue and Foot of Three Adults

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Background: Leiomyosarcoma is an uncommon malignant tumour with smooth muscle differentiation that often occur in the soft tissue of the gastrointestinal tract, reproductive organs and retroperitoneum. The tumour may however be seen in any anatomic site where smooth muscle is found. Cases: We describe three adults; a 28 year old female student and two males aged 35years and 36years with leiomyosarcoma of the dorsum of foot, left parotid and tongue respectively. The female presented with a year history of swelling of the dorsum of the left foot, the younger man presented with two months history of ulcerated discharging left facial swelling and the elder man with a tongue nodule. Histology of tissue biopsies from the three lesions showed a malignant infiltrative tumours growing in diffuse and haphazard fascicles. They were composed of pleomorphic spindle cells having hyperchromatic to vesicular shape, blunt ended nuclei, prominent 1-3 nucleoli with fibrillary cytoplasm. Tumour giant cells and mitotic figures of over 6-15 per HPF were seen within a fibrillarized stroma. Conclusion: Leiomyosarcoma of soft tissue is relative rare and constitute 6.5% of all soft tissue sarcoma. It is an aggressive tumour with propensity for the extremity and less than fifty cases have been reported in these three sites combined. Diagnosis is based on hematoxylin- & eosin-stained histologic sections with or without special stains. Other diagnostic techniques include electron microscopy, immunohistochemistry and cytogenetics for increased accuracy and differentiation from other soft tissue sarcomas.
P16

The Diagnosis of Head and Neck Cancer Using Fine Needle Aspiration Cytology

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Purpose of Study: Head and Neck (H&N) cancer in the UK accounts for around 8000 cases/year. Fine Needle Aspiration Cytology (FNAC) is recommended as a first line investigation in palpable H&N masses, salivary gland and thyroid lumps. However, a particularly high level of expertise is required to achieve a precise and reliable diagnosis. This study aimed to assess the accuracy and value of cytology in diagnosis when compared to histopathology. Methods: 260 FNACs were reported at Bradford Hospitals from 2/2007 to 2/2008, of which 120 had subsequent histological assessment, 44 were insufficient and the remainder had no documented follow-up. All cyt- and histo-pathology was critically appraised for diagnostic testing (included analysis of positive/negative predictive value (PPV/NPV), sensitivity and specificity). Summary of Results: Analysis of the 120 cases returned a concordance of 80.83% (within each sub-category neck-nodes 76%, neck-lumps 95%, parent/salivary glands 87.5% and thyroid lumps 78%). Importantly, 17% of FNACs were considered insufficient and the diagnosis relied on histopathology. Overall, analysis showed that FNAC had a PPV=93% (95% CI 0.86-0.86), Sensitivity=86.95%, Pre-test probability (prevalence)=84.25%, NPV=48.15% (95% CI 0.31-0.66), Specificity=65%, Accuracy=83.46%. Conclusions: A recent meta-analysis has shown FNAC to be a highly effective in the diagnosis of H&N cancers with some limitations. Our results showed that FNAC had a relatively poor NPV (the proportion of patients with negative test who are correctly diagnosed) = 48.15%. Also, we found FNAC to be a sensitive but not specific test. The accuracy of FNAC is related to aspirator skill and the experience of the cytopathologist. FNAC has reduced the number of patients requiring surgery by 35-75%. Our analysis returned a NPV=44% and FNAC insufficiency rate=17%. Image guided FNAC may improve sample quality and potentially NPV and specificity.

P17

The Role of Postoperative Radiotherapy in the Management of Parotid Pleomorphic Salivary Adenomas: Is There Any Benefit?

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Introduction: Pleomorphic Salivary Adenoma is the most common tumour of the Parotid Gland. Currently no national management guidelines exist. The objective of this study was to evaluate the role of adjuvant radiotherapy. Methods A retrospective study of all patients with a histological diagnosis of PSA between 1981 and 2008 in Greater Glasgow and Clyde was undertaken. From intra-operative notes and pathology reports, adherence to facial nerve, margin status and postoperative radiotherapy were analysed. Two cohort groups were identified. The first cohort underwent surgery alone, while the second received postoperative radiotherapy. Post-operative recurrence, short and long term complications were compared in the two groups. Results 201 patients were identified. 167 (83%) had surgery alone and 34 (17%) received adjuvant radiotherapy. Medical notes were retrievable in all patients receiving postoperative radiotherapy and in only 58 surgical patients. The rate of recurrence was 1.7% (1/38) in surgical patients and 2.9% (1/34) in patients receiving adjuvant radiotherapy. Short term complications were significantly higher in the second cohort accounting for 100% compared to 38% in the first. While long-term complications 15/58 (25%) and 12/34 (32%) were observed in the first and second cohort respectively. Conclusions There was no significant difference in the recurrence rate between the two groups. Short term and long term complications were significantly higher in the postoperative radiotherapy cohort. Adjuvant radiotherapy is therefore not recommended in the treatment of PSA. As well as a higher long term complication rate, radiotherapy is less cost effective.

P18

Bone Marrow Fibrin Ring Granulomas in Epstein Barr virus infection

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Fibric ring granulomas are composed of a central lipid-filled vacuole surrounded by a ring of fibrin and epithelial macrophages. They are seen in the bone marrow and liver in association with a variety of aetiologies, including infective agents, T cell lymphomas and alloportulin hypersensitivity. Infective aetiologies include Coxiella burnetii (Q fever), cytomegalovirus, hepatitis A and, in isolated case reports in the English literature, Epstein Barr Virus (EBV). We present a 36 year-old Caucasian female who presented with paresis of unknown origin, generalised lymphadenopathy, abnormal LFTs and raised LDH. A monosop test for glandular fever at presentation was negative, and bone marrow trephine biopsy and cervical lymph node excision were carried out. Fibric ring granulomas were present in the bone marrow trephine whilst the lymph node showed features strongly suggestive of EBV infection, including positive in situ hybridisation (EBERs) and immunohistochemistry (LMP-1 and EBNA-2). A repeat monosop test was positive and the patient’s blood raised titres of EBV IgM and IgA, suggesting recent acute infection. Tests for CMV and hepatitis C were negative. The patient made an unremarkable recovery and was discharged shortly following diagnosis. Fibric ring granulomas are rarely encountered in pathological specimens, but their presence should stimulate an active workup of the patient for infectious agents, including EBV.

P19

Unrelated Clones and Acquired BCL2 Gene Abnormalities in Cutaneous Marginal Zone Lymphoma

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Lymphomas are believed to derive from a single transformed lymphoid cell. Translocations, and much less frequently amplifications, of the BCL2 gene are the initiating event in most follicular lymphomas (FL), the former occurring in the bone marrow during immunoglobulin gene rearrangement. The t(14;18)(q32;q21) involving the BCL2 gene has also rarely been reported in extranodal marginal zone lymphoma (MZL). Herein we document two unique cases of cutaneous MZL associated with BCL2 gene abnormalities.

Both patients presented with typical features of MZL: neoplastic infiltrates of small lymphocytes, numerous light chain restricted plasma cells and residual reactive follicles. One patient suffered 6 relapses with a common clone demonstrable by PCR in the 1st, 3rd and 4th, but an apparently unrelated clone in the 2nd. In addition, a previously undetected BCL2 gene translocation was found in the 5th and 6th relapses by interphase FISH. This correlated morphologically with a collection of neoplastic follicles in an otherwise typical MZL in relapse 5, whilst the pathological features in relapse 6 were of a typical FL. The other patient relapsed 3 times, genetically unrelated abnormal clones being demonstrated by karyotyping on each occasion. Marked amplification of the BCL2 gene was also identified by FISH in the third relapse but in none of the earlier biopsies. This coincided with acquisition of CD10 and BCL6 by a proportion of the neoplastic lymphocytes.

These two cases illustrate that abnormalities of the BCL2 gene may occur in cutaneous MZL. They occurred as secondary events, and unlike most previous cases of MZL with BCL2 gene abnormalities, coincided with an alteration in phenotype to one more closely resembling FL than MZL. Although not proven, the genetic findings also raise the possibility that relapses in some cutaneous MZL represent separate clonal events rather than recurrence of the original abnormal clone.
Review of EBV-Positive Diffuse Large B-Cell Lymphoma Occurring in Immunocompetent Patients

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Epstein-Barr virus (EBV) positive diffuse large B-cell lymphoma (DLBCL) of the elderly has recently been included in the WHO classification of malignant lymphoma. It usually occurs in the elderly with no underlying immunodeficiency and is associated with a poor prognosis. We have undertaken a review of EBV-positive DLBCL occurring in immunocompetent patients in the West of Scotland in order to define its clinical and pathological characteristics. All cases of EBV-positive DLBCL in patients with no known history of immunosuppression reported at Glasgow Royal Infirmary from 2001 to 2009 were reviewed. The clinical, morphological, and immunophenotypic features were recorded. 26 patients were identified with a median age of 66 (range 18 to 97) and a male female ratio of 1:2, representing approximately 7% of all DLBCL. There were 11 nodal and 15 extranodal presentations with 7 occurring in the nasopharynx or oral cavity. Three morphological patterns were identified. A typical DLBCL pattern (n=9), a plasmablastic (n=6) and a Hodgkin-like pattern (n=11). 17 cases in which full immunophenotyping was performed had an activated B-cell immunophenotype (MUM1+ CD10 neg). CD30 (n=6) and a Hodgkin-like pattern (n=11). 17 cases in which full immunophenotyping was performed had an activated B-cell immunophenotype (MUM1+ CD10 neg). CD30 was expressed in 88%. 58% of patients presented in stage 3 or 4 (slightly higher than the regional figure of 51% for all DLBCL). 7 patients died, 3 within the first month following diagnosis. The majority of those fit enough for chemotherapy achieved complete remission. EBV positive DLBCL in patients not apparently immunosuppressed occurs over a wide age range though is most common in the elderly. Extranodal presentations in the upper aerodigestive tract are particularly common. In cases of DLBCL, plasmablastic or Hodgkin-like morphology, activated B-cell phenotype and CD30 positivity should trigger testing for EBV by ESH. The prognostic implication of EBV positivity in this small cohort is unclear at the time of reporting.

A Review of Lymphoma in Non-transplant Patients on Immunosuppressive Therapy

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Iatrogenic immunodeficiency-associated lymphoma in non-transplant patients, now a specific category in the WHO classification of malignant lymphoma, is important to recognize as regression may occur following immunosuppression (IS) withdrawal. As there are many questions regarding management of these cases, we have undertaken a review of our experience in the West of Scotland.

We reviewed 125 cases of lymphoma developing in patients treated with Methotrexate (40) or Azathioprine (5) from pathology and rheumatology databases over a 10 year period. 43 patients suffered from rheumatoid arthritis, 4 from psoriasis and the remainder from other conditions. There were 20 cases of Diffuse Large B Cell Lymphoma (DLBCL), 12 of classical Hodgkin Lymphoma (CHL), 2 of Hodgkin-like lymphoma, and 11 of other lymphoma subtypes including Follicular Lymphoma and T-cell Lymphoma. Where EBV status was known, 55% of all cases, 61% of DLBCL, 75% of CHL and 100% of Hodgkin-like Lymphomas were positive. EBV-positive DLBCL had an activated B-cell immunophenotype in 82% of cases. Two patients are in remission as a result of IS withdrawal and 7 patients (2 DLBCL, 4 CHL and 1 Hodgkin-like) developed a transient response to IS withdrawal. One of the latter had a stable response with the addition of Rituximab. The remainder required chemotherapy or radiotherapy. Eight of the 9 cases responding to IS reduction were EBV positive. A wide variety of lymphoma subtypes occur in patients receiving immunosuppression for inflammatory diseases. Though most will eventually require chemo/radiotherapy, occasional cases will develop complete remission with IS withdrawal alone or in combination with Rituximab. A trial of immunosuppression reduction is worthwhile in all cases, independent of EBV status.

A Role of Small-Sized Cell Population in Tumourigenesis of Hodgkin Lymphoma Cells

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Tumours consist of heterogeneous cell populations derived from a single clone. Recently, it has been demonstrated that cells with tumorigenic potential are limited to a small population, called cancer-initiating cells or cancer stem cells (CSCs), in several tumours, such as leukemia, breast, brain, and colon cancers. To date, such a population has not been identified in malignant lymphomas. Here, we examined the presence of CSCs in Hodgkin lymphoma (HL) HE. In two cases of diffuse large B-cell lymphoma (DLBCL), 1HL cell line L1236 consists of heterogeneous sized cells; single-nucleated small-sized cells (S cells) like Hodgkin cells and multinucleated large-sized cells (M cells) like Reed-Sternberg cells. To examine the difference of tumourigenicity between S and M cells in L1236 cells, limiting dilution, semi-solid cultures, and injection into non-obese diabetic/severe combined immunodeficiency (NOD/SCID) mice were performed. In limiting dilution, S cells showed a more proliferative potential than M cells. S cells yielded both S and M cells. In contrast, M cells with less proliferative potential, yielded only M cells. In semi-solid cultures, S cells formed colonies more efficiently than M cells. In contrast to S cells, proliferative potential of M cells was rarely observed in limiting dilution assay. At injection into NOD/SCID mice, S cells formed tumours more efficiently than M cells. These results suggested that S cells were more tumorigenic than M cells. CSCs are known to contain a lower level of reactive oxygen species (ROS) than non-CSCs. A part of S cells contained lower levels of ROS than M cells. ROS-low cells are known to express FoxO3a, which enhances the expression of ROS-excluding enzymes, such as superoxide dismutase and catalase. FoxO3a was expressed in a part of S cells, suggesting that the FoxO3a-expressing cells might be a candidate for CSCs. These findings suggest that S cells might play an important role in tumorigenesis of HL.

The Relationship of Bone Marrow Trephine Length, Adequacy and Disease Process

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Bone marrow trephine biopsies are essential in the diagnosis and staging of haematological and non-haematological diseases. Absolute clarification of what constitutes adequacy is lacking, with 15mm having been suggested as the minimum adequate length. Ultimately, however, adequacy must be defined by the ability of a reporting pathologist to produce a definitive diagnosis from the trephine, accepting boundaries of good practice. We examine three increasingly specific bone marrow datasets to determine a pragmatic guide for adequacy that is useful for clinicians and can help pathologists. Our data-sets comprise: (i) a non-selected ‘base-line’ set, comprising 100 sequentially received cases; (ii) a set comprising 700 consecutive trephines taken as staging sequentially received cases; (iii) a ‘focal’ sub-set comprising 268 staging trephines for lymphomas associated with focal marrow involvement. We use a novel application of logistic regression to model the probability of a biopsy being regarded as adequate. For our base-line set, a length of 15.7mm is required in order to obtain a 95% probability of a specimen being regarded as adequate in our practice. For lymphomas in general, 95% probability is reached with a length of 17.2mm, whilst for our focal set 21.5mm is required. The average length in all our sets is less than optimum by these standards. We also find that, when trephine length is short, each 1mm more can make it up to 30% more likely to produce a diagnostic report. Conclusion, the likely adequacy of a bone marrow trephine relates to the disease being investigated as well as the absolute length of the specimen. Thus, the indication should be taken into consideration when assessing adequacy. To ensure the procedure serves its purpose, obtaining a longer biopsy in staging focal lymphomas would ensure more accurate results with prognostic benefits.
**P24**

**Plasma Cell Myeloma Presenting as a Testicular Mass: A Case Report**

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**Introduction:** This is a case report of plasma cell myeloma presenting as a testicular mass in an otherwise fit 58 year old man. Case: A 58 year old man presented to his general practice with a 2 month history of unilateral, painless testicular swelling. He did not complain of weight loss, back pain or bone pain and was otherwise fit and healthy. Clinical examination revealed a large testicular swelling, non-tender, which clinically resembled a hydrocele. Ultrasound examination performed shortly after showed a large tumour mass and urgent orchidectomy was performed. Tumour markers, alpha-fetoprotein and beta HCG were normal. Pathological assessment revealed a grossly enlarged 110cm testicle. The cut surface appeared lobulated and showed a white homogenous tumour replacing the entire testicle. Microscopically, the tumour was made up of numerous sheets of large lymphoid blast cells mostly resembling immunoblasts. Initial immunohistochemistry showed strong expression for MUM-1, patchy CD79a positivity and negative staining for CD20, CD10, BCL-2 and BCL-6. Further immunohistochemistry with plasma cell markers CD138 and CD56 showed strong positivity. CD 45 however was negative. A diagnosis of plasmacytoma or possible deposit of plasma cell myeloma was suggested which prompted further investigation and haematological referral. Subsequent investigations including laboratory tests and serum electrophoresis which were supportive of the diagnosis. The bone marrow trephine performed confirmed the presence of plasma cell myeloma. Discussion: Plasma cell myeloma is a rare neoplasm composed of plasma cells that usually involves the bone marrow. However, extramedullary disease is sometimes encountered. The most common sites of extramedullary involvement are the liver, spleen and lymph nodes. Localisation to the testis is considered rare, particularly as an initial presentation.

**P25**

**Paratrabecular Distribution of Lymphoplasmacytic Lymphoma in Bone Marrow**

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**Lymphoplasmacytic lymphoma (LPL) is a rare neoplasm composed of small B lymphocytes, plasmacytoid lymphocytes and plasma cells that usually involves the bone marrow.** Marrow involvement may be nodular, diffuse and/or interstitial and can also show paratrabecular aggregates. Published data suggests that one-third of LPL cases show a paratrabecular component. This study looked at a large series of LPL to determine the proportion showing paratrabecular disease and to quantify the extent of the paratrabecular component. A search over the last 5 years yielded 126 bone marrow cases with a diagnosis of LPL. All cases with a CD20 and/or Pax5 were reviewed (106 cases) and percentage involvement by LPL and percentage paratrabecularity were assessed. Cases showing no evidence of disease (10 cases), where there was >75% involvement, and/or where the specimen was <5mm in length were excluded. Of the 69 remaining cases, 33% showed 50-75% overall involvement by LPL, 26% showed 25-50% involvement, and 42% showed <25% involvement. A paratrabecular component (>10%) was seen in 62% of cases. Further quantifying this component showed the following; no cases were >90% paratrabecular, 19% of cases showed 50-90% paratrabecular disease, and 43% of cases were 10-50% paratrabecular. 38% of cases were <10% (i.e. not) paratrabecular. Our study indicates that the proportion of lymphoplasmacytic lymphomas in bone marrow with a paratrabecular component is higher than that previously published, and that this pattern may be a useful diagnostic feature in LPL.

**P26**

**Audit of Central Review Cases to Identify Trends in Light of the NICE IOG on Haematological Cancers**

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A review of all lymphoma cases received, during a period of just under one year, for central review at a specialist referral centre in one cancer network was undertaken. 300 cases were reviewed. Out of these the original report was not available in 41 cases. Of the remaining 259 cases, the original (referring pathologist’s) diagnosis was agreed with in 196 cases. There was discordance between the referring pathologist’s diagnosis and the diagnosis after specialist review in 63 cases. The discordant diagnoses were subclassified into categories 1-3 based on the Royal College of Pathologists guidelines on categorisation of discrepancies in histopathology (2008). Of the 63 cases, 26 were found to be category 1 discrepancies which included a diffuse large B-cell lymphoma being diagnosed a Seminoma, Nodular Lymphocyte Predominant Hodgkin Disease being called classical Hodgkin Lymphoma and no report on transformation to diffuse large B-cell lymphoma in follicular lymphoma, amongst others, which were known to have therapeutic and clinical ramifications. Also, 25 cases were found to be category 2 discrepancies which included wrong subclassification of B-cell lymphomas (e.g. lymphoplasmacytic lymphoma being called marginal zone lymphoma), 12 cases were found to be category 1 of which the commonest reason was grading of follicular lymphoma and classical Hodgkin lymphoma. Although the last category includes criterion which are subjective, in any cancer centre which undertakes research, accurate subclassification is important. This highlights the importance of specialist referral in haematopathology as per NICE guidance for both diagnostic and research work.
Is Endoglin a Particular Marker for Endothelial Cells in Glioblastoma Multiforme?

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Abstract background: Angiogenesis is an important factor in the growth of solid tumours that can be used in their diagnosis and treatment. Aim:To compare CD31 and CD105(Endoglin) staining in Glioblastoma multiforme angiogenesis. Methods:This study was performed on 50 Glioblastoma multiforme(GBM) samples, referred to Al-Zahra hospital pathology lab between 2001 to 2006. We prepared 3 slides from each sample which were used for immunohistochemistry for CD31, CD105(Endoglin), and CD67(proliferation Index) monoclonal antibodies. Microvessel density(MVD) was evaluated by immunostaining for CD31 and CD105 and the results were compared between the two and also with Ki67 expression. Results:We showed that CD105-MVD was significantly higher in Glioblastoma compared with normal tissue(P=0.012). We did not find such difference for CD31. The mean of CD105-MVD was significantly higher than CD31-MVD in Glioblastoma tissue(P<0.001) although there was a significant positive relationship between them(Pearson’s r=0.630 P<0.001). CD105 odds ratio was 11.1:1. 95% confidence interval: 3.54-36.53. The mean of proliferation index was more closely correlated with CD105-MVD(Pearson’s r=0.611 P<0.001) than CD31-MVD(Pearson’s r=0.360 P=0.01). Conclusion:We suggest that Endoglin can be used as a specific and sensitive marker for evaluation of angiogenesis in Glioblastoma which can be used in the diagnosis and treatment of this tumour. Comparing these results with previous studies revealed the importance of Endoglin in the prognosis of Glioblastoma. Keywords:CD105,CD31,Angiogenesis,Glioblastoma Multiforme (GBM),Vascular Endothelial Growth Factor (VEGF)

Figure 1: Mean of CD105 microvascular density (MVD) and CD31-MVD in glioblastoma and normal brain tissue.

- Student P =0.807 for CD31-MVD
- Student P =0.012 for CD105-MVD

Figure 2: Correlation between CD105 microvascular density (MVD) and CD31-MVD in glioblastomas (Pearson’s r=0.630 P<0.001).
P30
Trends in Primary Cutaneous Melanoma: A 10 Year Single Institution Review

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Purpose: To retrospectively analyse all primary cutaneous melanomas submitted to the Histopathology Department over a ten year period (2000-2009). Our aim was to determine disease incidence and demographics and identify changing trends in presentation including a possible seasonal variation in tumour distribution. Methods: A review was conducted within our institution (University affiliated teaching hospital, catchment area 290,000) to identify all primary cutaneous melanomas resected between 2000 and 2009. The reports were audited using agreed dataset criteria including: age, sex, month of resection, site, subtype (nodular, superficial spreading, lentigo and other) and Breslow thickness. The data was analysed in spreadsheet format using Excel statistics. Results: We identified 263 cases in the defined study period. Females outnumbered males in 1.66:1 ratio (n=164:99) with a predominance of patients > 50 (n=167, mean age at presentation 58.5 years). The number of cases per annum increased between 2000 (n=19) and 2009 (n=40) with an increase in male cases from 21% (n=4) to 57.5% (n=23). A seasonal peak in presentation was seen in summer with an overall summer/winter ratio of 2.39. Additionally, melanomas presenting over the summer had a greater Breslow thickness than those over the winter months (summer: winter ratio of 2.86 for those > 4mm). Conclusions: Our study has identified three interesting trends. The first is confirmation of the seasonal variation in presentation and thickness of melanomas in concordance with other international studies. The second is documentation of the increasing incidence of the disease over a decade of study and the third is the increasing number of male patients presenting with this tumour. This is the first study within Ireland to subclassify the distribution of primary cutaneous melanoma with summer: winter ratios based on patient and tumour characteristics.

P31
An Audit of Subtyping Basal Cell Carcinoma in Diagnostic Biopsies

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Basal cell carcinoma (BCC) is the most common type of invasive skin malignancy. Preoperative biopsy is recommended when there is a clinical doubt or a specialized treatment is required. In addition to the risk of recurrence, identification of a high risk histological subtype is important to reduce the local destructive potential of the tumour. The aim of the audit was to identify the percentage of BCC reports which recorded the histological subtype in diagnostic biopsies in our department. The accuracy of subtyping was also assessed by comparing with subsequent excision biopsies. The search for all BCC cases reported for one year was achieved electronically using the SNOMED coding system on telepath. This search revealed 847 BCC reports. 94/847 BCC reports of diagnostic biopsies with subsequent excision biopsies were identified by manual search. 11 cases were excluded as there was no residual BCC or the subtype was not recorded in the subsequent excision biopsies. The final number of cases included was 83. The subtype in diagnostic biopsies was reported in 61/83 (73.5%). Diagnostic biopsies correctly identified the BCC subtype in 47/61 (77%) cases. A total of 22 cases (26.5%) were not assigned a subtype on diagnostic biopsy. Of these 50% (11/22) were found to be a high risk subtype on subsequent excision biopsy. These cases included 7 punch biopsies, 2 curettages, 1 shave biopsy and 1 case where the biopsy type was not specified. In conclusion, the accuracy of histological subtyping in diagnostic biopsies was high (77%) and similar to published data, however, it was recognised that failure to report a high risk subtype in diagnostic biopsies may have a direct impact on the prognosis.

P32
Human Dirofilariosis in a 53 Years Old Female Patient: An Uncommon Entity in the Alpine Region

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Introduction: Dirofilaria repens and Dirofilaria immitis are well known parasites, which are endemic in the climate conditions of Europe. Their natural hosts are carnivores (e.g. cats, dogs). Infection is transmitted by mosquitoes. Humans get accidentally infected, showing subcutaneous dirofilariosis in most cases. Dirofilaria repens and immitis are not endemic in the Alps. Patient Presentation: A 53 years old female patient, who lives in Southern Tyrol, was biopsied due to a re-occurring swelling of the right parotid region in an outward hospital. Radiological examinations were unhelpful. Outward histological examination of the specimen showed a non-specific inflammatory reaction. In fact the patient was treated in a conservative way. Due to persisting symptoms the patient was presented at the University Department of Dermatology, and due to being suspicious for sialadenitis transferred to the Department of Dental Surgery, where she underwent a surgical biopsy. Parasite infection was diagnosed by histology. The diagnosis Dirofilaria repens was confirmed by PCR analysis. No recent travel history was positive for Dirofilaria spp. Conclusion: Human Dirofilariosis is a parasite infection rarely seen in the Alpine region. Between 1981 and 2008 only 13 cases of subcutaneous Dirofilariosis have been reported in Austria. Climate changes are discussed as possible source for increasing infections in central Europe. Although most unlikely in our region, the possibility of a parasite infection has to be excluded in unclear subcutaneous swellings. Histology and PCR Analysis are mandatory for diagnosis.

P33
MELAN-A Expression in Atypical Fibroxanthoma and Pleomorphic Dermal Sarcoma

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Atypical fibroxanthoma (AFX) is a solitary dermal-based tumour that primarily occurs on sun-damaged skin of the head and neck area of the elderly. If confined to the dermis behaviour is benign following complete excision. Invasion of deeper structures is associated with risk for local recurrence and those tumours are best regarded as pleomorphic dermal sarcomas. The diagnosis is one of exclusion using a broad range of immunohistochemical markers. We report three patients with AFX/pleomorphic dermal sarcoma showing aberrant expression of MELAN-A. All three tumours were dermal based and composed of plump spindle cells with admixed large bizarre giant cells in varying proportions. All tumours involved the subcutaneous fat and in all cases, MELAN-A was focally expressed in large giant cells. Tumour cells stained positively for CD68, CD10 and focally for SMA. They were negative for desmin, multiple cytokeratins, CD31, CD34, S100 and HMB-45. S-100 protein expression was noted only in scattered dendritic cells. Aberrant expression of MELAN-A in AFX/pleomorphic dermal sarcoma represents an important diagnostic pitfall, particularly when tumours invade beyond the dermis similar to desmoplastic or spindle cell melanoma. Expression of MELAN-A limited to the giant cells and the absence of S-100 are helpful clues to the diagnosis, as is the fact that expression of second line melanoma markers in desmoplastic melanoma is rare.
Audit of Incomplete Excision Rates of Basal Cell Carcinomas

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Purpose: Incomplete excision of basal cell carcinomas (BCCs) can have significant impact on morbidity. As part of reflective practice and improvement in service, an audit into the rate of incompletely excised BCCs by various clinical groups was carried out. This would help identify the need for improvement in current practice and allow maintenance of clinical standards. The data would also identify factors associated with an increased risk of incomplete excision and correlate with the current literature. Criteria and standards: Various regional audits and literature from the British Association of Dermatologists have shown acceptable incomplete excision rates to range from as low as 4.7% to as high as 13%. From such existing data, a local agreement of the minimum standard of incomplete excision was established and a minimum requirement of 13% was set as the standard. Method: Data was derived retrospectively including up to seven regional hospitals. 1246 reports on BCC skin excisions were analysed according to their gender, clinical groups, tumour site, tumour size, histological subtype and completeness of excision. Results: The overall excision rate of incomplete BCCs was found to be low at 4.3% and no change in management was advised. Factors associated with an increased risk of excision included the following: tumours arising from the periorbital region, scalp and ear; Tumour size greater than 1 cm; histological subtype of micronodular, morphoeic and mixed subtypes; excisions performed by general practice.

Detection and Quantification of MicroRNAs in Laser Microdissected Formalin-Fixed Paraffin Embedded (FFPE) Breast Cancer Tissues

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MicroRNAs (miRNAs) are a class of endogenous non-coding RNAs that target protein coding mRNAs for cleavage or translational repression. Both profiling and functional studies demonstrate deranged miRNA expression in many human cancers including breast tumours. Research in this field is increasing and the potential of miRNAs for being used in clinical settings emphasises the need for sensitive detection techniques. In this study, techniques for the analysis of miRNA expression in microdissected FFPE breast cancer tissues were developed and optimised. Full face sections from three invasive breast tumour samples and different microdissected areas (1,000 to 1 million im2) and section thickness (10 to 200μm) were analysed. Total RNA was extracted using commercially available RNA extraction kits (miRNeasy FFPE Kit, Qiagen; RecoverAll™ Total Nucleic Acid Isolation Kit for FFPE, Ambion; PureLink FFPE RNA Isolation Kit, Invitrogen). Three miRNAs (miR-21: highly expressed, miR-29c: intermediate expressed, and miR-127: low expression in breast cancer) extracted from both gross and microdissected invasive breast cancer tissues were quantified using real-time PCR. The PureLink kit produced largest quantities of total RNA from FFPE breast tumours. All three miRNA (21, 29c and 127) were successfully detected by real-time PCR and levels of sensitivity were comparable between extraction methods. Our data showed that relative miRNA levels gradually decreased with diminishing amounts of microdissected tissue used but reliable miRNA quantification was obtained using at least 5 million im2 from 20μm thick FFPE breast tissue sections. In contrast to previously published results, quantity of miRNA detected in breast tissue samples depends on the amount of tissue used, and cannot be performed reliably from one or a few cells.

Co-existent Granulomatous Vasculitis and Leukaemia Cutis in Resolving Herpes Zoster

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An 80-year-old man with a 5 year history of small lymphocytic lymphoma (SLL) being managed conservatively under a "watch and wait" protocol, subsequently presented with a six month history of indurated tender purple papules. These coalesced to form plaques with some central scarring, and had a dermatomal distribution on the left arm, immediately following herpes zoster infection at this site. Skin biopsy showed marked interstitial granulomas and prominent granulomatous vasculitis, supporting the clinical impression of a post-herpes zoster granulomatous reaction. In addition, there was a dense monoclonal small B-cell lymphocytic infiltrate indicating Koebnerisation by SLL - a finding which previously has not been reported with concurrent post-herpetic granulomatous vasculitis. Although benign pseudolymphomas occur in post-herpetic settings, this case shows that even in association with benign vasculitic features true lymphomas occur. Furthermore it highlights the value of the appropriate use of detailed immunohistochemical analysis, and the importance of clinicopathological correlation.

Suppression of Tissue Autofluorescence with Copper + Hydrogen Peroxide

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The simultaneous immunohistochemical staining of multiple tissue antigens has largely been the preserve of immunofluorescence. In addition, it is probably the only technique that facilitates multiple staining for confocal microscopy. Tissue autofluorescence remains a serious problem, however, and is particularly troublesome where low levels of antigen require illustration. A number of techniques have been developed to suppress tissue autofluorescence such as treatment with copper sulphate, or masking of specific fluorescent substances, such as lipofuscin, with dyes. Here we describe the use of copper sulfate + hydrogen peroxide (a technique that was originally developed to suppress tissue argyrophilia) for suppressing tissue autofluorescence. To evaluate the technique, 4μm sections of paraffin wax-embedded 1% glutaraldehyde-perfusion fixed rat kidney were treated with 10 mM copper sulfate or 10 mM copper sulphate followed by 3% hydrogen peroxide. Compared to untreated tissue, copper treatment produced a noticeable reduction in autofluorescence, but when combined with subsequent treatment with hydrogen peroxide, a further and dramatic improvement was observed. To evaluate the utility of this technique in immunofluorescence staining, further sections of rat kidney were pre-treated with copper + hydrogen peroxide and immunofluorescently stained for aquaporin-1. Staining was compared with untreated sections and with post-staining treatment with copper. In untreated sections, positivity was barely discernable against the intense background autofluorescence. In contrast, immunopositivity could be clearly seen in tissue sections that had been pretreated with copper + hydrogen peroxide.

Post-staining treatment with copper suppressed autofluorescence, but also reduced immunofluorescence.
P38

Raman Microspectroscopic Mapping of Thin Histopathological Tissue Sections

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Disease diagnosis of a biopsy sample is performed routinely by the examination of stained tissue section under a light microscope. Raman spectroscopy shows considerable promise as an optical technique for disease diagnosis, due to its ability to provide valuable biochemical information from tissue samples at the molecular level. As most pathologists and other clinicians are not spectroscopically trained, Raman spectroscopy will only be useful to them if there is a way to present the thousands of Raman signals, obtained from different parts of a tissue section, in a format that is easily interpretable i.e. a Raman map. Paraffin-embedded clinical tissue samples were obtained from the archival files of the Pathology Department, Ninewells Hospital, Dundee with ethics approval from the Tayside Tissue Bank. 4-6μm thick unstained sections were cut and placed onto quartz slides and de-paraffinsed. Raman mapping was performed by raster scanning the tissue using a home-built Raman system. Multivariate analysis was performed by hierarchical cluster analysis (HCA) of the Raman spectra associated with the different tissue types using normal cervical tissue, we successfully mapped squamous epithelium and the epithelial-stromal interface, and Raman maps were generated using the resultant cluster. Using normal cervical tissue, we successfully mapped squamous epithelium and the epithelial-stromal interface, muscular artery and endocervical glands. Analysis of a tissue section containing a cervical intraepithelial neoplasia (CIN) grade 2 lesion adjacent to normal squamous epithelium demonstrated that the CIN lesion clustered predominantly with the basal epithelial cells of normal epithelium and allowed visual discrimination of these areas using the Raman map. These findings suggest that Raman mapping has the potential to provide images that are useful for disease diagnosis. In particular, the discrimination between normal cervical squamous epithelium and CIN is of relevance to cervical screening pathology.

P39

Abstract Withdrawn

P40

Virtual Microscopy Meets the Microsoft Surface: a Multi-Touch Experience for Digital Pathology

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Virtual microscopy provides enormous opportunities for supporting educational, research and diagnostic applications in pathology. Traditionally, whole slides scans are viewed using a standard computer interface, where slides are navigated on a computer monitor using a mouse or keyboard. The Microsoft Surface provides an alternative multi-touch software interface where software control is through natural finger movements and hand gestures across the table surface. The aim of this study was to explore the Microsoft Surface and development of multitouch control for virtual microscopy. We developed a software interface which allows high resolution virtual slides to be viewed on the Microsoft Surface. This was built using the Surface SDK on the .NET framework using Surface libraries and integrated with PathXL (i-Path Diagnostics) for image serving. The virtual slide can be navigated in x and y, and focussed using finger movements across the touch sensitive surface. By swiping a finger from left to right the virtual slide will move to the left. By positioning two fingers close together and dragging outwards, the image magnification will increase. Annotations can be drawn by hand allowing convenient marking of key morphological observations. These natural movements make the use of virtual slides more intuitive. Controls also allow mutliuser interaction locally, where several users can sit around the table and discuss a slide, and also for remote consultation. While education in pathology would be the biggest beneficiary of this technology we are already implementing a tissue microarray interface which allows automatic core marking of key morphological observations. These natural movements make the use of virtual slides more intuitive. Controls also allow mutliuser interaction locally, where several users can sit around the table and discuss a slide, and also for remote consultation. While education in pathology would be the biggest beneficiary of this technology we are already implementing a tissue microarray interface which allows automatic core marking of key morphological observations. These natural movements make the use of virtual slides more intuitive. Controls also allow mutliuser interaction locally, where several users can sit around the table and discuss a slide, and also for remote consultation.

P41

PCR Based Tissue Identification- the UCLH Experience

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PURPOSE OF THE STUDY Accurately identification of tissue from an individual is crucial in the laboratory if mislabelling of slides or carryover of samples is suspected. Equivocal samples, including sub-divided fragments can be identified by PCR amplification of simple tandem repeat (STR) sequences. Here we report our experience of this technique from 2003-2010. METHODS PCR was performed using primer sets designed to target small fragments covering STR regions, to permit analysis of degraded DNA samples and products analysed on polyacrylamide gels. All submitted cases for UCLH patients were reviewed and their contribution to patient management assessed. SUMMARY OF RESULTS Eighteen cases, including one from cytology were included. Six cases (33%) were of clinically significant ‘carry over’. Five of these were confirmed as having extraneous tissue present on the slide and the provenance of one of these cases was identified. In 7 cases (39%) a mix-up, either of forms and tissue, of tissue alone or of mislabelled slides was suspected. In all cases the analysis identified tissue to an individual and resolved the mix-up. In 2 cases prostatic carcinoma was diagnosed in young individuals. At the patient’s request, peripheral blood and the corresponding tissue samples were compared in order to confirm identity. In both cases the tissue was correctly labelled. In 3 cases two consecutive biopsies showed a significant histological discrepancy, but PCR confirmed that no mistakes had been made. CONCLUSIONS The PCR STR analysis was reliable, robust and easy to perform in cases where the origin of tissue samples was in doubt. The results enabled improved patient management with consequent cost saving and quality control benefits.
Epithelial Mesenchymal Transition: Does it happen in Gastric and Oesophageal Cancer?

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Epithelial Mesenchymal Transition (EMT) is a proposed mechanism for cancer metastasis and is characterised by the acquisition of mesenchymal markers, vimentin (VIM) and n-cadherin (CDH2), and the loss of epithelial markers, e-cadherin (CDH1) and cytokeratin (CK). In the upper gastrointestinal tract information on the occurrence of EMT is very limited. Our research aimed to investigate the frequency of EMT in gastric adenocarcinomas and oesophageal squamous and adenocarcinomas in relation to clinicopathological data.

We used immunohistochemistry to evaluate CK and VIM expression in 31 full sections as well as in tissue microarrays of 368 gastric adenocarcinomas (GC), 108 oesophageal carcinomas (OeC) and 26 GC cell lines. In addition, 31 GC full sections, 52 squamous OeC and 26 GC cell lines were stained for CDH1 and CDH2.

23% GC cell lines expressed VIM compared to 2% primary GC. A complete EMT with VIM/CDH2 positivity and reduced CK/CDH1 was found in 12% of GC cell lines but not seen in primary GC. VIM expression was significantly higher in squamous OeC than in adenOeC (65% vs. 14% of cases; p<0.001) and complete EMT occurred in 8% of squamous OeC. No relationship with clinicopathological data or survival was observed.

This is the first study to demonstrate (i) a higher rate of EMT in GC cell lines compared to primary GC which may be related to the artificial in vitro environment of cell culture and (ii) a higher rate of EMT in squamous cancer compared to adenocarcinoma in the upper GI tract. The latter may suggest that EMT is regulated differently depending on morphological subtype. These findings need to be confirmed in a second independent large series and extended to small and large bowel cancers.

P53 Dependent Repression of PLK1

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We investigated the repression of PLK1 in a number of cell lines. PLK1 is an important regulator of the cell cycle as reflected by its expression. PLK1 is expressed as low levels at G1, increasing into S phase and becoming most elevated in G2/M where it acts as a checkpoint to allow G2/M transition. In addition, P53 is required for maintenance of the G2/M checkpoint and without P53 cells are pushed into mitosis. Previous research has shown that as P53 levels augment, PLK1 decreases in expression, however the mechanism for this remains unclear. We have examined the effects of DNA damage in cells and confirmed that PLK1 expression is repressed following P53 up regulation. In addition successful knockdown of P21 by siRNA has shown that PLK1 depletion is independent of P21. Furthermore, we find that P53 is recruited to the PLK1 promoter under conditions of etoposide induced stress and when linked to a luciferase reporter gene, PLK1 promoter activity is repressed. These findings suggest that at the G2/M checkpoint, PLK1 is suppressed in a P53 dependent manner. Over expression of PLK1 is often observed in tumour cells and consequently may offer therapeutic interest.
Properties of Exosomes Derived from Normal and Malignant Prostate, Breast and Bladder Cell Lines.

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Exosomes are small vesicles 50-100 nm in size that are secreted from both normal and tumour cells. They have a wide ranging activity being able to modify the immune response to tumours and having the potential to act as tumour markers. Exosomes were isolated in the supernatant from normal and tumour cell lines. They were concentrated by centrifugation, firstly by collecting the supernatant after a 10,000g spin then pelleting the exosome rich fraction at 100,000g. The exosomes were further characterised by FACS analysis following exposure of the cells to carboxyfluorescein succinimidyl ester (CFSE) and to immunoblotting for exosome markers. The exosomes express Tsg101 and ALIX detected by immunoblotting. These are well characterised exosome markers. FACS analysis following calibration with beads revealed that the particles exhibited a size consistent with that reported for exosomes. The particles in this size range were labelled with CFSE indicating that they had been synthesised by the cells. Fetal calf serum was depleted of exosomes by differential centrifugation. The exosome fraction expressed the markers Tsg101 and ALIX. The growth rates of mammary epithelial cells and the MDA MB231 breast tumour cell line were decreased in exosome depleted medium. The ability of prostate tumour cells to attach to prostate fibroblasts was also compared in exosome depleted medium and with exogenous exosomes added. The ability to attach was modified by the exosomes. Exosomes derived from tumour cell lines modify the growth and attachment of tumour cells.

Non-Technical Skills in Histopathology: Definition, Relevance and Potential Application

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The NHS is a high risk organisation where there is a 10% possibility of adverse events for hospital patients. Most safety incidents in health care and other high risk industries like aviation are associated with ‘human factors’, failures in cognitive and social skills, classified as non-technical skills, comprising situation awareness, decision making, communication, team-working, leadership, managing stress and coping with fatigue. We explore how non-technical skills are relevant to histopathological practice where these risks apply. Histopathologists make hundreds of decisions that affect patients. Getting these correct requires extensive training and professional development, audit and EQA. While these processes improve performance, they may not be sufficient to ensure a high level of safety. Delivery of high quality care requires more than diagnostic acumen. Communication between medical, scientific and administrative staff in laboratories is crucial, as is that with multidisciplinary care teams. Clarity within departments about leadership responsibilities and accountability is necessary. These factors are acutely relevant in the stressed environments in which many histopathologists work. The aviation and nuclear power industries have recognised the need to understand the factors influencing human performance in safety critical occupations. They have identified non-technical skills that are protective for safety and train them to reduce the likelihood of human error. Anaesthesia and surgery have recently developed non-technical taxonomies relevant to their practice leading to training to assist skill development. This paper explores how developing non-technical skills in histopathology could enhance our ability to provide a safe accurate service, help us to construct training that is more safety-sensitive and improve the quality of our practice.

Emergency Requests for Histopathology–Standard Setting and Audit

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We noted high numbers of apparently inappropriate "urgent" requests for histopathology reports using time and diverting resources. Many lacked clinical details justifying the "urgency" and contact details. We sought to establish the nature of these requests and thus try to change behaviours in requestors. We identified 102 consecutive urgent requests (Series 1, S1; September - October 2008) and collected details of these electronically. Results were fed back to requestors. Over the same time interval in 2009, we carried out an audit following the intervention using the same methods (Series 2, S2), collecting 76 cases. This study presents our findings.

Most specimens in both series were gastrointestinal biopsies although many other specialties were represented. Clinical contact details were absent in 59% of S1 and 47% of S2 cases and in many clinical details were scanty. Specimens spent between <24hours to 5days to reach the department. Cases were reported by consultants alone in 54% (S1) and 53% (S2). Telephoned reports took on average 1day 18hours (S1) and 2days 8hours (S2). Trainee involvement did not affect this. Clinical diagnosis varied between S1 and S2: malignant 38%, 86%; benign 19%, 5%, inflamed 43%, 4%, none given 0%, 5%. Pathological diagnosis also varied: malignant 25%, 57%; benign 32%, 37%; inflamed 37%, 11%; not diagnostic 1%, 0%.

Overall, there was a good correlation between the clinical and pathological diagnoses (p<0.00001) although only 64% of clinically malignant cases were classed as such pathologically. Discussion with clinical colleagues resulted in fewer urgent requests over the same time period one year later and a higher proportion of possibly malignant cases in this group. Concluding, we find that feedback can influence requesting behaviours. We concede that there is still room to improve the provision of contact details and clinical justification of urgent requests.

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The induction is fundamental to ensuring effective transition for specialist trainees into new roles and departments. PMETB and the MMC both set out standards for trainee induction. The aim of this audit is to compare the current ST1 induction in histopathology with these standards, from the trainees’ perspectives. This audit is being carried out in parallel to one looking at induction from the trainers’ perspectives.

A questionnaire was created using ‘Survey Monkey’, covering the PMETB and MMC standards for induction and distributed to all current ST1 histopathology trainees in England and Wales. The response rate was 40.6%. 96% of trainees had a departmental induction. The majority of the aspects of induction included in the standards were received by >80% of trainees. The two standards for which <80% of trainees received induction were provision of information about the service the trainee is working within and provision of information about when RCPath events were. For the majority of the standards audited, >85% of trainees felt the information provided relating to that standard was adequate or excellent. The areas where ≤15% trainees felt induction was poor were information about support systems available; information about the service they were working within; information about the on-line portfolio and information about when RCPath events were.

This audit indicates parts of the induction period that could be improved to bring it in line with national standards. Introduction of a national framework for induction in histopathology would provide consistent induction across the SHO training schools, incorporating the PMETB and MMC standards and focusing on the specific needs of new ST1s in histopathology.

References
1 PMETBs Generic Standards for Training
P52
Perceptions of the Teaching of Pathology Amongst Medical Students: A Comparison Between a Problem-Based and a Traditional Lecture-Based Learning?

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Purpose of Study: The reform of undergraduate medical teaching has led to an integrated problem-based learning (PBL) style replacing the traditional lecture-based (TLB) learning. The Royal College of Pathologists state “the low profile of pathology teaching in the undergraduate medical curriculum has become increasingly damaging to the recruitment of quality UK medical students.” This study evaluated the perceptions of Pathology teaching amongst medical students from both PBL and TLB medical schools. Methods: An on-line survey was sent to medical students from 24 medical schools. They were asked about the quality of Pathology teaching (including what facilities were provided) at their medical schools and their understanding of Pathology. Summary of Results: 1126 students from 17 universities responded, with even representation over years 1-5, the data was analysed using the Mann-Whitney-U test. Approximately 75% of students from PBL courses compared to 38% from TLB courses said Pathology teaching was neglected (p<0.001) on their curriculum and only 20% (PBL) versus 52% (TLB) felt they had a good understanding of Pathology (p<0.001). Approximately 10% (PBL) and 17% (TLB) said they were specifically examined on Pathology during their end-of-year/final exams. The TLB courses provided far superior teaching facilities compared to PBL, e.g. 63% providing microscopes compared to 11% of PBL courses. Furthermore, 74% (TLB) practiced cadaver dissection compared to only 24% of PBL courses, 34% (TLB) of which had some formal pathalogy during these sessions compared to only 6% in PBLs. Conclusions: Pathology underpins a majority of clinical diagnosis and decisions that are made. It’s understanding (through effective teaching) is paramount to good medical practice. This study demonstrates that Pathology is poorly assessed in medical exams and more worryingly that PBL is poor in disseminating pathological principles.

P53
Students’ Deep, Strategic and Surface Approaches to Learning and Studying Over a Medical Degree Programme

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Students combine three approaches to learning and studying: deep, where learners aim for long term retention of subject matter thorough understanding, surface, which implies learning by rote with little understanding, and strategic, which concentrates on achieving high grades. Learning approach may change with environment. We used the Approaches to Study Skills Inventory for Students (ASSIST) questionnaire to measure the scores of medical students. We previously showed little change between early first year and late years of the medical degree programme. Reliability (Cronbach alpha) was >.7 for scales and >.5 for subscales. At the start of year 1 students in both cohorts gave high scores for deep and strategic, but relatively low scores for surface (Tables). Spearman correlation of matched pairs between first and later years showed no significant increase in scores for deep and strategic and a slight but not significant fall in surface. This slight tendency for surface scores to decrease is in keeping with results from studies in other subject areas at university. Various factors could explain the findings. Students enter with established approaches, scoring highly on deep and strategic approaches and it may be difficult to increase the scores further. Assessments were deliberately designed to test for competence and may not sufficiently promote a deep approach. Some students may succeed in assessments by using a surface approach and see no need to change. Finally, the questionnaire may not detect changes in approaches in learning and studying in medicine, either because some questions are inappropriate or do not reflect students’ real study practice.

P54
Attitudes of First Year Medical Students from Different Religious Backgrounds to the Autopsy

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Introduction: The role religion plays in shaping attitudes towards the autopsy is an important one and can impact the way in which doctors take consent for autopsies. Conversely doctors can also face resistance from bereaved relatives to autopsy based on religious grounds. Aims: To investigate the attitudes of first year Muslim, Christian and Atheist medical students to establish whether religion affects their views on the autopsy and their thoughts about taking consent from bereaved relatives after qualification. Methods: First year medical students responded to an advert on a medical student intranet site. Three semi-structured focus group discussions of the respective groups were audio taped. Their religious views, personal experiences of autopsy, the role of the coroner and taking consent for autopsy were discussed. Recordings were transcribed verbatim and subjected to a qualitative analysis by defining codes and sub-codes. Subsequent collation of the data allowed direct comparisons to be made between the three groups. Results: Most participants felt uncomfortable with the physical procedure of the autopsy, especially on a member of their own family. Findings from the Christian and Atheist groups were very similar with no objections to autopsy based on their religious or personal beliefs. The Muslim group believed that the deceased should be buried immediately and were concerned an autopsy would delay this religious obligation. Discussion: This study demonstrates that religion affects the personal beliefs of students and influences their behaviour in their personal lives. They are aware that their beliefs could infringe on their professional responsibilities as doctors, and their interactions with patients of other beliefs. They are keen to learn about other religions so that they can manage those interactions.
The Delivery of Pathology Teaching in the Medical Curriculum: How Often are Medical Students Taught and Examined in ‘Pathology’

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Introduction: The Royal College of Pathologists (RCPath) response to the 2007 NHS Employers paper ‘The Future of the Medical Workforce’ stated "lack of exposure to modern scientific principles during undergraduate... medical training results in a total workforce that is significantly deficient in a modern comprehension of pathological processes" and that "the low profile of pathology teaching within the undergraduate medical curriculum has become increasingly damaging to the recruitment of quality UK medical students." Leading on from these statements an audit group from the RCPath sought to determine at what stage and how often medical students were taught pathology as a surrogate marker for the extent and profile of pathology teaching and whether pathology is formally examined in end of year and final examinations as a surrogate for sufficient comprehension of pathology.

Methods: An on-line survey was sent to Medical Students in all years of study from 24 medical schools in England and Wales. Students were asked to provide information regarding the frequency and timing of pathology teaching and examinations at their medical school.

Results: Responses were received from 1126 medical students from 17 medical schools in England and Wales, distributed between years 1-6 (Graph 1). Students reported pathology to be predominantly taught during years 1 and 2 (Graph 2) and only 4% reported pathology teaching in all years of medical school. Less than 15% reported having a form of pathology teaching weekly. 50% of the respondents reported being specifically examined in pathology in their end of year/final year examinations.

Discussion: The results of this survey support the views held by the RCPath and highlight potential areas for future development of medical curricula to enhance medical student perceptions and comprehension of pathology.

Continuous Analysis of Histopathology Trainee Reports as a Means of Assessment

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Aim: We sought to determine the feasibility of a continuous assessment method by way of analysis of trainee reports. Secondarily, we hoped to evaluate the quality of reports to advocate or counter graded independent reporting by trainees.

Method: Seven histopathology trainees were consented for the 6 month study. For each case they determined whether or not, if given the opportunity, they would report independently. All cases were thus categorised as either confident or non confident. Trainee reports were then compared to final issued report using a scoring system for macroscopy, microscopy examination and report formulation. Attention was given to report errors which would have led to an untoward clinical event. Other criteria included conveyance of appropriate certainty, use of relevant clinical comments and overall clarity. Data was compiled onto Microsoft Excel. Results: Entries focused on the microscopic examination whilst macroscopic and report formulation criteria were largely ignored. The two junior trainees were both confident of 73% of cases. Their overall accuracy rates were 87 and 75%. On average senior trainees (ST5s) confidence rate was 93% and overall accuracy ranged from 88 to 96%. The rate of major errors was 3 - 4% for juniors and 1 - 2% for seniors. For cases considered 'confident' the major error rate was below 0.8% for all trainees.

Discussion: There was moderately low acceptability of data entry because it was deemed too time consuming. Fewer categories and criteria are likely to increase acceptability. Confidence and report accuracy increased with trainee experience. However, all trainees were adept at recognising cases where they were likely to make errors. Graded responsibility for independent reporting is supported by the low incidence of errors in confident cases.
P57
Do Medical Students Understand The Role of a Pathologist?
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1University Hospitals of Leicester, Leicester, United Kingdom; 2St James University Hospital, Leeds, United Kingdom; 3The Royal London Hospital, London, United Kingdom
The Royal College of Pathologists states that pathology is the hidden science at the heart of modern medicine, vital for the diagnosis and clinical management of disease. The pathology experience of medical students is declining and very few spend time in a pathology department. If they do not understand what the role of a pathologist is how can they be expected to be interested in a career in pathology? Method: To establish what medical students understand about the role of the pathologist, each medical student from 24 medical schools in England and Wales were sent an online survey. Results: 1126 students replied from 17 universities with even representation over years 1-5. Only 866 students agreed with the statement ‘a pathologist needs to be a medically qualified doctor’ and 57 did not think a pathologist needed clinical knowledge and expertise to carry out their work. 99% and 92% thought pathologists’ work involved post mortems and disease diagnosis respectively. 310 students thought pathologists did not need good communication skills and only 31% would consider a future career in pathology. Discussion: The findings show that the majority of medical students understand a pathologist’s work involves diagnosis of disease and performing post mortems. However, the understanding of the attributes one must have to train and become a pathologist is clearly a problem and this may be as a result of lack of exposure to the specialty. Pathology is slowly increasing its profile and medical students should be our number one target audience.

P59
Examination of a Large Series of Temporal Artery Biopsies Shows That EVG Staining does not Contribute to the Diagnosis - a Follow on Study
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BACKGROUND: Elastic Van Gieson (EVG) stain continues to be used routinely to demonstrate disruption of the internal elastic lamina in clinically suspected giant cell arteritis (GCA). Recent reviews, however, have shown high variability for all features of GCA except the presence, extent and severity of mural inflammation. Previous audit of a small case series of positive biopsies confirmed that routine use of special stains in temporal artery biopsies does not increase diagnostic sensitivity, but this did not include review of EVG appearances in negative biopsies. PURPOSE: To re-assess the contribution of EVG to the diagnosis of GCA, compared with standard haematoxylin and eosin (H&E)-stained sections alone. METHODS: A retrospective case series of 525 temporal artery biopsies (Jan 1999-Oct 2009) was identified from computerised hospital records, yielding 105 biopsies positive, and 406 biopsies negative, for GCA. Positive biopsies were reviewed histologically against standard diagnostic criteria and comparable information obtained from reports of negative biopsies. RESULTS: Review of H&E-stained sections demonstrated diagnostic features of GCA in 97.2% (n=102) of positive cases. Disruption or reduplication of the internal elastic lamina was apparent in 96.1% (n=101) of EVG-stained sections, but was also reported as present in nearly two thirds of negative biopsies. CONCLUSIONS: Results confirm that use of an EVG stain does not contribute to the recognition of diagnostic features in most cases of GCA and should therefore be limited to those with a strong clinical suspicion of GCA, but equivocal findings on H&E-stained sections. Inclusion of pre-biopsy treatment information on histopathology request forms would assist clinicopathological correlation in this group.
**P61**

**Qualifying an IHC Pharmacodynamic Biomarker - Androgen Receptor in Skin**

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Quality assuring a pharmacodynamic biomarker can be divided into three steps for sufficient robustness to use for go/no go decisions in clinical development. The three steps are: Feasibility, Reproducibility, Positive control.

In clinical development proof of mechanism (PoM) biomarkers can evaluate if the drug hits the target to support go/no go decisions. Therapies targeting the androgen receptor (AR) e.g. bicalutamide, are important treatment options for prostate cancer patients.

Collection of paired prostate biopsies to assess biomarker modulation before and on treatment can be challenging. Skin may be a surrogate tissue and potentially easier to collect.

This study evaluated if AR expression in skin could be quantified (feasibility) by immunohistochemistry (IHC) and to assess reproducibility, using prostate tumour as positive control. Twelve male healthy volunteers aged over 50 years were enrolled. Skin biopsies were collected at 3 time points on each of 2 days, one week apart. Biopsies were formalin fixed (24 hours), paraffin embedded. Sections were cut and stained with routine IHC method for AR (Dako). Stained slides were assessed by histopathologist and image analysis (Chromavision ACISII). AR expression was measured in the nuclear compartment of epidermis and sweat gland.

Overall variability of AR expression was high and dominated by the intra-subject (intra-day, inter-time) component (Coefficient of variability = 83%).

Conclusion: AR expression can be measured by IHC in skin. Whilst it may be feasible to assess AR expression for PoM in single centre healthy volunteer studies, given the biological variability it is unlikely to be useful in multicentre patient studies.

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**P62**

**A Rare Cause of Childhood Death: Clostridium Perfringens Sepsis in a Gastrostomy Fed Child with Cerebral Palsy**

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A 13 year old boy with cerebral palsy had a 24 hour history of fever and diarrhoea prior to unexpected death at home. His body was received in the mortuary 24 hours after death, after appropriate refrigeration at the funeral home. The body was unusually foul-smelling and there was a bloated appearance to the body, with x-ray confirming extensive subcutaneous emphysema. Full post mortem examination revealed a gastrostomy in situ, repair of a previous atrial septal defect and a fundoplication. The stomach showed intramural gas with overlying mucosal splitting, and the small and large bowel were markedly distended by gas. The Airways were erythematous and there were haemorrhagic changes in the lungs. The liver showed generalised necrotic softening with large gas bubbles. Histological examination revealed extensive growth of gram positive rods throughout most tissues, including the small bowel, with surrounding tissue necrosis and gas spaces. Microbiology revealed a pure growth of Clostridium perfringens from the spleen. Anaerobic cultures had not been performed on other samples, but the morphology of the gram positive rods seen throughout numerous organs is fully consistent with Clostridium perfringens. Death from Clostridium perfringens infection is rare in humans, and is usually associated with type C strains which cause necrotising enteritis. Unfortunately strain type was not available in this case, but the histology was consistent with necrotising enteritis. This child was gastrostomy fed with a sterile liquid feed which was found not to be contaminated on testing. Infection must therefore have originated from endogenous bowel bacteria. It is possible that some children with cerebral palsy have reduced splanchic perfusion, and therefore mucosal ischaemic damage could be the initiating factor for infection in this case, in a situation analogous to Clostridial necrotising enterocolitis in premature neonates.

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**P63**

**Pulmonary Hyperplasia Secondary to Bronchial Atesia**

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During the first pregnancy in a 26 year old mother, a fetal anomaly scan at 20 weeks’ gestation showed significant abdominal ascites and an enlarged echo bright right lung with cardiac displacement. These findings were consistent with a type III congenital cystic adenomatoid malformation (CCAM). Labour was induced at 32 weeks gestation due to increasing polyhydramnios and maternal dyspnoea. Labour was complicated by abdominal distocia and fetal paracentesis was performed, draining 800mLs of fluid. A fetal bradycardia developed and unfortunately the baby was stillborn. Post mortem examination revealed atresia of the right lower lobe bronchus, and the right middle and lower lobes were markedly enlarged. The abdominal skin was lax due to previously drained ascites. Some haemorrhagic ascites remained, and the intestines and kidneys showed haemorrhagic venous infarction, attributed to impaired venous return due to the right lung mass. Histology of the lung mass showed a marked increase in alveolar and broncholar spaces. The features are typical of those traditionally described as type III CCAM, but in the context of bronchial atresia, are better described as pulmonary hyperplasia, similar to the changes seen in laryngeal atresia. This case is instructive in showing the profound haemodynamic disturbances that an intrathoracic fetal lesion causes, with fetal hydrops and haemorrhagic infarction of intra-abdominal organs due to impaired venous return. Current concepts of congenital cystic lesions that challenge Stocker’s original classification are also discussed.
P64
Reporting of Lymphoma by Paediatric Pathologists: Five Year Experience of a Regional Children’s Hospital
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BACKGROUND: Current national guidance indicates that a specialist haematopathologist should be involved in multidisciplinary team (MDT) review of all paediatric lymphomas. In our institution, like other children’s hospitals in the UK, lymphomas are reported by paediatric pathologists, and discussed at the Paediatric Oncology MDT with paediatric oncologists. Expert haematopathology review is carried out only when the paediatric pathologist decides to refer the case. METHODS: An audit of 5 years of haematopathology specimens reported by our department was carried out, to assess the workload in comparison to other paediatric tumours, and to look at referral patterns and concordance of diagnosis between paediatric and haematopathologists. RESULTS: From 2005-2009, 69 haematological malignancies and 254 benign conditions were reported. More than half of lymphomas were reported (62). Visit our website: www.pathsoc.org

CONCLUSIONS: Paediatric lymphomas are among the commonest of paediatric malignancies. If appropriate and cautious referral to an expert is used, paediatric pathologists should be able to report lymphomas safely. Reporting by paediatric pathologists aids discussion of patients with paediatric oncologists, and turnaround times are far shorter than would be possible if samples were sent away to another centre.

<table>
<thead>
<tr>
<th>Tumour Type</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical Hodgkin’s Lymphoma (CHL)</td>
<td>25</td>
</tr>
<tr>
<td>Nodular Lymphocyte Predominant HL (NLPHL)</td>
<td>4</td>
</tr>
<tr>
<td>Precursor B Lymphoblastic Lymphoma (B-LBL)</td>
<td>3</td>
</tr>
<tr>
<td>Burkitt’s Lymphoma (BL)</td>
<td>14</td>
</tr>
<tr>
<td>Diffuse Large B Cell Lymphoma (DLBCL)</td>
<td>2</td>
</tr>
<tr>
<td>Follicular Lymphoma (FL)</td>
<td>2</td>
</tr>
<tr>
<td>Precursor T Lymphoblastic Lymphoma (T-LBL)</td>
<td>8</td>
</tr>
<tr>
<td>Anaplastic Large Cell Lymphoma (ALCL)</td>
<td>5</td>
</tr>
<tr>
<td>Langherhan’s Cell Histiocytosis (LCH)</td>
<td>3</td>
</tr>
<tr>
<td>Myeloid Sarcoma</td>
<td>2</td>
</tr>
</tbody>
</table>

Reason for Referral | Haematopathology Opinion |
---------------------|--------------------------|
2 cases unusual reactive pattern, rule out interfollicular Hodgkin’s lymphoma | One EBV infection, one reactive |
2 cases florid reactive pattern with progressive transformation of germinal centres | Agree |
1 case clearly benign histology, referred due to strong clinical and radiological suspicion of malignancy | Agree benign |
1 autopsy case, rule out immunodeficiency | Normal |
1 case, immunohistochemistry suggestive of myeloid sarcoma in leukemic patient | Reactive with mast cells and small vessels, no blasts |

CONCLUSIONS: Paediatric lymphomas are among the commonest of paediatric malignancies. If appropriate and cautious referral to an expert is used, paediatric pathologists should be able to report lymphomas safely. Reporting by paediatric pathologists aids discussion of patients with paediatric oncologists, and turnaround times are far shorter than would be possible if samples were sent away to another centre.

P65
Congenital Cystic Malformation of the Oral Cavity: An Indication for Exit Procedure?
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Aims and Backgrounds: Congenital Cystic Malformations of the oral cavity are rare entities of fairly unknown etiology. Heterotopy or embryonal maldevelopment are discussed as possible causes. Many heterogeneous differential diagnoses, such as benign and malignant tumours have to be considered. Due to their potential of airway obstruction after birth a sudden clinical and/or surgical intervention may become necessary. Patient Presentation: A male fetus showing a cystic tumour (about 1 cm in diameter) (3rd child of a 39 years old G6P2A3) by prenatal routine ultrasound scan was identified in the 19th week of gestation. During pregnancy the tumour showed a slightly increase of size (up to about 2.5 cm in diameter in the last trimester). A cesarean section with possible exit procedure was made in the 37th + 6 week of gestation because of the possibility of airway obstruction and respiratory distress. The newborn (3780 g body weight at birth) showed a 2.3 cm sized cystic tumour at the tip of the tongue. No disturbances in tongue movement nor respiratory distress were observed. Due to tumour size a decision for tumour excision was made. The specimen was examined histologically showing a mucous filled connective tissue cyst with squamous and cylindrical epithelium. Postoperative outcome was uneventful. Conclusion: Congenital tumours of the tongue are rare entities of unknown origin, which may be diagnosed accidentally by prenatal ultrasound or postnatal. Several differential diagnoses, such as other benign (e.g. ranula) or malignant tumours (malignant teratoma) are known, all of them may cause respiratory problems. Depending on site exit procedure can be necessary. Indication for postnatal surgical depends on tumour size and histology.

P66
Congenital Abdominal Cyst in a Female Patient – A Challenging Case
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Aims and Backgrounds: Congenital Abdominal Cysts are heterogeneous entities. Several differential diagnoses, e.g. ovarian cysts, hepatic cysts, intestinal duplications, cystic lymphatic malformations, have to be considered. In female fetuses ovarian cysts are the most frequent observed abdominal cysts. Treatment ranges from conservative procedure (wait and see) to fine needle aspiration and surgical intervention. Patient Presentation: A 29 years old G1P0 presented in the 35th + 3 week of gestation at the Department of Gynaecology due to her female fetus showing sonographically a subhepatic cystic structure (52 x 31 x 45 mm) with sediment. No further anomalies were detected. The placenta was sonographically inconspicuous. Decision for cesarean section to avoid hemmorhage complication by compression of the cyst was made and performed without problems in the 38th + 4 week of gestation. The baby was observed postpartum and at the age of 11 weeks, the child, who appeared constantly diseased, developed an acute abdomen. By surgery a conglomerate tumour of the known cystic part (6 cm), which showed adhesions with inflammatory altered small bowel loops and the greater omentum, was found. The cyst was examined histologically, presenting a hemorrhage infracted, non malignant soft tissue cyst with some calcifications, focal circular smooth muscle layers and a local peritonitis. No characteristic structures (not intestinal-, neither hepatic- nor ovarian-tissue) were found. Conclusion: Torqued ovarian cysts are observed more frequent before birth than postnatal. Sonographic verified segment suggests a hemorrhage process or torsion. Complications associated with conservative treatment or fine needle aspiration have to be considered. Postpartual surgical treatment is, as well as indicating operative intervention on the cyst size (> 4 cm) discussed controversial, due to high tendencies of cyst regression in the further course.

62 Visit our website: www.pathsoc.org | Summer Meeting (198th) 29 June – 1 July 2010 | Scientific Programme
Changing Patterns of Infant Death over the Last 100 Years: Autopsy Experience from a Specialist Children’s Hospital

Introduction: Paediatric autopsies have been performed at a specialist children’s hospital in the United Kingdom since the 1880’s, with the original hand written reports available for at least the last century. This study reviews the major findings from infant autopsies performed in 1909 and 2009 at this specialist centre.

Methods: Retrospective analysis of autopsies performed in the same unit 100 years apart.

Results: In 1909, 357 autopsies were performed at the centre including 178 infants (50%), compared to 347 autopsies in 2009, including 128 infants (37%). The causes of death and patterns of disease identified at autopsy were significantly different between 1909 and 2009, namely, infection in 132 (74%) including 10 tuberculosis and diphtheria, and 19 meningitis) and 25 (20%; zero) respectively. Congenital heart disease was diagnosed in 4 (2%) and 9 (7%) infants with gastroenteritis in 19 (11%) and 1 (1%) and other gut anomalies in 17 (10%; including 8 congenital pyloric stenosis and 4 congenital absence of bile ducts) and 2 (2%) respectively. Only 11 (7.5%) was classified as unknown in 1909 compared to 48/128 (38%) in 2009.

Conclusion: During the last century, autopsy findings from a single paediatric centre demonstrate the changing pattern of fatal infant diseases, the earlier period associated with significantly more infectious deaths, especially due to meningitis, TB and diphtheria, and deaths from structural anomalies which are now surgically correctable, such as pyloric stenosis and congenital liver disease. Due to changes in referral patterns, disease epidemiology and pathology practice, unexplained infant death (SIDS) is now the commonest group, being almost never encountered, or reported, in 1909.

Autopsy Findings in 885 Consecutive Sudden Unexpected Deaths in Infancy Examined at a Single Specialist Paediatric Centre

Introduction: Sudden unexpected death in infancy (SUDI) remains the commonest presentation of post-neonatal infant death, with various hypotheses regarding the cause and mechanism of death. This study reviews the findings from a consecutive series of SUDI autopsies performed in a single specialist centre over a 14 year period (1996 to 2009).

Methods: Data from >2,750 consecutively performed paediatric autopsies performed by specialist paediatric pathologists at one centre according to a standard protocol were retrospectively recorded into an autopsy database. SUDI cases were identified and autopsy findings reviewed.

Results: Of 2,762 consecutive autopsies, 1,228 were infants between the ages of 7-365 days. Of these, 885 presented as SUDI. 334 cases (38%) were explained following autopsy leaving 551 unexplained cases, representing SIDS / unexplained SUDI. Of 334 explained deaths, 188 (56%) were infection-related, 35 due to cardiovascular system abnormalities (4%; including 32 congenital heart disease). There were 33 cases (4%) with features of non-accidental / inflicted injury as the cause of death. Of 458 unexplained SUDI in whom death was recorded as during normal sleep, 237 infants were co-sleeping (52%), compared to 14% co-sleeping in the explained death group (19/138).

Conclusion: In a large series of SUDI autopsies at a specialist centre, including ancillary investigations, around 60% of deaths remain unexplained, with more than half of these being co-sleeping associated. Infection represents the commonest currently detectable aetiology of explained SUDI cases.

Autopsy Findings in Sudden Unexpected Early Neonatal Death: Results from a Specialist Centre

Introduction: Sudden unexpected early neonatal death (SUEND) in the first week of life shares some features with sudden unexpected death in infancy (SUDI; 7-365 days) but is not usually included in SUDI statistics. This study reviews findings of >100 consecutive SUEND autopsies performed at a specialist centre.

Methods: Data from >2,750 consecutively performed paediatric autopsies performed by specialist paediatric pathologists at one centre according to a standard protocol were retrospectively recorded into an autopsy database. SUEND cases were identified and autopsy findings reviewed.

Results: Of 2,762 paediatric autopsies, 299 were deaths in the first week of life, including 101 (34%) presenting as SUEND of an apparently clinically well infant. 64 (64%) were explained following autopsy, whilst 36% remained unexplained. 10 (27%) of the unexplained deaths were associated with co-sleeping with an adult. Of the explained deaths, 17 (27%) were infection-related, 11 (18%) due to metabolic causes and 15 (24%) undiagnosed congenital abnormalities, mainly congenital heart disease.

Conclusion: Two-thirds of SUEND are explained following autopsy, compared with around one third of SUDI, but one third remains unexplained, analogous to SIDS in older infants. In this group of explained deaths, infection is the commonest cause of death, followed by unexplained congenital abnormalities and metabolic disease.

Autopsy Findings in Paediatric Sickle Cell Disease

Introduction: Sickle Cell Disease (SCD) is a common single gene disorder, with significant morbidity and mortality despite improvements in healthcare. Death in childhood from SCD is rare. This study reviews findings from paediatric autopsies in a single specialist centre of cases with SCD.

Methods: Data from >2,750 consecutively performed paediatric autopsies at one centre were retrospectively recorded into an autopsy database. Deaths where the patient was known to have SCD were identified and autopsy findings reviewed.

Results: Of 2,762 paediatric post-mortem examinations, only 11 (0.4%) patients were identified with SCD. At time of presentation, one was not known to have SCD, being diagnosed after collapse. One patient had been diagnosed immediately prior to collapse. Three patients suffered from previous sickle crises requiring hospital admission. One patient presented with a fatal first crisis. Seven were referred as sudden unexpected deaths. 8 (73%) patients showed extensive sickling, with or without haemorrhage, in at least one site. Of all cases, 6 (55%) died from direct consequences of SCD (splenic sequestration, sickle cell crises, acute chest syndrome, acute cerebral infarct). Three died from infections, including viral gastroenteritis and pneumococcal sepsis, and one case, the youngest death in the group (22 days of age), did not show sickling on histology but died directly from bronchopneumonia. One died from a ruptured aneurysm of the posterior cerebral artery, with subarachnoid haemorrhage, a known association with SCD.

Conclusion: The autopsy revealed expected and unexpected findings in these cases with SCD. Around half died due to sickling complications, the others from related or unrelated causes. In 20%, the death was the initial presentation of SCD. These findings emphasise the need for aggressive management of patients with SCD in order to reduce mortality and morbidity.
P71

Autopsy Findings in Pediatric Immunodeficiency: Cases from a Specialist Paediatric Centre

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Introduction: The diagnosis of primary immunodeficiency diseases has improved over the past 10 years with advancing medical knowledge, in particular with regards to the genetics of such diseases, most presenting clinically with recurrent infection of systemic disease. This study reviews autopsy findings of such cases.

Methods: Data from >2,750 consecutively performed paediatric autopsies performed by specialist paediatric pathologists at one centre according to a standard protocol were retrospectively recorded into an autopsy database. Cases where a diagnosis of primary immunodeficiency had been made were identified and the autopsy findings reviewed.

Results: Of 2,762 consecutive autopsies, 17 (0.6%) cases were identified with a diagnosis of immunodeficiency, including one case of common variable immunodeficiency (CVID), five of severe combined immunodeficiency (SCID), five of presumed primary undetermined immunodeficiency (based upon clinical and autopsy findings) and six cases with DiGeorge syndrome. 2 presented as sudden unexpected death in infancy, all others cases being clinically unwell and undergoing investigations prior to death, including all six DiGeorge syndrome cases with congenital cardiac disease. 7 deaths (41%) were associated with atypical infections (including Pseudomonas, Pneumocystis jiroveci, and Cytomegalovirus), 6 were due to complications of congenital heart disease and the remainder due to other causes.

Conclusion: Primary immunodeficiencies are rarely seen in paediatric autopsy practice, most presenting clinically prior to death, but occasionally presenting as sudden unexpected death in infancy, the diagnosis being made at autopsy. Of the non DiGeorge cases without congenital heart disease, two-thirds were deaths associated with atypical infection.

P72

Autopsy Investigations Suggestive of Metabolic Causes of Death

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Introduction: Metabolic disease can be challenging to detect clinically and may present as Sudden Unexpected Death in Infancy, posing difficulty with autopsy interpretation of ancillary investigations.

Methods: Data from >2,750 consecutively performed paediatric autopsies performed by specialist paediatric pathologists at one centre according to a standard protocol were retrospectively recorded into an autopsy database. Infant deaths with Oil-Red-O staining of frozen sections and blood or bile Tandem Mass Spectrometry (TMS) Guthrie results were identified and autopsy findings were reviewed.

Results: Of 2,762 consecutive autopsies, 870 were infants in whom Oil-Red-O (ORO) staining was performed on frozen samples of heart, muscle, kidney and liver. 93 (11%) showed significantly increased fat in at least two tissues. TMS results demonstrated 13 metabolic diagnoses (mainly fatty acid oxidation disorders). Of 22 cases of abnormal fat staining in only 2 tissues, 1 had a positive TMS result (9%), of 24 with abnormal staining in 3 tissues, 4 (17%) had positive TMS results, and of 47 with abnormal staining in all 4 organs, 8 (17%) had positive TMS results. Bile Guthrie results were in accordance with Blood Guthrie results in all cases. Only one autopsy with equivocal staining on ORO had a positive TMS result.

Conclusion: Ancillary testing with Oil-Red-O staining for metabolic disease is a cheap and effective screen for most metabolic disorders presenting as infant death and identifies cases at increased risk of metabolic disease in whom formal TMS testing should be performed.

P73

Metabolic Causes of Neonatal and Infant Death: Autopsy Findings from a Specialist Paediatric Centre

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Introduction: Metabolic diseases can present as sudden unexpected infant death and can be challenging to detect in the neonatal and infant period. This study reviews cases of infant death due to metabolic disease examined at autopsy at a specialist centre.

Methods: Data from >2,750 consecutively performed paediatric autopsies performed by specialist paediatric pathologists at one centre according to a standard protocol were retrospectively recorded into an autopsy database. Metabolic causes of death were identified and the autopsy findings reviewed.

Results: Of 2,762 consecutive autopsies, 1,527 represented liveborn infants (<366 days). In total, 59 (4%) cases were identified where either by pre-mortem findings (including clinical history), autopsy findings or ancillary testing were either suspicious for, or diagnostic of an underlying metabolic disorder. 38 (64%) presented as sudden unexpected death with 18 in the first week of life, and 20 aged 7-365 days. 21 presented with preceding clinical features of disease. Of the 59 cases, 31 (53%) occurred within the neonatal period. Causes included mitochondrial defects, fatty acid oxidation disorders and other inborn errors of metabolism.

Conclusion: Metabolic disease may present as neonatal or infant death, more than half of fatal cases presenting as sudden unexpected death, the diagnosis being suggested at autopsy. Selection of appropriate tissue sampling during the autopsy procedure and appropriate ancillary investigations can help confirm the diagnosis and be of help with genetic counselling for parents with future siblings.

P74

Autopsy Findings in Neonatal Deaths; >500 Consecutive Cases from A Specialist Paediatric Centre

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Introduction: Neonatal autopsy rates have fallen in recent years, and only highly preselected cases are referred for autopsy. This study reviews findings from a series of >560 consecutive neonatal autopsies performed in a single specialist centre. Due to the tertiary nature of the centre, and the bias in clinical history of cases referred for autopsy, the cases undergoing autopsy are not representative of unselected neonatal deaths.

Methods: Data from >2,750 consecutively performed paediatric autopsies performed by specialist paediatric pathologists at one centre according to a standard protocol were retrospectively recorded into an autopsy database. Metabolic causes of death were identified and autopsy findings reviewed. Results: Of 2,762 consecutive autopsies, 564 represented deaths of liveborn infants in the neonatal period (<28 days), of which 245 (44%) presented as sudden unexpected deaths, either in the first week of life (sudden unexpected early neonatal death (SUEND)) or at 7-28 days (sudden unexpected death in infancy (SUID)). Overall, 411 deaths (73%) were explained following autopsy; 131 (32%) being due to congenital abnormalities (including 102 congenital heart disease), 85 (21%) were infection-related deaths (including 66 bacterial, 18 viral and 1 fungal) with respiratory tract infection being the commonest infectious process.

Conclusion: The majority of neonatal deaths referred for autopsy to a tertiary centre are explained following post-mortem examination. Congenital abnormalities, especially congenital cardiac disease, and infection, represent the commonest aetiologies of death. Almost half of referred cases represent SUEND or SUID, with about half of these remaining unexplained. Deaths due to common clinically recognisable neonatal complications such as prematurity-related disorders (respiratory distress syndrome, necrotising enterocolitis), are now rarely referred for post-mortem examination.
**P75**

**Difficulty of Interpretation of Post-Mortem Microbiology Results in Unexpected Infant Deaths: Evidence from a Multidisciplinary Survey**

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Introduction: Interpretation of post-mortem microbiology results in investigation of sudden unexpected death in infancy (SUDI) remains difficult. A cross-specialty questionnaire survey was performed to assess interpretive differences and difficulties. Methods: 109 consultant specialists involved in infant death management were contacted (including Paediatric Pathology, Histopathology, Microbiology, Paediatric Infectious Diseases and Paediatrics/Child Protection) with information on 5 standardised SUDI cases differing only in their PM microbiology findings from blood, spleen and lung. Respondents classified each case regarding likely cause of death into 4 categories (definite bacterial infection through post-mortem contamination). Findings were chosen to represent definite infection/non-infection cases and more difficult cases. Results: 63 specialists responded (57%). There were no scenarios in which all specialists agreed. Concordance rates varied: Case 1-76% agreed definite bacterial infection and 20% probable bacterial infection. Case 2, 70% agreed probable bacterial infection. Case 3, 58% agreed post-mortem overgrowth/contamination. Case 4, (Staphylococcus aureus positive cultures) caused the most disagreement with 50% suggesting probable bacterial infection. Case 5, 82% agreed post-mortem contamination, including all paediatric pathologists. There were no other significant differences in responses between specialties.

Conclusion: Interpretation of PM microbiology results in SUDI is difficult with no agreement of interpretation by specialists, discordant opinions regarding the significance of the same findings being seen both within and across specialties. The interpretation of S. aureus positive cultures is particularly challenging. Paediatric pathologists are more likely than paediatricians to attribute findings to PM overgrowth. Further research to aid correct interpretation is urgently required.

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**P76**

**Clinicopathological Features of Paediatric Deaths due to Cardiomyopathy: An Autopsy Series**

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Introduction: Cardiomyopathy is an uncommon but potentially fatal condition which encompasses many types with a range of aetologies and modes of presentation. This study reviews clinical and pathological features of children presenting with cardiomyopathy-associated death at a single specialist centre.

Methods: A retrospective review was carried out of 1,516 paediatric autopsies carried out at the centre from 1996 to 2005 inclusive, to identify cases in whom a diagnosis of cardiomyopathy was made at autopsy.

Results: 32 potential cardiomyopathy deaths were identified, 13 of which were excluded from further analysis (11 post-cardiac transplant deaths; 2 mycardiitis). Of 19 cases included, the final diagnosis was dilated cardiomyopathy in 11 (58%), hypertrophic cardiomyopathy in three (16%), arrhythmogenic right ventricular cardiomyopathy in two (11%), metabolic cardiomyopathy in two (11%), and one case of histiocytoid cardiomyopathy. The age at death was 10 days to 15 years (median 18 months), with nine (47%) infants under one year of age, five (26%) aged 1-4 years, and six (32%) older children. Cardiomyopathy-associated deaths represented 0.9% of all 965 infant autopsies, 1.9% of 261 childhood deaths at 1-4 years of age, and 4.1% of paediatric autopsies aged 10-18 years. The majority (16.8%) manifested some symptoms prior to death, whilst 3 (15%) presented as apparently sudden unexpected death without prodromal features. In more than half (10, 33%) of symptomatic deaths the diagnosis of cardiomyopathy was only established at autopsy.

Conclusion: Cardiomyopathy is an uncommon but recognisable cause of death, representing about 1% of paediatric deaths referred for autopsy to a single specialist centre over a 10-year period.

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**P77**

**Co-Sleeping and Sudden Unexpected Deaths in Infancy (SUDI): Autopsy Series from a Single Specialist Centre**

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Introduction: It is suggested that co-sleeping increases risk of sudden unexpected death in infancy (SUDI), particularly when associated with maternal smoking, or parental alcohol or drug use. This study determines the prevalence of co-sleeping in SUDI deaths referred for autopsy to a single specialist centre.

Methods: Retrospective analysis of >1,500 consecutively performed post-mortem examinations at a single centre over a 10-year period (1996-2005). SUDI was defined as death of an infant 7-365 days that was sudden and unexpected, deaths were categorised into explained (cause of death was found at autopsy) or unexplained SUDI. Results: Of 546 SUDI, 314 infants died during sleep in whom sleeping arrangements were well documented; of these, 174 (55%) were co-sleeping-associated deaths. More than half (59%) of unexplained SUDI were associated with co-sleeping, usually with one or both parents, compared to only 44% of explained SUDI (difference 14.4%, 95% CI 1.0-27.2%, p=0.03). In both groups, co-sleeping-associated deaths were more common in younger infants; however, co-sleeping-associated deaths were significantly more common in unexplained SUDI than explained SUDI only in the first six months of life (66% unexplained SUDI vs. 47% explained SUDI, difference 18.6%, 95% CI 3.5-33.2%, p<0.01), but not in older infants aged to 12 months (27% vs. 35%; difference 8.6%, 95% CI -15.1-33.5, p=0.38). Overall, 32 (18%) co-slept on a sofa. Conclusion: Co-sleeping is common, associated with more than half of SUDI, and is especially associated with unexplained SUDI in infants aged less than six months, suggesting that co-sleeping may be related to the pathogenesis of sudden death in younger infants.
P79
Staphylococcal Toxins in Sudden Unexpected Death in Infancy (SUDI)
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Introduction: Two-thirds of sudden unexpected deaths in infancy (SUDI, aged 7-365 days) remain unexplained following autopsy. It has been postulated that some deaths may be caused by toxicogenic Staphylococcus aureus (SA). This study compared prevalence of toxigenic SA in unexplained and explained SUDI (those in whom a cause of death is determined).

Methods: A retrospective review of SUDI autopsies as part of a larger review of >1,500 paediatric autopsies over a 10-year period was performed. SUDI cases were categorised as unexplained, explained with histological evidence of infection (bacterial infection group) or explained due to non-infective causes. Toxin gene profiling was carried out by PCR as part of routine investigation in cases with positive SA cultures.

Results: Of 507 SUDI, bacteriological investigations were performed in 470. SA was isolated on post-mortem cultures in 173 (35%). There were significantly more cases with SA identified in unexplained SUDI (40%) than in the non-infective SUDI group (21%), further supporting the hypothesis that a subset of SUDI may be related to the production of bacterial toxins, but toxin gene testing does not demonstrate differences in frequencies between groups.

P80
Cardiac Causes of Sudden Unexpected Deaths in Infancy and Childhood: Autopsy Series
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Introduction: Cardiac disorders are a recognised cause of sudden unexpected death (SUDI) in infancy and childhood. This study examines the frequency and characteristics of sudden cardiac deaths referred for autopsy to a single specialist centre.

Methods: From a review of autopsies carried out in a single paediatric centre over a 10-year period, sudden unexplained cardiac deaths were identified, those in which the underlying cardiac abnormality was first detected at autopsy. SUDI in children with pre-existing cardiac pathology diagnosed during life were excluded.

Results: Of 1,372 paediatric autopsies (0-18 years), 855 (62%) were sudden and unexpected deaths. 416 (49%) deaths were explained by the autopsy findings, of which 55 (13%, 6% of all SUDI) were due to previously unsuspected cardiac pathology, accounting for 34% of explained sudden unexpected early neonatal deaths (<7 days), 13% of explained SUDI in infancy (7-365 days), and 6% of explained SUDI in children aged 1-4 years, 10% aged 5-9 years, 27% aged 10-14 years, and 29% aged ≥15 years. Causes included structural congenital heart disease (CHD) in 23 (42%), myocarditis in 20 (36%), cardiomyopathy in 8 (15%) and other in four (7%), Kawasaki disease, coronary artery atheroma with homogenous familial hypercholesterolaemia, infarction of the atrioventricular node, and dilated (primary) endocardial fibroelastosis. Whilst myocarditis occurred in all ages, death due to previously undiagnosed CHD was limited to children <4 years of age, and cardiomyopathy to infants (<365 days) and older children (≥10 years).

Conclusion: Carriage of toxigenic strains of SA is more common in unexplained SUDI, but these differences were not statistically significant (Fisher exact test p=0.44).

P81
Variation and Uncertainties in the Classification of Sudden Unexpected Infant Deaths amongst Paediatric Pathologists in the UK: Findings of a National DELPHI Study
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Introduction: Paediatric Pathologists use diverse terminologies to classify sudden unexpected infant deaths (unexplained, unascertained, sudden unexpected death in infancy/SUDI, and sudden infant death syndrome/SIDS). This study used the DELPHI method to investigate views of UK paediatric pathologists on their use of these terms in order to identify areas of consensus and disagreement.

Methods: A standard DELPHI approach was used, with three email rounds. In the final one, once views had been collated, participants scored statements using a modified Likert scale (0-9). Scores were analysed using non-parametric statistics, statements with median scores ≤3 or ≥7 were considered to have reached consensus agreement.

Results: 25 of 36 UK Paediatric Pathologists who were approached contributed to the final round. There was consensus that ‘SIDS’ be used for otherwise unexplained deaths occurring during sleep; infancy was defined as up to one year of age but there was no consensus regarding the lower age limit for SIDS. SUDI was used for deaths with atypical but non-suspicious circumstances of death (e.g. co-sleeping-associated deaths), whilst unascertained was used for unexplained deaths in whom findings were suspicious of a possible non-natural cause.

Conclusion: There remains significant lack of agreement in terminology used by UK Paediatric Pathologists, suggesting that an acceptable alternative term be identified to classify infant deaths which remain unexplained following autopsy with no suspicious features but not necessarily typical for SIDS; we propose that ‘unexplained SUDI’ followed by a comment may represent the most factually correct compromise, but this requires further evaluation.

P82
Pneumocystis (Carinii) Jiroveci Identified at Autopsy: Findings from a Specialist Paediatric Centre
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Introduction: Pneumocystis (Jiroveci) (PCJ) is a unicellular fungus usually recognised as an opportunistic infection in immunosuppressed individuals. This study reviews autopsy findings from a single specialist paediatric centre in which PCJ has been identified.

Methods: Data from >2,750 consecutively performed paediatric autopsies performed by specialist paediatric pathologists at one centre according to a standard protocol were retrospectively recorded into an autopsy database. Cases in which PCJ were detected on immunofluorescence were identified and the autopsy findings reviewed.

Results: Of 2,762 consecutive paediatric autopsies, lung microbiology was performed in 1,057 liveborn infants. 29 cases in total had PCJ detected by immunofluorescence, all but one of which were infants (65-339 days of age), the prevalence in infant deaths being 28/1057 (2.6%). 23 of the 28 infants presented as sudden unexpected deaths. Histologically, PCJ was identified in lung tissue sections in 13 cases (46%) and apart from two cases, there was associated inflammatory change. In total, of these 29 cases, 18 showed an inflammatory process ranging from a mild peribronchial mononuclear infiltrate to a severe acute pneumonia. In 7 cases, no definite other cause of death was found, in another 7, co-morbidities were present as the cause of death including congenital defects and neurological insults. In the remaining 15, there was evidence of pneumonia (7), pneumonia (5) and systemic sepsis (3). There was associated co-infection in 9, including Cytomegalovirus, Streptococcus pneumoniae and Group B Streptococcus. In 4 cases, underlying immunodeficiency states were diagnosed.

Conclusion: Colonisation by PCJ appears to occur in the first year of life. In 7 of 1057 infants, PCJ may be identified in lung sections with no histological pneumonitis and no other cause of death. The significance of this finding remains uncertain.
P83
Mesocolic Excision with Central Vascular Ligation not Extended Longitudinal Excision may be the Key to Improved Survival in Colon Cancer: Lessons from Japan

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Coellic disease is a relatively common condition which is usually managed by placing patients on a gluten free diet. Follow up biopsies to confirm histological recovery are controversial with a considerable variation in practice observed. We aimed to determine the length of time to histological recovery in a group of coellic disease patients and assess its associations with clinicopathological data.

All patients attending a specialist coellic disease clinic prior to March 2009 were entered onto a database which recorded various clinicopathological data. The histopathology reports for all duodenal biopsies were reviewed and each biopsy was given a histopathological disease score based on a modified Marsh grade.

284 patients underwent index and at least one subsequent biopsy. 227 (80%) showed histopathological improvement and 100 (35%) returned to normal (median recovery time 1.9 years, IQR 1.0–4.8 years). Patients with less severe disease at diagnosis were more likely to show a better response (r=0.281, p=0.0001). Older patients demonstrated a shorter time to histopathological recovery (r=−0.200, p=0.001). Compliance with a gluten free diet was correlated with the best follow up biopsy score (r=−0.134, p=0.040) and degree of histological recovery (r=0.161, p=0.014).

Current guidelines for the timing of repeat biopsy after commencing a gluten free diet are unclear, although 4-6 months has been recommended. This study shows that time to histological recovery is longer than traditionally thought and may need to take into account the patient’s age at diagnosis, the initial disease score and the level of compliance with a gluten free diet.

P84
Measuring Colorectal Polyps Endoscopically and Histologically: Does it Matter?

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Colorectal polyps must be carefully examined to identify malignancy and determine the risk of developing further neoplastic lesions. An adenomatous polyp measuring 10mm or more in maximum size will trigger follow up by the NHS Bowel Cancer Screening Programme. It is important to determine the frequency of inclusion of size in endoscopy and histopathology reports, and the degree of correlation between the modalities. All endoscopic polypectomies performed in a 3 month period were identified, the endoscopy and histopathology reports, and the degree of correlation between the modalities.

Additional measurements of the maximum polyp size were performed on the glass slides using a ruler and a breast screening magnifier device. 222 patients underwent endoscopic polypectomy yielding 393 lesions including 264 adenomas. Of the adenomas, 89% showed low grade dysplasia, 9% high grade and 1% invasive adenocarcinoma. For all polyps, endoscopic size was reported in 83% (mean 6.7mm) and histological size in 15% (mean 12.2mm). There was a positive correlation between body mass index (BMI) and the area of mesentry removed (r=0.467, p<0.0001). The median lymph node yield was 20 (IQR 13 to 24) which was not significantly correlated to the amount of tissue removed or BMI. We have shown that Japanese surgeons predominantly resect colon cancer in embryological tissue planes with a high VT in a similar fashion to CME with CVL surgeons. However, they remove a shorter length of colon resulting in a lower lymph node yield. With impressive survivals reported, including in stage III disease, the principles of operating in the correct plane with a high vascular tie appears to be more important than the actual length of bowel removed.

P85
Investigating the Factors Linked to Histopathological Recovery in Coellic Disease

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Coellic disease is a relatively common condition which is usually managed by placing patients on a gluten free diet. Follow up biopsies to confirm histological recovery are controversial with a considerable variation in practice observed. We aimed to determine the length of time to histopathological recovery in a group of coellic disease patients and assess its associations with clinicopathological data.

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284 patients underwent index and at least one subsequent biopsy. 227 (80%) showed histopathological improvement and 100 (35%) returned to normal (median recovery time 1.9 years, IQR 1.0–4.8 years). Patients with less severe disease at diagnosis were more likely to show a better response (r=0.281, p=0.0001). Older patients demonstrated a shorter time to histopathological recovery (r=−0.200, p=0.001). Compliance with a gluten free diet was correlated with the best follow up biopsy score (r=−0.134, p=0.040) and degree of histological recovery (r=0.161, p=0.014).

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P86
No Relationship Between the Expression Patterns of CDH1, CTNNB1, BCL2 and EGFR in Gastric Cancer

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Aberrant E-cadherin (CDH1) expression is a common finding in gastric cancer (GC). It has been suggested that CDH1 is involved in regulating the expression of proteins involved in EGFR signalling, WNT signalling and apoptosis. Studies in the past have usually investigated VD/CDH1 expression in GC in isolation. We aimed to assess the concurrent expression of CDH1, beta-catenin (CTNNB1), BCL2 and EGFR and its relationship to clinicopathological data and patient survival.

Tissue microarrays were constructed from 110 GC and protein expression was studied by immunohistochemistry (IHC). IHC staining was categorised as positive/negative (BCL2), abnormal/normal (CDH1), negative/membranous/nuclear (CTNNB1) and negative/ weaker/equal/stronger than matched normal mucosa (EGFR).

11% GC were BCL2 positive, 41% GC showed abnormal CDH1 expression, 69% GC were CTNNB1 negative. 18%GC were EGFR negative, 59% GC showed the same or lower EGFR staining intensity than matched normal. 24% GC showed EGFR overexpression compared to matched normal mucosa. No relationship was found between the expression of CDH1, BCL2, CTNNB1 and EGFR on bivariate correlation analysis. Loss of CTNNB1 was more frequent in high pT (p=0.004). Loss of EGFR was related to poor patient survival whilst patients with normal-like EGFR expression survived longest (p=0.026, univariate analysis).

Disappointingly, bivariate correlation analysis did not show the hypothesised related expression pattern between CDH1 and its suggested downstream targets. Hierarchical cluster analysis may be required to show such a relationship. However, this is the first study to demonstrate that GC patients with complete loss of EGFR have a worse prognosis than those with EGFR overexpression. As EGFR is part of a complex regulatory network, further studies are warranted to analyse the effects of loss of EGFR protein expression in GC.
P87
Quantitative and Qualitative Relationship of Tumour Cells and Vessels in Gastric Cancer – Identification of Three Distinct Vascular Patterns

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Anticancer drug resistance is usually considered to be related to molecular changes of the tumour cell thus disregarding the potential influence of the tumour microenvironment. However, we think that drug response may depend on tumour cell density, overall tumour vessel density and spatial relationship between vessels and tumour cells (‘vascular pattern’). No data is available on the relationship of tumour cells and vessels in gastric cancer (GC). We undertook a pilot study to measure overall tumour vessel density (TuVD), tumour cell density (TuCD) and determine the vascular pattern (VP).

A wide variation of TuVD (median: 7%, range: 2 to 28%) and TuCD (median: 34%, range 13 to 88%) was noted. High TuCD was related to low TuVD (p=0.024). Three major vascular patterns were observed (A) vessels evenly distributed, compressed and directly adjacent to small groups of tumour cells (30% of GC) (B) vessels randomly distributed and directly adjacent to tumour cells (40% of GC) and (C) vessels randomly distributed and separated by clearly visible stroma from tumour cells (30% of GC). VP-B was more frequent in diffuse type GC (p=0.037). No relationship with pT, pN, grade or survival was found in this pilot study.

This is the first study that quantified both, overall tumour vessel density and tumour cell density demonstrating that there is a relationship between the two, a finding which may be important for anticancer drug resistance. Furthermore, three qualitative different vascular patterns were identified in GC for the first time. These could be related to different molecular phenotypes of tumour cells. Further studies in larger series are necessary for confirmation and validation.

P88
Loss of MLH1 and MSH2 Expression Varieties Significantly between Sporadic Cancers of the Gastrointestinal Tract – No Relationship With Survival in 1027 Cases

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Mismatch repair proteins, MLH1 and MSH2, play a crucial role in a DNA repair. Loss of MLH1/MSH2 expression results in microsatellite instability, one of the two major forms of genetic instability in cancer. The incidence of oesophageal (OeC), gastric (GC), small bowel (SBC), and colorectal (CRC) cancers varies substantially from 1.9/100,000 per year in SBC to 49.1/100,000 per year in CRC. The aim of our study was to investigate the frequency of loss of MLH1/MSH2 expression and its relationship to tumour location, clinicopathological data and patient survival.

Tissue microarrays and immunohistochemistry were used to assess and compare different molecular phenotypes of tumour cells. Further studies in larger series are necessary for confirmation and validation.

P89
Systematic Audit of Upper GI Cancer Biopsies: Are We Missing Opportunities for Earlier Diagnosis?

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During the last year in Leeds, cancer was diagnosed in 193 out of 3737 gastric and oesophageal biopsy specimens (5.2%). These were taken by 70 endoscopists working in 4 endoscopy suites. We propose a routine audit should be carried out for quality assurance to avoid missed/delayed diagnosis of malignancy.

We piloted an audit of previous endoscopy in patients with a biopsy diagnosis of cancer as a quality assurance tool for the endoscopy service. A monthly list of upper GI cancer was checked against the endoscopy database to identify patients who had a previous endoscopy in Leeds in last 2 years. We reviewed endoscopy and biopsy reports of previous examinations, and histology slides of negative biopsies.

The results cover a 6 month period, March-Aug 2009. There were 95 patients with a biopsy diagnosis of gastric/oesophageal cancer; 68 had not had an endoscopy in the previous 2 years. Of the 27 who had an endoscopy within the last 2 years 12 had a previous biopsy diagnosis of cancer and 15 had a previous negative endoscopy. In conclusion 15/85 (18%) new cancer patients had non-diagnostic endoscopy in preceding 2 years. Review of endoscopy/histology can identify avoidable factors in delaying diagnosis and provides quality assurance of the service.

P90
Invasive behaviour of the OE33 oesophageal adenocarcinoma cell line is dependent on co-operation with fibroblasts.

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BACKGROUND: Cell-cell and -matrix interactions play a critical role in influencing tumour cell behaviour, but conventional culture systems fail to capture these aspects of the tumour microenvironment. To investigate the pathogenesis of oesophageal adenocarcinoma we have developed a tissue-engineered model of the oesophagus which includes epithelial and stromal cells and a microanatomically realistic extracellular scaffold. In this study we examined the impact of fibroblasts on tumour cell behaviour.

MATERIALS & METHODS: OE33 oesophageal adenocarcinoma cells were seeded on the superficial surface of sterile, decellularised porcine oesophageal mucosa, in the presence or absence of fibroblasts on the deep surface. All experiments were repeated with two different media: RPMI and a 3-stage media with increasing calcium that we have previously used in culturing normal oesophageal squamous epithelium. Tissue cultures were maintained at air-liquid interface for 14 days. The resultant tissues were fixed and examined histologically. RESULTS: In all conditions the tumour cells proliferated and formed epithelial and glandular structures, histologically in keeping with a moderately differentiated adenocarcinoma. Non-invasive extension of the tumour into pre-existing ductal and glandular structures was frequently observed. Experiments incorporating fibroblasts showed extensive destructive invasion of the tumour into the extracellular matrix. Where fibroblasts were absent there was damage to the collagen matrix beneath the tissue surface above the damaged matrix. DISCUSSION & CONCLUSIONS: These results indicate an essential role for fibroblasts in indirectly promoting invasive behaviour in tumour cells, and demonstrate the power of this experimental system to model aspects of tumour behaviour that are not captured in conventional culture systems.
A Case of Epithelial Dysplasia Arising in the Abdominal Wall Following Loop Colostomy Formation

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We report a case of a 77 year old female who presented in 2009 with a cystic mass in relation to a colostomy scar dating back to emergency surgery for an obstructing diverticular stricture 20 years earlier. An ultrasound scan showed a suspected recurrent incisional hernia. A previous incisional hernia at the same site had been repaired with mesh 10 years earlier at which time a small mucinous cystic lesion was found. Microscopy of this showed fragments of benign mucinous epithelium thought to represent residual colonic epithelium from the colostomy.

At subsequent operation in 2009 a further mucinous cystic lesion was found in association with the residual mesh alongside a recurrent incisional hernia. Microscopy showed fibrous tissue partly lined by a columnar epithelium showing low grade dysplasia with no evidence of invasion. Immunohistochemical staining was positive for CK20, CEA and CDX-2 indicating large bowel origin. The patient experienced a self-limiting post-operative ileus confirmed on CT scan but soon recovered and was asymptomatic at three months’ follow up. To the best of our knowledge, low grade dysplasia arising in a previously benign residual colonic epithelium from a previous colostomy has not been described before in the literature. Hernia sacs containing copious mucin and atypical epithelial cells within is a common finding in pseudomyxoma peritonei however in this case the cysts were discrete and localised with no clinical or radiological evidence of pseudomyxomatous disease.

CD133 Expression in Colorectal Cancer and its Prognostic Significance

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Background: CD133 is a glycosylated cell surface molecule which has been controversially, reported as a CSC marker in colorectal cancer. In this study, we sought to study the expression and the prognostic value of CD133 in a large series of CRC. Methods: The prognostic value of CD133 expression was studied in a large series of colorectal carcinoma using tissue microarray and immunohistochemistry. Association between CD133 expression and clinicopathological variables and patient outcome were investigated. Results: An association was found between CD133 expression and patient’s survival. It was found that CD133 negative expression associated with better survival, although it is not statistically significant but there is a trend. Moreover, multivariate analysis showed that CD133 was not an independent prognostic marker. Conclusion: In this series, CD133 was found not to be a good prognostic marker in colorectal cancer

The Expression of RNA Binding Proteins in Colorectal Cancer

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The heterogeneous nuclear ribonucleoproteins (hnRNPs) are a group of RNA binding proteins with a range of key cellular functions which are dysregulated in tumourigenesis including regulation of translation and RNA processing. The purpose of this study was to define the hnRNP expression profile in colorectal cancer and establish the significance of hnRNP expression. A tissue microarray containing 515 primary colorectal cancers, 224 lymph node metastasis of colorectal cancer and 50 normal colon samples was immunostained for 6 hnRNPs. hnRNPI, hnRNPK and hnRNPL displaying the most frequent strong immunoreactivity in primary colorectal tumour samples. hnRNPA1 (p=0.001) and hnRNPU (p=0.003) showed significant alterations in nuclear expression in tumours compared with normal while hnRNPA1 (p=0.001), hnRNPI (p<0.001) and hnRNPK (p<0.001) all showed significant increases in cytoplasmic immunoreactivity in tumour cells. There were significant differences in cytoplasmic immunoreactivity between the primary tumour and the corresponding lymph node metastasis for hnRNPA1 (p=0.001), hnRNPI (p<0.001) and hnRNPK (p<0.001). There was a significant relationship between strong nuclear hnRNPH expression and survival (chi-squared=14.97, p<0.001). This study has defined the expression profile of hnRNPs in colorectal cancer and shown that there are significant alterations in individual hnRNP expression in this type of tumour.
**P95**

**Colorectal Cancer Biomarker Identification: A Proteomics Approach**

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Colorectal cancer (CRC) is the third most common cancer in the UK and the second most common cause of cancer death, with a 5 year survival rate of 40-45%. Early diagnosis is essential for increased survival while improving response and outcome to chemotherapy may provide significant benefits to patients by reducing toxicity. Biomarkers have considerable potential to impact current understanding and outcome by providing prognostic or predictive information, act as screening tools or therapeutic targets. The purpose of this study was to profile protein expression in colorectal cancer. Colorectal tumour samples (n=29, all Dukes B) and normal colorectal mucosa were dissected within 30 minutes of resection and samples immediately frozen in liquid nitrogen and stored at -80°C. No patient had received any form of neo-adjuvant therapy. Proteins were separated using 2D gel electrophoresis. Gels were analysed using Progenesis Same Spot software for identification of differential protein expression between tumour and non-tumour tissues. Protein spots of interest were identified following in-gel tryptic digestion and analysis by liquid chromatography-tandem mass spectrometry. Of the 220 significantly differentially expressed proteins identified, 111 were up-regulated in tumour tissue. Initial analysis indicates nucleophosmin (2.1fold change, p=0.001), 14-3-3 protein (1.2 fold, p=0.004), translationally controlled tumour protein (1.6 fold, p<0.001) among others, are all up-regulated in colorectal tumour tissue compared to non-tumour tissue. Nucleophosmin, 14-3-3 protein and translationally controlled tumour protein are amongst a number of potential biomarkers of colorectal cancer identified using a 2D gel electrophoresis and mass spectrometry proteomic approach.

**P97**

**Diagnostic Accuracy of Endoscopic Ultrasound Guided Fine Needle Aspiration of Pancreatic Lesions**

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Purpose of Study: Endoscopic ultrasound (EUS)-guided fine-needle aspiration (FNA) of the pancreas allows the evaluation of pancreatic neoplasms without the need for exploratory surgery. We review our recent experience of EUS-FNA and report the diagnostic accuracy.

Method: Data was collected from cytology reports for all patients who underwent EUS-FNA of pancreatic lesions between 1st January 2008 and 31st November 2009. Subsequent histology reports were reviewed where available to assess the diagnostic accuracy of the preceding cytology. We compared our results with those reported in the literature.

Summary of Results: 51 patients underwent EUS-FNA. 82% of samples were adequate for cytological assessment. 65% of these were given a benign cytological diagnosis and 35% were given a neoplastic diagnosis. Subsequent histology was available for review in 32% of cases. The sensitivity, specificity and accuracy of EUS-FNA for a neoplastic diagnosis were 78%, 100% and 85%, respectively. Studies from the literature report ranges of 64-94% for sensitivity, 88-100% for specificity and 74-94% for accuracy.

Conclusion: EUS-FNA is an accurate method for the evaluation of pancreatic neoplasms. Our centre has limited experience of EUS-FNA and we have identified a need for improvement in the diagnostic accuracy of the technique. Our recommendations to improve the sensitivity and diagnostic accuracy include; cytopathologists to attend the hepatobiliary multi-disciplinary team meetings, cytology technical support available in the radiology suite for specimen preparation and the completion of a pro-forma for all pancreatic EUS-FNA specimens to maximise the clinical and radiological information available for correlation.

**P96**

**Immunohistochemical Analysis of Colorectal Cancer with Gastric Phenotype: Claudin-18 is Associated with Poor Prognosis**

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Claudin-18 plays a key role in constructing tight junctions, and altered claudin-18 expression has been documented in various human malignancies; however, little is known about the biological significance of claudin-18 in colorectal cancer (CRC). The aim of this study is to investigate the significance of claudin-18 expression in CRC and its association with clinicopathological factors. We performed immunohistochemical analysis of claudin-18 expression in a total of 569 CRCs by immunohistochemistry. Moreover, we investigated the association between claudin-18 and various markers determining gastric/intestinal phenotype (MUC5AC, MUC6, MUC2, CD10 and CDX2). Claudin-18 expression was detected in 21 of the 569 CRCs (4%) and was seen exclusively on the cell membrane. Corresponding non-neoplastic colorectal mucosa and colorectal adenomas did not express claudin-18. Expression of claudin-18 was not correlated with T grade, N grade, staging, or histological type. Positive rates of various markers determining gastric/intestinal phenotype in 569 cases are as follows: 86 (15%) cases for MUC5AC, 11 (2%) cases for MUC6, 370 (65%) cases for MUC2, 200 (35%) cases for CD10 and 448 (79%) cases for CDX2. Positive expression of claudin-18 showed a significant correlation with positive expression of MUC5AC and negative expression of CDX2. The prognosis of patients with positive claudin-18 or MUC5AC expression was significantly poorer than in negative cases. In contrast, the prognosis of patients with negative CDX2 expression was significantly poorer than in positive cases. Multivariate analysis revealed that T grade, M grade and claudin-18 expression were independent predictors of survival in patients with CRC. In summary, we revealed that claudin-18 expression correlates with poor survival in patients with CRC and is associated with the gastric phenotype. Claudin-18 may be a useful marker to predict CRC and its prognosis.

**P98**

**Gastric Lymphangioma**

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Lymphangiomas are benign vascular tumour that usually arise in the neck, head and axilla of infants. Gastrointestinal lymphangioma is a solitary, localized benign tumour composed of multiple dilated lymphatic channels of various sizes lined by endothelial cells. The pathogenesis has been presumed to be sequestered lymphatic tissue that is separated from the normal lymphatic system. These are extremely rare with an incidence of 1 per 50,000 subjects examined by GI radiography. There have been very few cases of gastric lymphangiomas reported in the literature. Most of the GI lymphangiomas occur in the intestine and they are rarely found in the stomach. The location and rare occurrence makes this tumour a diagnostic challenge. When present near the lesser curvature these can be confused with pancreatic pseudocysts, gastrointestinal stromal tumours and other pancreatic related cystic tumours radiologically. We present a rare case of gastric lymphangioma which includes its clinical, radiological, intraoperative and histological findings.
Audit of Changes in Diagnostic Practice of Hyperplastic Type Lesions in the Colon

P99

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Aims Hyperplastic polyps (HPs) are benign but several subtypes and mimics of HP have been described, including sessile serrated adenoma (SSA). Molecular studies suggest that SSAs may have a malignant potential but the distinction from HP is problematic and several papers describe high inter- and intra-observer variatbility. The overall aim of this study was to determine the overall and site specific (right versus left colon) incidence of SSAs in a primary referral centre and secondarily to determine the robustness of the histological diagnosis of SSA versus HP. Methods All 299 cases of HP from 2001-2 (prior to 2003 where SSA was first described in detail) were examined by a consultant pathologist and a medical student. All cases considered possible SSA were then reviewed by a second pathologist. Both pathologists were blinded to the site. Finally, all biopsies from the right colon, regardless of initial diagnosis, were reviewed by the 2 pathologists. Results 271 of 299 cases were included (others were discarded due to other pathology). Initially 27 biopsies were identified as possible SSAs but when reviewed by a second pathologist both agreed on 16 biopsies (overall incidence 6%) which included a second review of all biopsies from the right colon. SSAs accounted for 37% of all biopsies in the right colon (7 of 19) and 3.5 % of all biopsies in the left colon (9 of 252). Conclusions SSAs are more common in hyperplastic lesions of the right colon (37% vs 3.5%). The differential diagnosis between HP and SSA is difficult and the most useful criteria were architectural features. Until diagnostic criteria are in common use and the biological differential diagnosis between HP and SSA is difficult, SSA remains a problematic entity.

Gain of Chromosome 13 is a Cause of CDK8 Overexpression Associated with Colorectal Adenoma to Carcinoma Progression

P101

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Introduction: Colorectal adenomas are common precursors of colorectal cancer (CRC). About only 5% of adenomas progress to cancer and this progression is mostly associated with overall onset/increase of chromosomal instability. Gain of 13q is often implicated in this progression of adenoma to carcinoma (1). Until recently however no genes were identified to be the drivers of this amplicon. Recently, Firestein and collaborators (2) showed that cyclin 8 (CDK8), at 13q12.13, functions as an oncogene in CRC. The aim of this study was to evaluate CDK8 gene dosage effects in colorectal adenoma to carcinoma progression. Material and methods: Sixty seven colorectal tumours (34 adenomas and 28 carcinomas) were analysed by array CGH (5k BAC platform, including contig coverage of 13q) and by expression microarray (36k CompuGen library). Integration of DNA copy number dosage and gene expression was performed using the Ace-it tool (3). Results: In the tumours analysed we observed 13q copy number gain in 9% and 46% of adenomas and carcinomas, respectively. Integrating copy number and mRNA expression with the differential upregulation of genes between carcinomas and adenomas, provided us with a list of 43 genes. Within this list, CDK8 ranked 7th in significancy (p=0.003). Upregulation of CDK8 was confirmed by real-time RT-PCR. Conclusions: Copy number gain of 13q has a gene dosage effect on CDK8 mRNA expression, indicating a role of this gene in colorectal adenoma to carcinoma progression. (1) Hermesen M et al. Colorectal adenoma to carcinoma progression follows multiple pathways of chromosomal instability. Gastroenterology 2002 Oct;123(4):1109-19. (2) Firestein R et al. CDK8 is a colorectal cancer oncogene that regulates beta-catenin activity. Nature 2008 Sep 25;455(7212):547-51. (3) van Wieringen WN et al. ACE-it: a tool for genome-wide integration of gene dosage and RNA expression data. Bioinformatics. 2006 Aug 1;22(15):1919-20.

Monoclonality and Immunophenotype of Intraepithelial Lymphocytes in Lymphocytic Gastritis

P100

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Lymphocytic gastritis (LG) is an uncommon condition associated with autoimmune and infective diseases (e.g. H pylori, coeliac disease (CD), Crohn’s disease) characterized by an increased number of intraepithelial lymphocytes (IELs) in the foveolar epithelium, primarily CD8+ T-cells. Its pathogenesis is poorly understood and the presence of monoclonal T-cell populations and the potential risk of T-cell lymphoma (similar to Enteropathy-associated T-cell lymphoma) have not yet been investigated. Methods: The study included 27 cases of LG. Clinical information regarding H pylori (Hp) infection and CD was recorded. Immunohistochemistry for Hp, CD3, CD4 and CD8 and PCR amplification of the T-cell receptor (TCR) gamma gene was performed in each case. Results: 8/27 cases were positive for Hp and 2/27 had histologically confirmed CD. In all cases the IELs showed a CD3+/CD8+ immunophenotype. In 19/27 cases DNA quality allowed PCR analysis and in 4/19 cases a monoclonal expansion of T-cells was seen. Two cases were associated with Hp and the remaining cases had no evidence of Hp infection or CD. In one case there was clinical / endoscopic improvement after Hp eradication and in 1/4 LG persisted despite treatment. None of the patients have developed lymphoma (median follow up 21 months).

Conclusion: Hp infection may trigger LG and induce infiltration of T lymphocytes in the gastric mucosa. In a significant proportion of cases (14% in our series) a T-cell clonal expansion may develop and in these cases repeat biopsy and close follow up should be mandatory. Some patients with monoclonal T-cell expansion are not Hp related and other host-related factors may play a role. It is important to include immunohistochemical analysis and TCR gene rearrangement tests in the diagnosis of lymphocytic gastritis.
P102
Audit of Colorectal Cancer Pathology Reporting in Kent & Medway Cancer Network: Compliance with National Guidelines

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**Introduction:** There is evidence in the literature of great variability in reporting of colorectal cancer pathology, which clearly can impact therapeutic decisions and prognosis prediction. We audited the compliance of pathology reporting, across Kent and Medway cancer network, with national guidelines. Patients and methods: 519 Patients with Primary colorectal adenocarcinomas treated with radical cancer resections in Kent and Medway cancer network from April 2008 - April 2009 were included in the study. Data collection: Minimum data set paper forms, pathology reports and Pathosys database were used, with data entered into Bento 3 database and then exported to Excel Spreadsheet for analysis. Data collected: Size, stage, type, grade and appearance of the tumour, depth of invasion & presence of tumour perforation. Total number of lymph nodes excised and number involved. Tumour involvement at surgical margins, including circumferential margins and in rectal cancers involving of distal margins and quality of mesorectal resection. Presence of extramural venous invasion. Whether Neoadjuvant therapy was used or not prior to surgery. Results: 12 nodes or more were harvested in 75-85% of patients. A median of 16-18 nodes were harvested per case across the network. Positive nodes were found in 41% - 50% of specimens. All reports mentioned whether margins were clear or involved. Reporting on circumferential margins was variable. Some variations also occurred in reporting Quirke grade in rectal specimens, which was not reported in all rectal cases. Colonic and rectal serosal involvement was reported in 30-35% and 14-17% of specimens respectively across the network. Extramural venous invasion was reported in all patients. It was positive in 37-49% of cases. Conclusion: Colorectal pathology reporting fulfilled the minimum data set across the network.

P103
A Case of Muir-Torre Syndrome

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We report a case of Muir-Torre syndrome (MTS), an autosomal dominant disorder with variable phenotypic expression characterised by the association of sebaceous gland neoplasms and visceral malignancy, usually colon cancer. It is a rare condition with just over 205 cases identified in a recent review. The patient was a male aged 56, who attended for routine colonoscopy in 2009, following abdominopelvical resection for adenocarcinoma of the sigmoid colon in 1985. This showed an annular tumour in the transverse colon. Subsequent right hemicolectomy showed a Duke's C2 adenocarcinoma. Because of the history of metachronous carcinomas of bowel and his relative youth at the time of the first carcinoma, his previous medical history and family history were investigated. A sebaceous adenoma of the eyelid and a basal cell carcinoma with sebaceous differentiation of the nipple had been resected in 2001 and 2008 respectively. There was a strong family history of bowel cancer, the patient’s mother, maternal uncle and two maternal cousins being affected. The most common skin tumours associated with MTS are sebaceous carcinomas, sebaceous adenomas and basal cell carcinomas with sebaceous differentiation. The most common visceral malignancy found in MTS patients is adenocarcinoma of the large bowel. The diagnosis of sebaceous gland neoplasms precedes visceral cancer diagnosis in 22% of cases, occurs concurrently in 6% and after visceral malignancy in 56%. Cutaneous findings can precede the diagnosis of internal disease by up to 25 years or follow it by up to 37 years. The genetic basis for MTS is defects of mismatch repair proteins (MMR). The importance of this condition is that diagnosis is often delayed and in some cases missed. The onus for prompt diagnosis lies mainly with pathologists and dermatologists.

P104
Villous Adenoma of the Bladder: Vogelstein Revisited?

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Villous adenoma of the bladder is a rare lesion that morphologically resembles villous adenoma of the colon. We present a case of a 71-year-old lady with a history of recurrent urinary tract infections. Computed tomography scan revealed a polypoid bladder mass and on cystoscopic examination a 4 x 5 cm mucous-secreting exophytic tumour was identified at the dome. Transurethral biopsies showed a papillary tumour composed of dysplastic enteric-type glandular epithelium consistent with a villous adenoma. The patient underwent further deep resection of the residual tumour and on this occasion foc of invasive mucinous adenocarcinoma were identified in association with villous adenoma. The patient went on to have a radical cysto-urethrectomy which confirmed the presence of a large villous adenoma with focal invasive adenocarcinoma of stage pT3. Although, in its pure form, villous adenoma of the bladder has an excellent prognosis with complete resection being curative, a significant proportion of cases have been reported to show co-existent invasive malignancy, with a risk of nodal spread and distant metastases. This case highlights the importance of complete resection of villous adenomas, as invasive carcinoma may not be apparent on initial biopsies. Where invasive carcinoma is identified, clinical and radiological correlation is essential to exclude direct invasion or metastasis from other primary sites including colon or female genital tract, which may show similar morphological and immunohistochemical features. Finally, the presence of adenocarcinoma arising within a villous adenoma of the bladder suggests an adenoma-carcinoma sequence of tumourigenesis similar to that identified in the colon. However, whilst the latter has been extensively studied at a molecular biology level, relatively little is known about the sequence of events in the bladder. Further research in this field is required.
P105

Epithelioid Haemangioendothelioma of the Penis

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A 50 year-old man presented with a 6-month history of a small painful nodule on the dorsum of his penis. Examination by ultrasound showed a well-circumscribed 8mm nodule within the subcutaneous penile tissue, superficial to corpus cavernosum, with evidence of vascular flow. The nodule was resected under general anaesthetic and histopathological examination revealed a lesion composed of sheets of plump epithelioid cells with evidence of vessel formation, particularly at the periphery of the lesion. There was a florid infiltrate of lymphocytes and eosinophils, but no significant cytological atypia and only a few mitoses. Immunohistochemistry showed the epithelioid cells were positive for CD31 and CD34 and negative for S100 and desmin. A diagnosis of epithelioid haemangioendothelioma was made. At 3 month follow-up there was complete resolution of symptoms with no evidence of local recurrence. Epithelioid haemangioendothelioma is an uncommon vascular lesion of uncertain aetiology and pathogenesis, most commonly arising on the head or distal extremities. Rare cases involving the penis have been reported. The lesion behaves in a benign manner and is best treated by local excision with regular follow-up to monitor for local recurrence. Clinically, it is important to distinguish this condition from Peyronie’s disease, which is not normally biopsied or excised. Histologically, exuberant examples of epithelioid haemangioendothelioma can potentially be misdiagnosed as malignant epithelioid vascular tumours such as epithelioid haemangioendothelioma or epithelioid angiosarcoma.

P106

Sequence Variation in the SDHD Gene in Renal Oncocytoma

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Succinate dehydrogenase (SDH) is a nuclear encoded mitochondrial protein involved in both the Kreb’s cycle and the electron transport chain. Heterozygous germline mutations in the genes encoding SDH subunits B, C and D are known to cause hereditary paragangliomas and phaeochromocytomas. Renal cell carcinomas (RCC) have also been described in around 4% of patients with germline SDHB mutations. Recently SDHB mutation has been described in oncocytoma and oncocyctoma like renal tumours. DNA was extracted from 28 formalin fixed paraffin embedded (FFPE) sporadic renal oncocyctomas (RO) and 4 chromophobe renal cell carcinomas (ChRCC) samples and analysed. Adjacent normal renal cortex DNA was extracted to allow demonstration of LOH. The use of these tissues for our research was approved by the Ethical Committee of the Regional Tissue Bank. Validated and SNP checked primer sets were available in the laboratory for the SDHB and SDHD genes that include all coding regions and intron-exon boundaries A panel of microsatellite markers close to the SDHB and SDHD loci on chromosomes 1 and 11 respectively were used to examine RO tissue for evidence of LOH. No significant mutations were identified in the SDHD gene. However, two samples from the 21 RO cases that were successfully sequenced for SDHD exon 2 were found to be heterozygous for the SDHD c.149A>G / p.His50Arg variant (9.5% RO, 0 from ChRCC samples). This variant was also present in normal tissue from each patient, representing a germline change. This variant has a very low frequency in the general population. There was no evidence of LOH at the any of the chromosome 11 markers flanking SDHD. LOH for chromosome 1 was found in a proportion of RO but this is a well described event. In conclusion we have identified germline sequence variation in the SDHD gene in a proportion of renal oncocyctoma patients.

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This abstract is not available for publication before the Summer Meeting.

P108

Caveolin-1: an Oncogene that Promotes Growth and Invasion of RCC Cells via Potentiation of AKT/mTOR and MAPKinase Signalling

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Immunohistochemical studies of Renal Cell Carcinoma (RCC) have shown that the over-expression of caveolin-1 (cav-1) correlates with increased tumour size, high tumour grade, presence of vascular invasion and shorter disease-free survival. However, the molecular mechanism(s) underlying the role of cav-1 in RCC pathophysiology remains unresolved. In a panel of clear cell RCC cell lines we have examined signalling mechanisms underlying the contributions of cav-1 to RCC cell growth and invasion. The siRNA targeted down-regulation of cav-1 led to decreased cell growth in all RCC cell lines examined, with respective reductions of 30% and 50%, respectively in the primary, VHL (+ve) caki-1 cell line (p<0.001). Using Matrigel™-coated chambers the inhibition of cav-1 decreased the invasive capacity of the RCC cell lines (p<0.05). Immunoblotting revealed that silencing of cav-1 caused reduced expression of phosphorylated (activated) forms of AKT, S6K1 and ERK paralleled by lower expression levels of the down-stream mTOR effector molecules eIF4E and cyclin D1. The of cav-1 inhibition upon growth, invasion and altered cell signalling were demonstrably greatest in the caki-1 cell line. This study shows for the first time that cav-1 is an important oncogene in RCC promoting tumorigenesis through increased cell proliferation and invasion and that cav-1 promotes the activity of AKT/mTOR and MAPKinase signalling pathways. We conclude that cav-1 represents a novel target for the treatment of advanced RCC disease and underlines its importance as a biomarker for RCC progression.
**P109**

**Morphology of Recurrent Dense Deposit Disease is Not Typical of Native Disease: A Report of Two Cases**

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Dense deposit disease (DDD) commonly recurs in renal allografts; this may result in graft failure and correct diagnosis has important implications for immediate treatment and management of subsequent grafts. We present two females with primary renal failure due to DDD that illustrate the varied morphology; one was treated by rituximab. Case 1 had a renal allograft at 7 yrs after developing renal failure at 11 yrs age. At 14 months an acute increase in creatinine was investigated by renal biopsy. Histology showed an acute diffuse endocapillary glomerulonephritis with no GBM abnormality on silver stain and no interstitial inflammation. C3 was present on capillary loops; electron microscopy (EM) showed typical linear dense deposit. Treatment with plasmapheresis resulted in poor but stable renal function for the next 6 months. Case 2 developed renal failure at 20 yrs age and had a renal allograft at 23 yrs. A biopsy at 3 weeks for secondary dysfunction showed glomerular intracapillary thrombus only. Biopsy at 7 weeks showed an acute focal segmental proliferative GN without significant scarring or tubulo-interstitial changes. The GBMs were normal on silver stain; however on EM linear dense deposits were seen. Treatment with plasmapheresis and rituximab resulted in clinical recovery; a protocol biopsy carried out at 28 weeks showed focal segmental sclerosis with no active lesions and resolution of the dense deposit at EM. At 38 weeks relapse resulted in further decline in renal function. Recurrent DDD rarely presents with a classical MPGN histological pattern, intracapillary thrombi and a focal segmental proliferative GN appear to be novel findings. This variety of morphologies emphasizes the importance of electron microscopy. Initial success, including histological resolution, with rituximab is encouraging. Further assessment of this treatment can only be made on a multicentre basis.

**P110**

**Tubular Amyloid Casts in Myeloma**

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Myeloma may result in a variety of renal lesions. Cast nephropathy is the result of precipitation of monoclonal light chains in the renal tubules; occasionally these may form crystalline structures. The deposition of amyloid, also due to light chain organisation, usually occurs in the glomeruli or interstitial space and not in lumen of the tubules. To your knowledge there are only three previous reports of tubular amyloid casts. We here report two cases in association with multiple myeloma. Case 1: 71 yr. old male with 3.9 gm proteinuria and rising creatinine to 268 was investigated with a renal biopsy. This showed soft eosinophilic casts in tubules at the cortico-medullary junction with a prominent giant cell reaction. These stained strongly including histological resolution, with rituximab is encouraging. Further assessment of this treatment can only be made on a multicentre basis.

**P111**

**ElF4E and Caveolin-1 Co-operate to Drive the Aggressive Features of Clinically Confined RCC**

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ElF4E is an important translational regulator that acts down-stream of the AKT/mTOR pathway. It is associated with chemo-resistance and inhibition of p53-induced apoptosis. We have recently shown in a panel of RCC cell lines that caveolin-1 (cav-1) is an important oncogene in RCC that serves to promote the over-expression of elF4E. However, no information is available regarding the clinical significance of elF4E or its potential association with cave-1 in RCC. Immunohistochemistry for elF4E and cav-1 expression was performed on tissue microarrays (TMA)s constructed from 174 clinically confined RCC cases. Specimens were scored semi-quantitatively according to previously validated criteria and converted to a binary simple covariate (positive or negative) according to the most informative split on Kaplan-Meier using the log-rank statistical test. A significantly decreased mean-free survival was observed when elF4E was co-expressed with cav-1 (2.6 yrs 6.0 yrs; p = 0.001) compared to when elF4E or cav-1 were expressed alone. On multivariate analysis, the composite co-variates of elF4E/cav-1 was a significant influential indicator of poor disease-free survival with a hazard ratio of 3.4 (95% CIs 1.6–7.1). Tumours that co-expressed elF4E and cav-1 were more likely to be larger, of higher grade and showvascular invasion. These results provide clinical evidence that elF4E and cav-1 co-operate to drive disease progression in primary RCC tumours and that the cav-1/AKT/elF4E axis may be an important molecular target for preventing metastasis and restoring chemo-sensitivity.

**P112**

**WT1, PTEN and phosphoPTEN Staining in an Ovarian TMA**

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WT1 was first described as a tumour suppressor gene in Wilms tumour, classically WT1 is now used as a marker of ovarian serous adenocarcinoma and is thought to be largely negative in the other ovarian malignancies. PTEN is the second most common tumour suppressor gene in human cancer and acts as a negative regulator of the AKT pathway which controls cell growth and proliferation. We created an ovarian TMA containing a variety of different ovarian malignancies & stained it with both the WT1 C19 and WT1 6F-H2 antibodies, PTEN and pPTEN antibodies. Each core was scored (cytoplasmic and nuclear staining) from 0 – 3. There was a significant difference between WT1 and WT1 6F-H2 staining (n to n staining p = 1.2986x10-15), with no specific non-staining seen in WT1 C19. Table 1 shows the overall mode of each antibody together with the serous carcinoma.

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Cytoplasmic Staining</th>
<th>Nuclear Staining</th>
</tr>
</thead>
<tbody>
<tr>
<td>WT1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6F-H2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PTEN</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PhosphoPTEN</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

There is a significant difference between WT1 nuclear staining and PTEN nuclear staining (p = 0.0006), & WT1 nuclear & PTEN cytoplasmic staining (p=7.6492x10-18). Overall there appears to be similar staining of the active PTEN and the inactive pPTEN but there is a significant difference seen between cytoplasmic staining (p= 0.00020) it would appear that WT1 6F-H2 does stain positively in the majority of ovarian serous carcinomas 73% of cases stained 1-3 nuclear positivity, however the majority of these cases displayed weak staining only. While 97% of cases showed no cytoplasmic WT1 staining. 64% of cases showed absent PTEN nuclear positivity 58% showed weak cytoplasmic PTEN positivity and 36% no staining. 94% of cases showed absent nuclear pPTEN staining 53% and 28% showed grade 1 and 2 cytoplasmic staining. In light of the significant differences between WT1 and PTEN there is evidence to suggest that they may play different roles and may even interact with each other, and further investigation is required to examine this.
P113
This abstract is not available for publication before the Summer Meeting.

P114
This abstract is not available for publication before the Summer Meeting.

P115
Audit of the Reporting of Invasive Cervical Carcinoma in Loop Excision Specimens
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Careful reporting of loop excision specimens that contain invasive cervical carcinoma is important for determining the management, prognosis and follow up of patients. In this audit, reports were identified retrospectively using a computer-based search of the pathology reporting database at Ninewells Hospital, Dundee to retrieve all loop excision specimens that contained invasive carcinoma over the period from January 2002 to January 2010, which spans the introduction of proforma reporting in 2006, and modification of the dataset in 2008. Of the 70 reports identified, 19 used the 2008 proforma, 12 the 2006 proforma and 39 no proforma. Reports were anonymised and their content compared with the 2008 dataset. Introduction of the proforma in 2006 led to improvement in the inclusion of parameters describing the invasive tumour (type, size measurement, presence of lymphovascular invasion (LVI)), and the involvement of resection margins. The 2008 modification led to a further improvement in report content, with all 19 reports containing tumour type, differentiation, LVI, assessment of all tumour dimensions and all resection margins. However, the proportion of summaries of these reports that contained each of the 5 required parameters ranged from 53 — 95%. Whilst this represents an improvement over reports that did not use a proforma (10 — 41%) and those based on the 2006 dataset (17 — 92%), there is clearly room for improvement in this component of the report. In conclusion, the introduction of proforma reporting of loop excision specimens containing invasive cervical carcinoma has led to the inclusion of clinically important parameters in almost all reports. However, report summaries are often incomplete.

P116
Classical Carcinoid Tumour Arising from an Intestinal Structure Within a Mature Cystic Teratoma
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We present a case of an insular type carcinoid tumour arising within a recapitulated segment of bowel within a mature cystic teratoma. Well differentiated structures are commonly identified within mature cystic teratomas (MCT) but the presence of well formed organoid structures is relatively rare. Several studies have reported the presence of well-differentiated intestinal structures within MCTs, several of which appeared to give rise to separate neoplasms. A single case reported the presence of an intestinal structure within a MCT with a concomitant carcinoid tumour: however, the precise origin of the carcinoid tumour remained uncertain. The case presented provides strong evidence for an "intestinal" origin of the carcinoid tumour through immunohistochemical studies and on morphological grounds. The carcinoid tumour cells expressed CK7 and 19, which were also strongly co-expressed by the glandular epithelium lining the intestinal structure. Similarly, synaptophysin was expressed by neuroendocrine cells present in the lining epithelium and was strongly expressed by the carcinoid tumour. The presence of infiltrating islands of the carcinoid tumour within the apparent muscularis propria further support its origin from the segment of "intestine". This is an unusual case that highlights the diversity of findings present within the spectrum of mature cystic teratomas and provides evidence that carcinoid tumours arising in this context may be of true intestinal origin.
P117

An Audit Assessing the Adequacy of Liver Biopsy Specimens Sent Over a One Year Period.

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Background: Liver biopsy is an important tool in the evaluation of patients with liver disease. Biopsies are commonly collected via ultrasound guidance or through a transjugular approach. It is recommended that an optimal liver biopsy should be longer than 20mm or have 11 or more complete portal tracts (CPTs). This audit aimed to assess the proportion of liver biopsies collected over a one year period which met this standard.

Method: Data was collected from the reports of biopsies collected over one year; data included patient demographics, the method used to obtain the biopsy; the number of cores taken, and the size and number of CPTs per biopsy. Cases where the samples were obtained from surgery were excluded. Results: Data was collected from 53 reports. 85% of the biopsies had been collected through ultrasound guidance. The mean age of the patients was 59.7 years. The mean length of the samples was 16.2mm; biopsies collected through ultrasound guidance were on average 16.7mm, the corresponding figure from transjugular specimens was 12.4mm. The specimens collected with ultrasound guidance were more likely to be in excess of 20mm than those collected through the transjugular approach (47% and 20% respectively). The number of CPTs was only documented in 13% of all the cases, in these specimens the mean number of CPTs was 8.4. Only 47% of the biopsies met our standard. Conclusion: Our results showed that less than half our sample met the standard. The standard was more likely to be met on the criterion of sample size. The mean number of CPTs was infrequently documented and therefore we recommend that the number of CPTs be routinely documented in reports. Furthermore, our data suggest that an ultrasound guided approach may be more likely to yield an adequate biopsy sample. However, due to our small sample size further study is required in this area to assess the adequacy of liver biopsy samples on a wider scale.

P118

Is Oil Red-O and Digital Image Analysis the Gold Standard for Quantifying Steatosis in the Liver?

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Background & Aims: The NAFLD Activity Score (NAS) is a well validated score for determining the severity of NAFLD using an H&E slide. The degree of steatosis contributes up to 3 of the 8 points to NAS and hepatocyte ballooning (which may be confused with fat) a further 2 points. Therefore, it is important to correctly identify steatosis in a liver biopsy. Oil Red-O (ORO) stain is the gold standard for identifying fat in tissue. Our aim was to compare two pathologists with digital image analysis (DIA) using both H&E and ORO to assess the degree of fat in mice with NAFLD.

Methods: We studied histological steatohepatitis exhibiting a spectrum of steatosis in C57BL/6 mice with high fat and/or high fructose diets. Slides were stained with H&E and ORO and examined by two pathologists. DIA was used to calculate the percentage of steatosis on H&E and ORO stained slides and size distribution of fat droplets. Triglyceride concentrations in the tissue were measured biochemically as a true reflection of tissue lipid content.

Results: ORO staining identified fat in the control and fructose groups where no fat was identified by pathologists on H&E slides. Most of this fat was macrovesicular.

The two pathologists showed strong interobserver agreement (Pearson correlation R=0.991, p<0.001). However, compared to ORO DIA, they underestimated the amount of fat for the high fat (71.6% vs 46.2%) and high fructose (71.9% vs 47.0%) groups where was mainly macrovesicular fat (p=0.011 and p=0.003). ORO DIA accurately reflected the liver triglyceride concentrations and is therefore an accurate reflection of liver steatosis (R=0.706, p<0.001).

Conclusions: ORO staining can identify fat in cases where it cannot be seen on H&E staining. Although NAS is clinically valid, in research situations ORO DIA is warranted as the most reliable way to accurately assess liver steatosis and also give additional information on fat droplet size.

P119

Recognising Histological Regression in Colorectal Liver Metastases Treated with Oxaliplatin Based Chemotherapy: Inter-Observer and Inter-Tumour Variation

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Neoadjuvant chemotherapy is used to increase the resectability of colorectal liver metastasis (CRLM). Can histopathologists distinguish chemotherapy response from ‘biological’ necrosis in CRLM? Method: Patients with CRLM who were chemo-naïve or previously treated with oxaliplatin-based chemotherapy were identified. Tumour regression/necrosis was scored using Mandard criteria adapted for CRLM (1), and the % tumour necrosis estimated, by 2 histopathologists unaware of previous treatment. We compared inter-observer variation using kappa statistics, and variability of tumour regression among multifocal tumours. Results: Inter-observer variation kappa statistic (197 tumour blocks) was 0.87 for major/ partial/no response and 0.81 for necrosis scored 0-4. Evidence of tumour regression by patient is shown in the table.

<table>
<thead>
<tr>
<th>Reg / Necrosis</th>
<th>Inter-Observer Kappa</th>
<th>Inter-Tumour Kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>No chemotherapy (20)</td>
<td>Neoadjuvant chemotherapy (20)</td>
<td></td>
</tr>
<tr>
<td>Median age in years (range): male/female</td>
<td>73.5 (55-40); 14.6</td>
<td>68.5 (44-75); 11.9</td>
</tr>
<tr>
<td>Number with 21 tumour</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Number of tumours/case (range)</td>
<td>2 (1-7)</td>
<td>2 (1-23)</td>
</tr>
<tr>
<td>Median tumour diameter (range)</td>
<td>21mm (3 - 150mm)</td>
<td>21mm (14 - 80mm)</td>
</tr>
<tr>
<td>No regression, any tumour (Score 0-5)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Partial regression at least 1 tumour (score 3)</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Major regression at least 1 tumour (score 1-2)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Of regression, number with unresponsive tumour (score 6-5) elsewhere</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Average necrosis score, all tumours</td>
<td>7.5</td>
<td>3.3</td>
</tr>
<tr>
<td>Cases with necrosis score &gt;50%</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusion: Major tumour regression with fibrosis (score 1-2) was seen in 8/20 chemotherapy patients and 1 untreated patient, 15/22 with regression also had non-responding tumours. Some tumour necrosis was universal and independent of chemotherapy. Inter-observer agreement was excellent. Features suggestive of chemotherapy response also occurred in untreated patients, and regression was usually heterogeneous in patients with multiple tumours. Reference: 1) Rubbia-Brandt et al, Annals of Oncology 18. 299-304, 2007

P120

Nodular Lymphoid Hyperplasia Occurring Concurrently in the Pancreas and Liver

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A 64-year-old woman presenting with weight loss was found to have a suspicious mass in the tail of the pancreas and a smaller mass in the liver following investigations. Two fine needle aspirations showed features suggestive of chronic pancreatitis, but an elective distal pancreatectomy and a non-anatomical liver resection were performed to exclude a neoplastic process. The liver mass was a fairly well-circumscribed pale nodule measuring up to 30mm, the pancreatic tail mass was ill-defined, stellate-like and pale measuring up to 26mm. Microscopically, both lesions were composed of lymphoid follicles with polarised germinal centres containing tingible body macrophages and surrounded by well-defined mantle zones. These were also present in peri-pancreatic adipose tissue and lymph nodes. There was associated fibrosis, and a mild chronic inflammatory cell infiltrate in the pancreatic tail but no evidence of periductal inflammation. Immunohistochemistry demonstrated preserved B and T cell compartmentalisation with bcl-2-negative follicles throughout. In situ hybridisation demonstrated a polyclonal light chain population. The overall appearances were of nodular lymphoid hyperplasia, a benign, localised lymphoid proliferation, which produces a tumour-like lesion. It has been described in various anatomic locations; however, to our best knowledge this is a first description of it occurring concurrently in the pancreas and liver. There are reported associations with immune-mediated disorders and immunodeficiency, but these were absent in this patient. It is important to be aware of this phenomenon and to exclude low grade lymphoma. We advocate an avoidance of the term ‘pseudolymphoma’ to describe what is essentially a reactive process.
Case Report: Congenital Hepatic Fibrosis Presenting in the Sixth Decade

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Congenital Hepatic Fibrosis (CHF) is a rare autosomal recessive fibropolycystic disease with hepatic manifestations of periportal fibrosis and bile duct proliferation, presenting in younger life with cholangitis or portal hypertension. We describe here the case of a 60 year old lady who presented with jaundice and right upper quadrant pain after a ride on the ‘Big Dipper’ at Blackpool pleasure beach. This was her first episode and her past medical history was unremarkable. Serum biochemistry showed an ALT of 169, an ALP of 165 and a bilirubin of 31. Ultrasound showed a thickened irregular CBD but no gall stones and the initial clinical impression was that of having passed a stone. MRCP did not show any calculi, instead there was irregular peripheral duct dilatation in keeping with primary sclerosing cholangitis. She was managed conservatively and was asymptomatic until a second episode a year later. A CT was performed and showed progressive worsening of the ductal disease with CBD dilatation (maximum luminal diameter 9mm). Subsequently a liver biopsy showed hyperplastic and ectatic bile ducts with an associated periportal neutrophilic infiltrate, fibrosis and evidence of cholestasis; features consistent with CHF. No Mallory’s hyaline, alpha – 1 antitrypsin bodies or HBsA positivity were seen. CHF is a challenging diagnosis to make and was particularly so in this unusual presentation and at this age. Liver biopsy was the definitive investigation in this case. CHF is a chronic disease which is often a challenge to manage, curative only by transplantation.
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