Intrarenal multiple and multilocular epidermoid cysts presented as an end stage kidney disease
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This report describes a case of large multiple and multilocular epidermoid cysts affecting the left kidney of 67 old male. The condition is accidentally discovered during investigations for left loin pain complaint. Ultrasonography revealed enlarged left kidney with the picture of hydrourephrosis. Grossly, the kidney is distorted by these cysts that were filled by cheesy like material. The histologic picture of an end stage kidney disease was apparent in the compressed renal parenchyma by these cysts that were identical to an epidermoid cyst elsewhere. In conclusion, although of the rarity of an epidermoid cyst of the kidney, it could cause serious kidney damage leading to eventual end stage kidney disease. Epidermoid cyst of the kidney could be presented as hydrourephrosis at least for nephrologists and radiologists so, awareness of the occurrence of this cyst would broaden the differential diagnostic categories.
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Evaluation of survivin expression in testicular tissues of infertile males

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Normal spermatogenesis represents a precisely regulated balance between continuous cell proliferation and apoptosis. Survivin is one of the inhibitors of apoptosis. We aimed to examine the testicular survivin expression in infertile men and to evaluate its possible role in defective spermatogenesis. 55 infertile male patients were included. Testicular biopsies were taken and were divided into 3 groups; normal spermatogenesis (NS), maturation arrest (MA) and sertoli cell only (SCO) groups. Immunohistochemical expression of survivin was detected in all groups but varied in degree of intensity. Only two specimens from SCO group were devoid of survivin expression. Survivin expression was detected in the cytoplasm of not only spermatogenic cells but also sertoli cells and interstitial cells of leydig. Most of patients of NS group (70%) and MA group (75%) showed marked survivin expression. In SCO group, 22% showed negative expression, 67% showed mild expression and 11% showed marked expression. The intensity of survivin expression was significantly higher in NS and MA groups when compared to SCO group (P=0.0198 & P=0.0008) respectively. However, there was no statistical significant difference in intensity of survivin expression between NS and spermatogenic failure (SCO and MA) (P=1). Also, there was no statistical difference between early and late MA group (P=1).

Conclusion: Survivin expression is not a specific marker for germ cells. Survivin expression is significantly reduced in sertoli cell only patients when compared to patients with maturation arrest or normal spermatogenesis however, survivin expression couldn’t correlate with the stage of maturation arrest.

P81

Urothelial Carcinoma with Rhabdoid Features: A Case Report

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Extranodal rhabdoid tumours have been described in a variety of primary sites with only rare case reports of urothelial carcinomas with rhabdoid features in the literature. We describe a rare case of poorly differentiated urothelial carcinoma with rhabdoid features, confirmed on immunohistochemistry. Bladder biopsies from three different sites were received from a large solid mass, all of which showed similar features. The tumour was poorly differentiated invasive urothelial carcinoma infiltrating the deep muscle and composed of high grade pleomorphic nuclei with frequent mitosis. Also present was the rhabdoid component composed of large rhabdoid cells with abundant pink cytoplasm, vesicular nuclei, and a prominent nucleolus in a myxoid background. Rhabdoid cells were discohesive and were present singly, in clusters, or in nests. Immunohistochemical stains for cytokeratin CK7, CK20, CD10, AE1/AE3 showed either dotlike positivity or diffuse cytoplasmic staining in the rhabdoid component of the tumours. The tumour cells with the rhabdoid features showed positivity with desmin and vimentin. Malignant tumours with rhabdoid features in adults in extranodal locations are considered to be phenotypic variants and have aggressive outcome. These have been described in all age groups and from multiple sites, including the extremities, brain, liver, mediastinum, orbit, heart, and is now accepted as a discrete entity. The tumours generally have a histological appearance similar to that of renal rhabdoid tumours. Immunohistochemical analysis usually demonstrates reactivity to vimentin, desmin, and keratin. Extranodal rhabdoid tumours do not demonstrate skeletal muscle components by immunohistochemical analysis.

P82

Tale of Two Urinary Bladder tumours – Myeloid Sarcoma as a Primary manifestation of Acute Myeloid Leukemia and Extranodal Marginal Zone Lymphoma

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Case 1: Myeloid sarcoma (MS) of the lower urinary tract is rare. We describe a 47-year-old man with pyuria, who underwent TURBT for a suspected bladder tumour and was found to have acute myeloid leukemia. Fragments of ulcerated bladder mucosa with underlying distinct monomorphic population of cells with granular and clear cytoplasm were noted. Immunohistochemistry revealed strong expression of myeloperoxidase and weak IRF4(MUM1) positivity. Expression of transcription factor PU-1 was accompanied by weak CD5, CD3, CD20, CD138, CD34, CD68, IRF8, MNF116 and Cam5.2 were negative. Blood count after one month was WBC-99.0x10^9/L, with predominant population of leukemic blasts. Expression of CD20, CD138, and CD68, which are usually present in lymphoma cells, were negative.

Case 2: Malignant lymphoma of the bladder can be classified into 3 groups: 1) Primary lymphoma localized to the bladder; 2) Lymphoma in the bladder as disseminated disease (non-localized lymphoma); 3) Recurrent bladder involvement by lymphoma(secondary lymphoma). Primary extranodal marginal zone lymphoma of MALT type of the urinary bladder is rare and generally has excellent prognosis. We present a 70 yr female with a newly diagnosed bladder tumour comprising of nonexpansive lymphoid infiltrate with focal nodular pattern and occasional lymphoid follicles. The focal nodular growth pattern was as a result of colonization of the germinal centres by the nonplastic lymphoid infiltrate. Immunohistochemistry showed these lymphoid cells to be CD20, CD79a and bcl-10 positive and CD5, CD3, CD10, cyclin D1 negative. Demonstration of light chain restriction was not possible. Bone marrow aspirate and trephine biopsy showed no evidence of lymphoma infiltration.
P83
Adenocarcinoma Arising in an Endocervicosis of the Urinary Bladder
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Endocervicosis is a non-neoplastic lesion exhibiting mullerian differentiation. A malignant tumour arising in endocervicosis has not been reported, except for a case of adenocarcinoma originating from a lesion of the vagina. Herein, we describe a case of adenocarcinoma arising in endocervicosis of the urinary bladder. The patient is a 58-year-old woman. She had a history of endometriosis, for which a total hysterectomy was performed 16 years previously. Cystoscopy revealed an elevated nodular mass, 4*4 cm in size, in the triangle area. Total cystectomy was performed. The tumour was composed of two different histological components. The dominant component was proliferation of multiple cystic glands lined with cuboidal epithelium. The lining epithelium had clear cytoplasm, which resembled an endocervical gland. The other histological component was proliferation of atypical cells with large nuclei, which infiltrated the surrounding connective tissue. This histological finding was the same as the biopsy specimen taken previously. From these findings, we suggest that this is the first case of adenocarcinoma arising in endocervicosis of the urinary bladder.

To determine the histochemical nature of the mucus of this tumour, we performed various histochemical stainings, including Alcian Blue (AB)-PAS, High iron diamine (HID)-AB. We then compared the results with four control populations (normal cervical gland, normal endometrial gland, adenocarcinoma of cervix, adenocarcinoma of endometrium). It is difficult to differentiate these groups based only on their staining characteristics, but endocervicosis is shown to have a similar histochemical nature to a normal endocervical gland.
Seminoma with Exclusive Intertubular Growth: Report of a Clinically and Grossly Inconspicuous Testicular Tumour

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Seminoma with intertubular growth pattern represents a rare but distinct clinicopathological subset of testicular seminomas. Such tumours do not present as mass lesions, and may be discovered during investigation of infertility, pain or metastatic disease. No distinct tumour is grossly apparent in most of these cases. Microscopic identification is difficult, as the tumour cells can be obscured by lymphocytic reaction and hyperplastic Leydig cells.

We present the case of a 43-year old man who had right orchidectomy suspected as a tumour on ultrasound. A left radical orchidectomy was performed. We received a testis with attached spermatic cord containing a 5 mm nodule at the periphery. Microscopically, the nodule was predominantly composed of benign spindle cells arranged in fascicles with no evidence of mitoses or necrosis. These were admixed with steroid cells with epitheloid and signet ring morphology. Immunostaining for S100, inhibin and SMA was positive, a pattern also seen in both adult and juvenile granulosa cell tumours; whereas desmin, CD34, c-kit and cytokeratin was negative. This concurrent presence of some morphological and immunohistochemical features of both steroid and granulosa cell lines in the tumour suggests its origin from a stromal stem cell, possibly capable of dual differentiation, but with an arrest of maturation at an early phase of differentiation.

Unclassified sex cord stromal tumours (SCSTs) of the testis can occur at all ages, but most common in children (30% in <1 yr). The behavior is mostly benign in prepubertal (<10yrs) children, but these have malignant potential in older individuals. Prognosis depends on the age, size, invasion beyond testis, necrosis, pleomorphism and mitosis.

Cervical Cytology Suggestive of Glandular Neoplasia: An Audit of Outcomes

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Seventy-seven cases having a cervical smear result showing abnormal glandular cells between 1st January 2005 and 31st Dec 2006 were identified and matched with the diagnostic histology result. Correlation with histology revealed the following results: ten cases (12%) were associated with invasive malignancy, one case of cervical squamous carcinoma, four cases of cervical adenocarcinoma and five cases of endometrial adenocarcinoma. In-situ neoplasia of the cervix was present in 41 (54%) of those with positive smears; fourteen (18%) had cervical squamous intra-epithelial neoplasia (CIN) only and twenty-seven (36%) had cervical glandular intra-epithelial neoplasia (CIGN) only. Eleven (14%) patients had negative histology, two were inadequate and thirteen (17%) had other non-neoplastic diagnoses including inflammation, metaplasia and reactive atypia.

The majority of women were asymptomatic (84%). Women who were post-menopausal and symptomatic were more likely to have an endometrial lesion than a glandular abnormality of the cervix.

Neurofibroma of the uterine cervix, case report and literature review

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Neurofibromatosis type 1 (Von Recklinghausen’s disease) is an autosomal dominant condition caused by a mutation in the NFI gene (chromosome 17) and has a prevalence of approximately 1 : 3000. Neurofibromas rarely involve the urogenital organs. There is a 12 - 29% risk of malignant transformation and therefore, long-term follow-up is warranted.

The female genital system is rarely affected in neurofibromatosis. The vulva is the most common part of the female genital system to be involved. Few cases of cervical neurofibroma have been described in literature. Despite its rarity, clinicians should consider the possibility of genitourinary involvement in patients with history of neurofibromatosis.
**P91**

**Immunohistochemical study on cell cycle related proteins (PTEN, p27, p53, cyclin D1, cyclin E) of ovarian cancers**

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The PI3K (phosphatidylinositol 3-kinase) / pAkt pathway is an important regulator of cell cycle progression and cell survival. PTEN (phosphatase and tensin homologue deleted on chromosome 10) with phosphatase activity regulates this PI3K / pAkt pathway, thereby functioning as a tumor suppressor. This study was conducted to clarify the significance of PTEN and its downstream proteins, such as p27, p53, cyclin D1 and cyclin E, that relate to the cell cycle, with a special focus on the relationship among these proteins in ovarian carcinomas. We examined among immunohistochemical expression in 64 cases of primary ovarian carcinomas comprised of 17 serous, 8 mucinous, 21 endometrioid, and 18 clear cell carcinomas. Immunohistochemical date were analyzed with a co-relation of histologic subtypes, nuclear grades and clinical stages. Significant differences of PTEN expression were identified in different histological subtypes. Percentage of positive staining of PTEN was lower in endometrioid carcinoma (38.1%) than those of other histologic subtypes (55.6-82.4%). PTEN expression did not correlate statistically with expression of p27, p53, cyclin D1 and cyclin E in Fisher’s exact probability test. In all histologic subtypes of ovarian carcinoma except for clear cell carcinoma, high-level cyclin D1 expression was more frequently found in stage I, II tumours than in stage III, IV tumours (p<0.01), and grade 1 tumours than grade 2, 3 tumours (p<0.05). The results suggest that activation of cyclin D1 might be an early event in ovarian carcinogenesis.

**P92**

**Primary Mucinous Carcinoid, a rare entity and a diagnostic dilemma**

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A previously well 34 year old woman presented with a large pelvic mass, found to be ovarian at laparoscopy. The resected ovarian mass was composed of small well formed acini with focal goblet cells, mucin containing signet ring cells that focally expressed chromogranin and contained sub nuclear argyrophil granules. A small epidermoid cyst was seen adjacent to the tumour. The case was diagnosed as a primary mucinous carcinoid of ovary and with a high mitotic rate (up to 6/10hpf), it was regarded as an atypical carcinoid. The other ovary was also involved. The tumour first recurred as a pelvic mass 3 years later and after another 2 years in the form of ileal and sigmoid metastasis. These cases present challenges for diagnosis and prediction outcome having an immunoprofile that overlaps with their gastrointestinal counterpart.

Reference:

**P93**

**Comparison of Mucin and CD10 expression among ovarian serous adenocarcinoma, clear cell adenocarcinoma, endometrioid adenocarcinoma, mucinous adenoma, mucinous borderline tumour, and mucinous adenocarcinoma**

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The aim of this study is to evaluate the immunohistochemical expression of mucin and CD10 in ovarian serous adenocarcinoma (SC), clear cell adenocarcinoma (CC), endometrioid adenocarcinoma (EC), mucinous adenoma (MA), mucinous borderline tumour (MB), and mucinous adenocarcinoma (MC), and to analyze the relationship between prognosis and these expressions.

Method: Formalin-fixed paraffin-embedded tissue sections from 35 cases of SC, 45 cases of CC, 25 cases of EC, and 26 cases of MC were immunostained using antibodies for MUC1, MUC2, MUC4, MUC5AC, MUC6, and CD10. The staining results were evaluated according to the proportion of positive cells. Results: MUC1 was more frequently expressed in EC, CC and SC than MC. MUC2, MUC5AC, and MUC6 were mainly expressed in MC and EC. In contrast, SC and CC revealed negative or low expression for MUC2, MUC4, MUC5AC, MUC6, and CD10. MC revealed more frequent expression for MUC2 and MUC5AC than the other histological types. MUC1, MUC2, and CD10 were increased from MA to MC. MUC5AC were decreased from MA to MC. Low proportion of positive cells for MUC2 and MUC4 in MC, high proportion of positive cells for MUC1 in EC, and CD10-negative SC showed better long-term survival rate.

Conclusions: These results suggest that the difference in mucin and CD10 expression among ovarian carcinomas may be useful for the prediction of clinical outcome. In mucinous tumour, the expression patterns of MUC2, MUC5AC, and CD10 suggest that there is close association between carcinogenesis and intestinal metaplasia in ovarian mucinous tumours.

**P94**

**The Origin of Gliomatosis Peritonei**

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Gliomatosis Peritonei (GP), Characterised by Peritoneal and Omental Gial Implants (GI), Occurs Almost Exclusively in Association With Ovarian Teratomas (OTs). Some Investigators Have Suggested That GI Originates Through Capsular Rupture of the Teratoma With Subsequent Implantation, or Via Angiolymphatic Spread. Others Advocate That GP Arises From Gliomatosis Peritonei (GP), Occurs Almost Exclusively in Association With Ovarian Teratomas (OTs). Some Investigators Have Suggested That GI Originates Through Capsular Rupture of the Teratoma With Subsequent Implantation, or Via Angiolymphatic Spread. Others Advocate That GP Arises From Gliomatosis Peritonei Stem Cells. In Contrast to Normal Tissue DNA Which Contains Maternal and Paternal Genetic Material, and Thus is Heterozygous at Many of Polymorphic Microsatellite Loci (PML), OTs Often Contain a Duplicated Set of Maternal Chromosomes, Demonstrating Heterozygosity of Alleles.

Twelve OTs Associated With GP Were Identified. DNA Was Extracted From Paraffin-Embedded Tumour Tissue, and Polymerase Chain Reaction (PCR) Was Used to Determine Their Genetic Pattern at Various PML. Eight Teratomas Arose Post-Meiosis I, Displaying a Predominantly Heterozygous Microsatellite Pattern. These Cases, Considered Non-Informative, Were Excluded From Further Investigation. Four Teratomas Arose Post-Meiosis I, Showing a Predominantly Homozygous Microsatellite Pattern. In These Informative Cases, DNA Was Extracted From Paraffin-Embedded Matched Normal Tissue and GI, and Analyzed Using PCR. In Two Cases, the Matched Normal Tissue and Associated GI Demonstrated a Predominantly Heterozygous Microsatellite Pattern in Contrast to the OT. DNA Analysis of the Other Two Cases Is Being Performed.

Thus, Our Preliminary Results Support the Theory That GP is Genetically Unrelated to the OT, Most Likely Arising From Pluripotent Cells Within the Peritoneum. Factors Responsible For Gliomatosis Peritonei Stem Cells In This Setting Are Poorly Established, Being an Important Area of Future Investigation.
Ovarian Neuroblastoma Arising Within a Mature Cystic Teratoma: A Rare Pathological Entity

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Mature cystic teratoma (MCT) are common ovarian neoplasms which undergo malignant transformation in 1-2% of cases with squamous cell carcinomas accounting for the vast majority. Malignant neural tumours arising from MCT are exceptionally rare. Here we describe a case of neuroblastoma developing within an ovarian teratoma in a 30 year old female.

Macroscopically the specimen was received from theatre in pieces containing a part of a cyst wall lined by hair bearing skin. Solid areas were identified showing a variegated appearance with firm white tumour and foci of haemorrhage.

Histologically the cyst was lined by stratified squamous epithelium with appendiceal structures, adipose tissue and mature neural elements. The solid areas consisted of sheets and nests of small pleomorphic blue cells, neurofibrillary stroma, focal Homer-Wright rosettes and multifocal anaplasia with bizarre uninucleated and multinucleated giant cells. No ganglion cell differentiation was identified.

Immunohistochemistry showed these cells to be neuroblastic in origin being positive for CD56, synaptophysin and NB84. The tumour was classified according to the International Neuroblastoma Pathology Classification (INPC) as stroma poor with an intermediate MIK1 (mitotic-karyorrhectic index). Fluorescent in-situ hybridization was carried out on paraffin sections and showed N-myc amplification and a relative 17q gain in the neuroblastic tumour.

Only a handful of cases of neuroblastoma arising in ovarian MCT have been described to date and all previous reports were in patients under 20 years of age. According to the age-linked INPC, this tumour is thought to carry an unfavourable prognosis.

Morules in endometrioid proliferations of the uterus and ovary consistently express the intestinal transcription factor CDX2

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Aims: To undertake an immunohistochemical analysis of squamous elements in endometrioid proliferations of the uterus and ovary and to compare the immunophenotype of typical squamous elements and so-called squamous morules.

Methods: Results: Cases of uterine or ovarian endometrioid glandular lesions with squamous elements were stained with CDX2, β-catenin, ER, CD10, p63 and high molecular weight cytokeratin LP34. Thirteen cases had typical squamous elements and 18 cases morules. Morules typically exhibited diffuse nuclear CDX2 and β-catenin immunoreactivity and were positive with CD10 and LP34. They were usually ER and p63 negative. In contrast, typical squamous elements were usually positive with ER, CD10, p63 and LP34. They were usually CDX2 negative or focally positive and exhibited no nuclear staining with β-catenin. Ten endometrioid carcinomas not exhibiting squamous differentiation were stained with CDX2; one was focally positive. Electron microscopy in two ovarian endometrioid adenocarcinomas with extensive morular differentiation showed that the morules exhibited epithelial features but no overt evidence of squamous differentiation.

Conclusions: Typical squamous elements and morules have an overlapping but differing immunophenotype. Morules exhibit no firm immunohistochemical or ultrastructural evidence of squamous differentiation, although immature squamous differentiation cannot be excluded. Nuclear β-catenin positivity is in keeping with the observation that endometrioid glandular lesions with morules are often associated with β-catenin gene mutation. The explanation for diffuse nuclear positivity with the intestinal transcription factor CDX2 in morules is not clear but may be a result of overexpression of nuclear β-catenin. We suggest that the term morular metaplasia is used instead of squamous morules.
Regulation of MUC16 in Ovarian Cancer by Micro RNA

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CA125 is a tumour antigen used to monitor progression and response to therapy in epithelial ovarian cancer, and is encoded by the MUC16 gene. Micro RNA’s (miRNA) are short non-coding RNA strands that can regulate gene expression through regulation of the stability or translation of mRNA. We investigated the possible regulation of MUC16 in ovarian cancer cell lines by four miRNAs predicted to target this gene.

Relative quantification real time PCR was performed on mRNA extracted from 22 primary ovarian tumour cell lines grown from ascitic fluid samples taken from 17 ovarian cancer patients. The established ovarian tumour cell line OVCA433 was used as a calibrator. The levels of miR-92, miR-193a, miR-452 and miR-651 miRNAs and MUC16 mRNA were measured relative to a standard internal control, β-actin. MUC16 mRNA levels were found to vary by three orders of magnitude between the 22 cell lines, compared to a variation of only 30-fold in the levels of CA125 found in the serum of the 17 patients at the time of ascitic fluid removal. We found very high (\(>0.8\)) or high (\(>0.6\)) positive correlations of 0.869, 0.773, 0.713 and 0.690 when MUC16 mRNA levels were compared to miR-92, miR-453, miR-193a and miR-651 levels respectively. These observations are consistent with the negative regulation of MUC16 mRNA translation, rather than stability, by each of four miRNAs predicted to target this gene transcript.

A Case of Cervical Squamous Cell Carcinoma and Schistosomiasis

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We report the case of a 26 year old female who presented with mild dyskaryosis on a cervical smear. At colposcopy examination, she was thought to have high grade cervical intraepithelial neoplasia (CIN) and a cervical biopsy was performed. The biopsy showed CIN II, CIN III and spherical bodies with terminal spines consistent with Schistosoma haematobium eggs. A LLETZ was performed and this showed high grade CIN, well-differentiated invasive squamous cell carcinoma and further schistosome eggs.

When schistosomiasis affects the female genital tract, it is most commonly seen in the cervix and is usually Schistosoma haematobium. The presence of Schistosoma haematobium in the bladder is known to be associated with the development of squamous cell carcinoma due to long-standing chronic inflammation and it is feasible that it plays a similar role in the cervix. We review the published literature looking at the role schistosomiasis of the cervix might play in the development of cervical squamous cell carcinoma.

The Diagnostic Utility of PCR in a Specialist Haematopathology Unit

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Molecular analysis of tissue using the polymerase chain reaction (PCR) is an important adjunct to diagnosis in haematopathology. PCR is used for the demonstrating T or B cell clonality and for detecting specific chromosomal translocations. A PCR technique is also available for the detection of tuberculosis (TB). The diagnostic contribution of PCR in our department was assessed by a twelve-month retrospective analysis of its use.

Our haematopathology unit receives around 2300 biopsies annually. In 2006 PCR was used on 118 biopsies (5\%) and on 15 cytology specimens. In 19 cases (14%) PCR could not be assessed due to insufficient or poor quality DNA; this was seen most frequently in skin biopsies suspicious for mycosis fungoides (7 cases). Where DNA was successfully extracted, PCR was performed for suspected lymphoma in 92 cases (91\%) and for TB in 22 cases (19\%).

In no case did TB PCR yield a positive result. In suspected lymphoma PCR made an important contribution to the final diagnosis in 84 cases (91\%), and amended an initial diagnosis in 7 cases (8\%). In 13 cases (14\%) PCR did not corroborate the provisional diagnosis, and was deemed non-contributory.

Our results show that PCR is a valuable tool in lymphoma diagnosis, but is less helpful in identifying TB or confirming the diagnosis of mycosis fungoides in skin biopsies, where the DNA extraction can be problematic. These findings may be useful in planning the appropriate use of PCR in haematopathology units.
Biopsy Pathology in HIV in the Era of HAART

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The introduction of highly active anti-retroviral therapy (HAART) has markedly improved patient survival in human immunodeficiency virus (HIV) infection. HAART prevents many opportunistic infections, but with increased survival times patients can go on to develop a range of other pathological conditions. To assess these conditions, we have examined the spectrum of disease seen in recent tissue biopsies from patients with HIV.

In 2006 we received 151 biopsies from HIV positive patients. The most common specimens (50%) were haematological in nature, and included 41 bone marrow trephines (27%), 29 needle core biopsies of lymph node (19%) and 21 whole lymph node specimens (14%). 25 biopsies (17%) were from the GI tract, and the remainder were from a variety of sites including skin, salivary gland, chest wall, breast and nasopharynx.

Lymphoproliferative disease was the commonest diagnosis, and was found in 22% of biopsies. Diagnoses in this category included classical Hodgkin lymphoma, diffuse large B cell lymphoma, plasma cell Castleman’s disease, Burkitt lymphoma and primary effusion lymphoma. In 20% of the biopsies (mainly in bone marrows) there were non-specific HIV related changes, and in 15% of the specimens the histology was non-diagnostic. Opportunistic infections were seen in only 9 cases (6%).

Our findings suggest that the most likely positive finding in biopsy specimens from HIV patients is lymphoproliferative disease, and that infectious disease is now relatively rare. This should be taken into account when determining reporting strategies for biopsies from HIV positive patients.

Atypical Morphology in Plasma Cell Myeloma

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Plasma cell myeloma (PCM) represents 15% of all haematological malignancies. PCM is a bone marrow-based multifocal plasma cell neoplasm characterised by a serum monoclonal protein and skeletal destruction with osteolytic lesions, pathological fractures, hypercalcemia and anaemia. The disease results from the expansion of single clone of immunoglobulin secreting, terminally differentiated end stage B cells (plasma cells). Histologically plasma cells characteristically show eccentric nuclei, “clock face” nuclear chromatin and abundant basophilic cytoplasm with focal perinuclear clearing (hof). We present a series of 6 cases of PCM where the plasma cells lacked this typical morphology, so that the diagnosis depended on the clinical history supplied and the immunohistochemical findings.

In 2007 we received 220 biopsies with a diagnosis of PCM. Whilst the majority showed characteristic plasma cells, we identified 6 cases (2.7%) that showed atypical morphology. In these cases the neoplastic cells variously resembled mast cells, histiocytic/monocytic cells, hairy cells, or melanoma. One case showed pleomorphic bizarre cells suggestive of a poorly differentiated carcinoma. Immunohistochemistry revealed positive CD138 staining and immunoglobulin light chain restriction in all cases, confirming the diagnosis of PCM. A history of previous myeloma was present in four of the cases, raising the possibility that the atypical features were treatment-induced. Pathologists should be aware that neoplastic plasma cells can show an abnormal histological appearance, and where there is a history or clinical suspicion of PCM should always include CD138 and light chains in their immunohistochemistry panel.

Rapid Reporting of Bone Marrow Trephine Biopsies – an Assessment of the Effects on Diagnostic Accuracy

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A departmental audit in 2006 identified a turnaround time (TAT) for bone marrow trephine biopsies (BMT) of 7 days. Streamlining fixation and decalcification and the use of a rapid processor reduced the technical time, but waiting for immunohistochemistry (IHC) remained a source of delay. At the clinicians’ request we instituted a new BMT reporting protocol whereby the Consultant issued a rapid initial report based solely on the H&E morphology. A supplementary report with the IHC findings was added later. These measures reduced the TAT to 2.5 days.

To assess the diagnostic effects of this strategy, all cases subject to rapid reporting between October 2006 and October 2007 were retrieved and the initial and supplementary reports compared.

Over the year 73 cases were reported under this protocol, and 61 (84%) had IHC. The initial reports were classed as diagnostically useful in 67 cases (92%), the remaining 6 reports (8%) were purely descriptive. In 12/67 cases (14%) a firm diagnosis was made on morphology alone. In the remaining 55 biopsies, IHC confirmed the morphological diagnosis in 44 cases (80%), added information in 2 cases (4%), and in 9 cases (16%) resulted in significant change to the initial diagnosis.

Overall approximately 20% of the rapid initial reports were diagnostically unhelpful, either being purely descriptive (6/73, 8%) or later turning out to be inaccurate (9/73, 12%). We and the clinicians now need to decide if this level of diagnostic inaccuracy is acceptable in order to produce faster turnaround times.

An Unusual Case of Granulomatous Lymphadenitis

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We describe an unusual case of a 61 year old man who initially presented with axillary lymphadenopathy, which was reported as granulomatous lymphadenitis (special stains for micro-organisms and a lymphoma panel were negative). Approximately one year later the patient presented with lethargy, abdominal pain, weight loss and subcutaneous nodules over his trunk and limbs. CT scan revealed persistent axillary lymphadenopathy and also splenomegaly. A second lymph node biopsy was performed and again histology showed granulomatous lymphadenitis (special stains and a lymphoma panel were negative). However, a biopsy of one of the subcutaneous skin nodules revealed a heavy dermal infiltrate of immature and atypical myeloid cells, which was confirmed by immunohistochemistry. Further immunohistochemistry was performed on the lymph node and this highlighted a heavy infiltrate of atypical myeloid cells that was not initially obvious on the H&E sections. A diagnosis of a myeloid neoplasm was then suggested and a recommendation made to exclude acute myeloid leukaemia (AML). Bone marrow aspiration and trephine were performed and the appearances were consistent with a myelodysplastic syndrome and acute myeloid leukaemia transformation. Granulomatous inflammation can be associated with Hodgkin’s lymphoma and some T cell lymphomas. This case describes an unusual presentation of AML involving axillary lymph nodes which presented as granulomatous lymphadenitis.
P107
Type and maturational status of dendritic cells in cutaneous B-cell lymphoproliferative disorders
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Emerging evidence suggests that cutaneous B-cell lymphoproliferations represent a continuous spectrum of disease, with polyclonal B-cell cutaneous lymphoid hyperplasia (BCLH) at one end and monoclonal cutaneous marginal zone lymphoma (CMZL) at the other. We believe it probable that dendritic cells (DCs) play a central role in the genesis and evolution of such cutaneous lymphoproliferations. As a preliminary step towards testing this hypothesis, we sought to compare the number, subtype and maturational status of DCs in biopsy specimens showing features of BCLH and CMZL. Immunohistochemistry was used to identify Langerhan’s cells (Langerin), dermal DCs (DC-SIGN) and plasmacytoid DCs (BDCA2), and to differentiate between mature (CD83) and immature (CD16a) DCs. The mean number of positive cells/mm2 was calculated for each antibody in all cases. There were significantly more Langerhan’s cells and dermal DCs in BCLH than CMZL, and significantly more mature DCs in BCLH than CMZL. No significant difference was seen in the number of plasmacytoid DCs or immature DCs.

Mature DCs function as antigen presenting cells and are involved in priming T-cells, suggesting that these functions are important in the genesis of BCLH, consistent with the hypothesis that persistent localised antigenic stimulation is the cause of these lesions. Conversely, immature DCs may play a more important role in maintenance of established CMZL through modulation of the anti-tumour immune host response, since persistence of DCs with an immature phenotype, as shown here, has been shown to lead to a state of immune tolerance.

P108
Identifying HIV Infection in Diagnostic Histopathology Tissue Samples
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Using immunocytochemistry, HIV-1 infection can be visualised in fixed tissue samples. AIM: To investigate the practicalities and utilities of routine HIV-1 p24 immunocytochemistry on tissue samples received in a London histopathology laboratory. METHODS: Over a 3-year period, 2005-7, fixed tissue samples from patients (age 2-65yrs) with and without known HIV infection, including primary diagnostic biopsies, consultation referrals and autopsy material, were stained with Dako anti-HIV-1-p24 antibodies. Cases were selected that, on H&E stains, morphologically suggested HIV infection, eg lymphoid hyperplasia in non-lymphoid organs, atypical germinal centres in lymphoid tissue (PGL), and encephalitis. RESULTS: Of 123 cases, 36 were HIV-1 p24+ve: 24/87 lymph node, 7/13 Waldeyer's ring, 1/3 parotid, 1/2 anus, 2/5 lung, and 1/2 brain samples. In 10/36 cases (28%), the p24+ staining was the first indication to clinicians that the case of these lesions. Conversely, immature DCs may play a more important role in maintenance of established CMZL through modulation of the anti-tumour immune host response, since persistence of DCs with an immature phenotype, as shown here, has been shown to lead to a state of immune tolerance. No significant difference was seen in the number of plasmacytoid DCs or immature DCs.

Mature DCs function as antigen presenting cells and are involved in priming T-cells, suggesting that these functions are important in the genesis of BCLH, consistent with the hypothesis that persistent localised antigenic stimulation is the cause of these lesions. Conversely, immature DCs may play a more important role in maintenance of established CMZL through modulation of the anti-tumour immune host response, since persistence of DCs with an immature phenotype, as shown here, has been shown to lead to a state of immune tolerance.

P109
Role of Tissue Biopsy in the Rapid Diagnosis of Nodal & Extranodal Lymphomas
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AIM OF THE WORK: To find out reliable means for rapid and solid diagnosis of lymphomas that can allow quick therapeutic intervention and save patient lives.

MATERIAL AND METHODS: Specimens from 10 patients : 2 children and 8 adults, were received in the Department of Pathology during December2007, January and February 2008; all with first presentation of their disease and requiring rapid and solid diagnosis to allow immediate intervention. Specimens were subjected to full pathologic examination including immunophenotyping. RESULTS: F.N.A.Cytology specimens from 3 cases, TRU-CUT BIOPSIES from 6 cases, and Multiple Endoscopic biopsies from 1 case, were received. Accurate diagnosis and typing of lymphoma was reached in 8 cases(i.e. 80% of cases), and was suggested in 2 cases which required open tissue biopsy for confirmation and immuno-pheno-typing of the disease. micrographs of the findings will be presented). Mean period required for initial reporting in each case ranged from 1 hour to 24 hours; and diagnosis was completed in up to 4days , including immunophenotyping.

CONCLUSION: F.N.A. CYTOTOLOGY specimens, TRU-CUT BIOPSIES, and ENDOSCOPIC BIOPSIES can be used reliably to allow rapid and solid definitive diagnosis of different types of lymphomas if two conditions are present: 1- Availability of ample amount of submitted specimen, e.g. multiple long intact cores of tissue, and enough aspirated fluid to allow multiple smear and/or cell block preparation. 2- Close clinico-pathologic communication before specimen taking.

P110
TTF-1 Positive Diffuse Large B-cell Lymphoma: An Unusual Finding Causing Diagnostic Dilemma
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Thyroid transcription factor-1 (TTF-1) is expressed in most thyroid carcinomas and in vast majority of lung carcinomas; hence it is one of the most useful markers in differentiating these carcinomas from other malignancies. Diffuse large B-cell lymphomas (DLBCL) form a heterogeneous group of high grade non-Hodgkin's lymphomas which show a variety of immunostaining patterns. They are typically positive with LCA (CD45) and B-cell antigens (e.g. CD20, CD79a), but negative with Cytokeratins and TTF-1; which forms the basis of its differentiation from many carcinomas. Here we present a case of DLBCL that stains positively with TTF-1.

A 73-year old lady presented with a left supraclavicular node. The lymph node architecture was completely effaced and replaced by a diffuse infiltrate of large cells having pleomorphic nuclei, vesicular chromatm, prominent nucleioli and scant amount of cytoplasm. Initial run of immunohistochemistry showed strong positivity with TTF-1. EMA stained a few cells, but HMWCK, S100, thyroglobulin, CD30, PLAP, CK20, CK7 and LCA were all negative; and it was thought to be a metastatic carcinoma. But further IHC revealed AE1/AE3 to be negative. Repeat IHC showed LCA, CD79a and CD20 to be positive. Therefore, the final diagnosis was a DLBCL.

The diagnostic dilemma created by TTF-1 positivity in this case of DLBCL has not been addressed in the literature. We do not know the significance of this finding, but it may be of concern if more cases are reported in future. 
YY1 is a Prognostic Marker in Follicular Lymphoma

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1Medical School, University of Manchester, 2Cancer Studies, University of Manchester

Follicular lymphoma is the second most common type of Non-Hodgkin’s Lymphoma worldwide. The majority of patients diagnosed with follicular lymphoma have an indolent, incurable form of the disease, however a subset of patients have aggressive disease with a shorter survival interval, but are potentially curable. In order for the correct treatment options to be considered it is important to distinguish between these patients.

The transcription factor YY1 has been shown to play an important role in cancer biology. PolyA RT-PCR has recently identified YY1 mRNA as being over-expressed in follicular lymphoma patients with a shorter survival interval. This study aimed to validate these findings at the protein level.

Quantification of the YY1 protein was carried out on 26 follicular lymphoma biopsy samples using Quantum Dot labelled immunohistochemistry. Expression levels of the YY1 protein were significantly increased in those patients alive after follow-up, in comparison to those dead (P<0.025). Kaplan-Meier survival analysis identified that higher expression levels of YY1 were associated with longer survival times (P<0.01). In order to identify the expression pattern of YY1 within follicular lymphoma tissue, co-localisation with CD20 was carried out. The results demonstrated that YY1 is expressed in CD20 positive and CD20 negative cells.

These observations indicate the presence of a negative feedback loop controlling YY1 protein and mRNA expression. They also support the hypothesis that YY1 can predict survival in follicular lymphoma, and indicate that YY1 could be a novel target in future anti-cancer therapies.

Grading Follicular Lymphomas by Counting and “Eye-balling”

W Al-Qsous1, DBegbie1, ME McKeen1, PW Johnston1
1NHS Grampian

Grading follicular lymphomas (FL) is recommended in current WHO guidance but the perceived accuracy of this process is controversial. This pilot study compares grading by eye – qualitatively assessing numbers of centroblasts in FLs – with formal counting. FL cases from 2003-2004 (n = 34) were retrieved from Departmental files. Three cases were excluded owing to missing material. Slides were reviewed independently by an SpR and two consultants and the results of their analyses correlated. These results were then compared with the formal grading of the tumours carried out at the time of reporting. Of the 31 cases assessed, 28 were nodal and 3 were extra-nodal. Overall, results show significant correlation (p<0.01) between the three reviewers’ eye-ball grading. In 8 cases, all grades were identical; in 15, two agreed and the third varied by one grade. In 5 low grade cases there was no agreement apart from classification as “low grade”. Comparison with the formal grading showed complete agreement by eyeball and counting about the one case graded formally as 3B. In three cases one of us disagreed by eye between Grades 3A and 3B – formal counting graded each of these as 3A. Cases graded 1, 2 and 3A by eye-ball were all graded by counting as “low grade”.

This pilot study suggests there is reasonable consensus in eye-ball and counted grading of low grade FLs but with variation in that range. “Eye-ball” 3A or 3B cases would benefit from formal counting.

Microphthalmia in the Himalayan Rabbit: a Teratogenic Effect

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Forty pregnant Himalayan does were exposed to a New Chemical Entity (NCE), a mitochondrial complex II inhibitor, as part of a GLP Regulatory Study to investigate teratogenic potential. Exposure was from Day 6 to Day 30 of gestation at doses of 0, 600, 800 and 1000 ppm. All animals gained weight, increased their food consumption and survived to the end of pregnancy, with no adverse clinical signs. Examination of the pre-term foetuses (Day 30) revealed gross evidence of a reduction in eye size in all treated groups, but not in control animals. The reduction in eye size varied from 25-50%; no dose relationship was observed (0/33, 10/37, 5/22, 14/44 respectively). The heads were fixed in Bouin's for 3 weeks and then processed to wax blocks. Coronal sections of each head were cut in a rostro-caudal direction through the level of the eyes and stained with haematoxylin and eosin. The number of sections obtained per foetus varied from 11-18. The sections for examination were chosen on the basis of sectional symmetry, presence of all eye structures and proximity to the middle of the globe. Histopathological examination (13/33, 24/37, 16/22, 27/44 respectively) revealed retinal dysplasia, choroidal hypoplasia, cataract and persistence of the lens vesicle (0/13, 15/24, 9/16, 17/27 respectively). Such findings are considered to represent an unusual teratogenic effect. The relationship to the mode of action of the NCE is to date unclear.

A three-year retrospective diagnostic review of CNS metastatic tumours

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We reviewed the pathological/ neurourology records of last 3 years (2005-2007) for metastatic tumour removal. Forty-six cases were identified including 42 craniotomies and 4 vertebral decompressions. Age of patients was 34-80 years (median = 60 years). In 12 cases the original primary was not known and by use of a panel of immunohistochemical stains the most likely primary site was identified in 10 of these cases. In two cases the patients had 2 separate known primaries. Breast cancer was the most common primary closely followed by lung. (Chart 1)

Chart 1 Site of primary cancer

<table>
<thead>
<tr>
<th>Primary Site</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>15</td>
</tr>
<tr>
<td>Lung</td>
<td>13</td>
</tr>
<tr>
<td>Colorectal</td>
<td>03</td>
</tr>
<tr>
<td>Stomach</td>
<td>02</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>02</td>
</tr>
<tr>
<td>GI Tract</td>
<td>02</td>
</tr>
<tr>
<td>Kidney</td>
<td>02</td>
</tr>
<tr>
<td>Bladder</td>
<td>01</td>
</tr>
<tr>
<td>Unknown</td>
<td>02</td>
</tr>
</tbody>
</table>

A total of 16 different immuno stains were used and were tailored for sex and previous diagnosis.

In conclusion a variety of distant metastasis of cancer are treated by surgical removal and the neuropathologist has a role in confirming the diagnosis and also identifying the site of primary when clinically not known.
A Meningeal-Based Neural Epithelioid Fibroblastic Tumour; a Neoplasm Related to Solitary Fibrous Tumour and Showing Neuroblastic Transformation

TS Bracey, DA Hilton, S Wharton, MEF Smith

This article describes a meningeal-based tumour with fibroblastic and epithelioid elements, arising in the anterior cranial fossa. The tumour cells were positive for CD34 and bcl-2, and negative for EMA, an immunophenotype suggesting relationship to solitary fibrous tumour, and effectively excluding meningioma. The tumour subsequently recurred at the same site, with more aggressive clinical course, invaded into the nasopharynx, and resulting in the death of the patient. Histological examination of the recurrent tumour showed a component similar to the previous sampling, admixed with high grade tumour with neuroblastic features consistent with effactory neuroblastoma. The radiological and histological co-localisation of the high grade neuroblastic recurrence raises the possibility of neuroblastic transformation of the original tumour.

Ischaemic fasciitis, unusual location and presentation

A Abedou, M Abd Elwahed

We present a case of ischaemic fascitis in a female patient aged 45 years old with unusual site and history. She presented with a hard infiltrating mass in the anterior axillary fold with a history of modified radical mastectomy and radiation therapy courses. The clinical presentation has led to the assumption that the ischaemia could be induced by previous surgical trauma.

A Large Extraperitoneal Myolipoma

A Merve, M Kamal, N Gul, A Clark

Myolipoma is a rare neoplasm, mostly occurring in adults, with female preponderance. It is characterised by the admixture of mature adipose tissue and smooth muscle tissue in varying proportions; most often the muscular component being predominant. Myolipoma have been described in the round ligament, eyelid, subcutaneous, pericardium, retroperitoneum, rectus sheath and abdominal cavity. In deeply situated tumours it is likely to be confused with a well-differentiated liposarcoma, extrarenal angiomylipoma and leiomyoma with fatty change.

A 44-year-old lady presented with gradual abdominal distension for 15 months. The CT scan raised a suspicion of an ovarian tumour with liposarcoma as a differential diagnosis. She underwent a debulking laparotomy, which surprisingly revealed a well-demarcated large extraperitoneal mass measuring 24x24x10cm, weighing 2.7kg and extending between the urinary bladder and the epigastrium. This partly cystic and partly solid mass was completely excised. The pelvic organs including the ovaries were normal.

Histologically, the tumour was encapsulated, composing of smooth muscle elements with rather oedematous and myxoid areas together with islands of inactive adipose connective tissue. The blood vessels within the tumour were not predominant. No mitotic activity was seen. A diagnosis of myolipoma was made. Immunohistochemistry revealed a positive staining for ER, PR, desmin and smooth muscle actin.

Myolipoma may be clinically or radiologically mistaken as a malignant lesion. Myolipoma is a benign tumour with good prognosis and pathologists should consider it in the differential diagnosis of fat-containing extraperitoneal masses. These tumours may show positive staining for ER and PR.

Case Report - Intra-abdominal Ossification

SS Roberts, AG Douglas-Jones

We present a case of a 76 year old man admitted for the surgical repair of an abdominal aortic aneurysm (AAA). Post-operatively he required six laparotomies; day 6: adhesiolysis for small bowel obstruction; day 11: abscess drainage secondary to pancreatitis; days 31 and 35: unexplained bleeding; day 52: two enterocolonic fistulae; day 162: closure of abdominal wound and fistulae. At wound closure hard, calcified deposits were found in the omentum and on the peritoneum of the anterior abdominal wall. These were sent for pathological examination.

Macroscopically, six solid, white nodules, labelled omentum, were sent together with two pale, brown peritoneal nodules. Histologically, the omental specimen actually contained skin with underlying scar tissue, foreign body granulomas and a 5mm focus of ossification with bone marrow elements. The peritoneal nodules contained cancellous bone with bone marrow elements. Intra-abdominal ossification is an unusual finding. Mature bone with haemopoietic elements present within the small bowel mesentry has been described as heterotopic mesenteric ossification (HMO), typically occurring after AAA repair. Mesenteric lesions were lacking in this case, however some reports include omental lesions as HMO. Heterotopic bone formation has been described in abdominal wounds; a strong possibility given the number of laparotomies performed. The most important differential is with an extraperitoneal osteosarcoma. Given the lack of cellularity and pleomorphism, this is unlikely.

The role of acute pancreatitis in this case is uncertain. Although saponification of fat with calcium deposition is well known, ossification with haematopoiesis has not been described.
Ossifying Fibromyxoid Tumour of the Parapharynx: A Case Report of a Rare Tumour at an Unusual Site

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Ossifying fibromyxoid tumour of soft tissue (OMFT) is a rare tumour that typically occurs in the extremities of adults with cases located in the head and neck being recognised as unusual.

We describe a case of OMFT of the parapharyngeal space in a 53-year-old female that initially presented as a lump in the right cheek. The tumour was resected and histopathological examination showed bland cells with ovoid nuclei in a fibromyxoid stroma and a focus of central ossification. Mitotic activity was absent (0 per 50 hpf). Immunohistochemistry was focally positive for S100 and CD68 but was negative for epithelial, vascular, smooth muscle and other neural markers. Cytogenetic analysis of the tumour using fluorescent in-situ hybridisation found no rearrangement of FUS [associated with a t(7;16) translocation], excluding the diagnosis of low-grade fibromyxoid sarcoma.

A diagnosis of OMFT was made. Because of the low nuclear grade, low cellularity and absent mitotic activity, the tumour was graded as a benign typical OMFT.

Localised Crush Injury to the Cricoid Cartilage: Vital Evidence Requiring a Meticulous Autopsy for Recognition

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Fractures of the cricoid cartilage are uncommon but when present, they are almost always indicative of significant violence to the neck. Injury usually occurs when the structure is crushed by antero-posterior force, such as a blow with the edge of the hand, a kick or forceful compression. We present a case of an elderly male, found dead after a four week post-mortem interval, where the identification of cricoid trauma was critical in establishing the nature of the death. Examination of the neck structures revealed fractures of the thyroid cartilage and vertical, paramedian, undisplaced fractures of the cricoid cartilage. Subtle associated bruising was revealed only on reflection of the cricothyroid muscles. A transverse cut, inferior to the cricoid cartilage in the fixed laryngeal specimen, revealed localised bruising that was otherwise not visible. Histological examination of the cricoid cartilage revealed five cartilaginous fractures, with a well-preserved haemorrhagic and fibrinous reaction, despite the post-mortem interval. Fractures to the cricoid cartilage may be easily overlooked at autopsy, particularly if the associated bruising is not great. This case highlights the need for meticulous identification and histological sampling of neck injuries in order to provide maximum forensic evidence, especially where subtle findings may be obscured by decompositional change.

Disseminated sarcoidosis and cardiac involvement: report of a post-mortem case

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A 46 year old lady with disseminated sarcoidosis died of cardiorespiratory arrest in the hospital. At autopsy there was serious pleural (2000mls each side) effusion and pericardial adhesions. There was no significant cardiomegaly (weight 263grams) and both atrial and ventricular wall thicknesses were within normal limits (15mm and 3mm respectively). On slicing there were focal areas of ill-defined scarring in the myocardium. The coronary arteries and valves were normal. There was no lymphadenopathy or organomegaly.

Histology of the lungs confirmed the established diagnosis of sarcoidosis by presence of multiple non-caseating granulomata. The areas of scarring within the myocardium showed fibrosis and non-caseating granulomata. Sarcoideal sarcoidosis is a multisystemic disease with an unclear aetiology. Direct cardiac involvement is seen in 20 to 27% of post-mortem cases of sarcoidosis. Cardiac sarcoidosis is mostly identified by impaired systolic left ventricular (LV) function, a feature of more advanced disease. Once symptomatic cardiac sarcoidosis develops in pulmonary sarcoidosis patients, the prognosis becomes very grim. In contrast, the prognosis in asymptomatic cardiac involvement in pulmonary sarcoidosis patients is good. In patients with sarcoidosis regular screening for cardiac involvement with regular methods is advised.

Audit of Post-Mortem Histology

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1Pembury Hospital, Maidstone and Tunbridge Wells NHS Trust

The 2006 NCEPOD report on the coroner’s autopsy raised concerns regarding the frequency of tissue sampling for histopathological assessment. We reviewed our current practice with regard to histological sampling in coronial autopsies.

The Royal College of pathologists’ guidelines recommend the sampling of all major organs in all autopsies. However, with the constraints which exist between the coronial system and pathologists we felt a standard of 100% unrealistic. The frequency of histopathological sampling in the NCEPOD report was 19% (baseline for early 2005) however the advisers raised concerns that this was not enough, therefore a standard of 19% could be considered too low.

As a compromise we chose a standard of 30% for this audit.

We also looked at the following questions: How do we word the preliminary report when histology is pending? Which cases do we take histology from? How often does the histology confirm the macroscopic appearances? How often does the histology bring a new unexpected pathology to light that was relevant to the cause of death? What disposal options are relatives choosing for handling retained tissues? How do we document tissue retention, consent and arrangements for disposal? Results & Conclusion: We sampled tissue for histology in 6% of cases and so did not meet the standard for this audit of 30%. Do we consider this enough bearing in mind the constraints? As a result of this audit we will be reviewing our criteria for selecting cases for histopathological assessment.
Sudden Death in Undiagnosed Graves' Disease
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A 54 year old lady was admitted to A&E with sudden breathlessness. She had tachycardia at rest and bilateral proptosis. Investigations revealed supraventricular tachycardia and cardiomegaly. The findings suggested thyrotoxicosis but the patient died before a definite diagnosis could be established. A coroner’s postmortem was ordered.

At autopsy the thyroid showed subtle enlargement. There was a thrombus in the left atrial appendage and an infarct in the right kidney. The lungs were congested and the liver had a mottled appearance. Tissues were sampled for histology. The thyroid showed characteristic features of Graves’ disease. Histology confirmed heart failure cells in the lung and chronic passive congestion in the liver. The A&E blood sample revealed a raised freeT4 confirming thyrotoxicosis. The renal infarct was probably a result of an embolus from the thrombus in the left atrial appendage. Formation and dislodgement of thromboemboli are known to be associated with supraventricular tachycardia. This case highlights some important points. It emphasises the importance of clinical information in order to interpret the autopsy findings in the correct context. It reiterates the value of postmortem histology. This is relevant in the current climate where postmortem histology is becoming increasingly difficult to take. It highlights the opportunity the antemortem A&E blood samples offer to carry out relevant investigations. Finally this was an opportunity to see the characteristic histological features of untreated Graves’ disease. These are rarely seen in surgical pathology specimens because of prior treatment.

Coronary artery thrombosis associated with a ruptured atheromatous plaque and sarcoid granulomas of the vasa vasorum. An autopsy case report
W Al-Qsous1, PAJ Brown1
1Pathology, Aberdeen Royal Infirmary

Sarcoidosis is a multisystem disease of unknown aetiology and approximately 20% of sarcoid patients have involvement of the heart at autopsy. The most involved area is the myocardium and the coronary arteries are only very rarely affected. We present a case of a 63 year old woman who died from acute myocardial infarction as a result of a ruptured atheromatous coronary artery plaque with a superimposed thrombus. An unusual incidental finding was the presence of giant cell granulomas associated with the vasa vasorum of the coronary arteries underlying the ruptured atheromatous plaque. Non-caseating epithelioid granulomas were also seen elsewhere in the coronary arteries and in the lungs and liver. An infectious aetiology was excluded by special stains and culture studies and the appearances were consistent with sarcoidosis. Our unusual case demonstrates involvement of the coronary arteries by sarcoidosis in a case that would appear clinically straightforward. It is speculation whether granulomas associated with vasa vasorum could contribute to plaque instability.

Blake and Rocket Drains, Which is Better in Cardiothoracic Surgery?
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1Leeds Teaching Hospital, 2Castle Hill Hospital

It has been a standard teaching that drainage of the mediastinum is best accomplished using rigid large-bore Rocket drains. Recent trends in cardiothoracic surgery have suggested using Blake drains (thin, flexible, fluted with sideholes). Our aim was to compare Rocket and Blake drains with regards to pain score, amount of pericardial effusion and risk of atrial fibrillation after drains removal.

METHODS
Retrospective audit on 100 patients with major cardiothoracic operations divided into two groups, Group-A (50 patients, Blake drain, Consultant SG) and Group-B (50 patients, Rocket drain, Consultant MC). Measured parameters: amount of pericardial effusion, incidence rate of atrial fibrillation during drains removal and pain-scores with a descriptive scale (1-10) before, during and after drain removal. Statistical analysis was carried out using the Wilcoxon signed ranks test.

RESULTS
Group-A had a median pain score of 2, 6, 2 while Group-B had a median pain score of 3, 8, 4 before, during and after drains removal respectively. This is clinically and statistically significant with p<0.02. The mean effusion drainage was 89ml/day, 92ml/day while the incidence rate of atrial fibrillation was 8%, 12% for Group-A and Group-B respectively.

CONCLUSIONS
Larger chest tubes are not necessarily better when it comes to draining the mediastinum. We believe that Blake system can replace standard chest tubes as it is significantly less painful, associated with less risk of atrial fibrillation and drains the same amount of effusion compared to Rocket drains.
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The effect of inhaled carbon dioxide on constricted airways in an animal model of asthma

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1University of Calgary

The objective of this study was to determine the effects of inhaled CO2 on constricted airways in a rat model of allergic asthma and to determine the mechanism of CO2-induced bronchial smooth muscle relaxation.

An animal model of chronic asthma was developed using Brown Norway rats sensitized and challenged with ovalbumin. Histologic examination of the airways showed most of the features of human asthma. The response to allergen and treatment was monitored using non-invasive whole body plethysmography.

Inhaled CO2 caused a rapid, reversible and dose-dependent relaxation of constricted airways during the late phase of the asthmatic response. The percent drop of the enhanced pause (an index of bronchoconstriction) was 6.9% ± 5.29, 15.8% ± 5.83, 43.7% ± 6.37 and 68.5% ± 11.1 (mean ± SE) with 2%, 5%, 8% and 20% CO2 respectively. Arterial blood gases during the late phase response in ovalbumin-challenged rats showed a significant increase in PaCO2, decreased arterial blood pH and decreased PaO2 compared with saline challenged rats.

CO2 caused rapid dose-dependent relaxation of constricted airways in an allergic model of asthma. Our results suggest that CO2 is a bronchial smooth muscle relaxant and support the notion that hypocapnia (low PCO2) seen in some asthmatics may play a role in the pathogenesis of their asthma.

P128

Frequency and significance of atypical histological features in pulmonary inflammatory myofibroblastic tumours

N Etessami1, M Dusmet De Smours1, P Goldstraw1, K Thway2, C Fisher2, A Nicholson1
1Royal Brompton Hospital, London, 2Royal Marsden Hospital, London

Inflammatory myofibroblastic tumour (IMT) is a rare mesenchymal neoplasm which may present in many organs including lung. Tumour behaviour is unpredictable although the WHO states ‘intermediate biological potential’. However, some pulmonary cases are still being classified as inflammatory pseudotumour (IPT), a term that likely includes varying reactive mass lesions with similar morphology, confounding prognostic data. Furthermore, within IMTs overall, atypical features (high cellularity, rounded/large polygonal cells, abundant ganglion-like cells, necrosis and giant cells) and lack of ALK-1 expression have recently been suggested to be associated with more aggressive behaviour.

We have retrospectively reviewed 38 cases reported as IPT, plasma cell granuloma or IMT between 1992 and 2008. Of these, 24 cases were classified as lesions other than IMT. In the remaining 14 cases, ages ranged from 5 to 70 years with 8 females. Tumour sizes ranged between 11-110mm. All lesions showed ill-defined borders, with 8/14 showing extrapulmonary spread into either chest wall or mediastinal structures. 9/14 cases show atypical features, two with extrapulmonary extension.

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Secondary vascular changes in pulmonary sequestrations

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1Royal Brompton Hospital

Pulmonary sequestrations, both intralobar and extralobar, are localised lesions comprising lung parenchyma receiving their blood supply via aberrant systemic arteries and lacking continuity with the upper respiratory tract. This study retrospectively reviews parenchymal changes within 27 resected cases, in particular concentrating on secondary vascular changes. All 27 cases (1982-2008) had H&E and EVG stains for review. There were 11 females and 16 males, with an age range of 2 months to 60 years (average = 13 years). There were 22 cases with intralobar and 5 cases with extralobar sequestration. A specific feeding vessel was identified in all but one extralobar case. 15 of 27 cases showed intimal fibrosis and/or medial hypertrophy characteristic of plexogenic changes in the pulmonary vasculature with additional plexiform changes seen in 6 cases. Vascular changes such as medial hypertrophy were also seen within otherwise normal lung adjacent to the mass lesions in 42 intralobar cases. In addition, one case each of dissection of systemic vessels and lymphangiomatosis were seen, both in extrapulmonary lesions. In terms of the parenchyma within the sequestrations, 17 showed features of type 2 congenital cystic adenomatoid lesions. Marked hypertensive vascular changes may be seen within the pulmonary vessels in sequestrations with lesser changes more rarely seen in adjacent lung, likely due to prolonged increased pressure from the systemic blood supply. In addition, dissection and coexistent lymphangiomatosis are reported in these lesions.

P130

Automated Scoring of Tissue Microarrays using Virtual Slides

A Wright1, D Magee1, P Quirke1, D Treanor1
1Pathology and Tumour Biology, Leeds Institute of Molecular Medicine, University of Leeds, 1School of Computing, University of Leeds

Inhaled CO2 caused a rapid, reversible and dose-dependent relaxation of constricted airways during the late phase of the asthmatic response. The percent drop of the enhanced pause (an index of bronchoconstriction) was 6.9% ± 5.29, 15.8% ± 5.83, 43.7% ± 6.37 and 68.5% ± 11.1 (mean ± SE) with 2%, 5%, 8% and 20% CO2 respectively. Arterial blood gases during the late phase response in ovalbumin-challenged rats showed a significant increase in PaCO2, decreased arterial blood pH and decreased PaO2 compared with saline challenged rats.

CO2 caused rapid dose-dependent relaxation of constricted airways in an allergic model of asthma. Our results suggest that CO2 is a bronchial smooth muscle relaxant and support the notion that hypocapnia (low PCO2) seen in some asthmatics may play a role in the pathogenesis of their asthma.

Tissue microarrays (TMAs) are a widely used tool in medical research to rapidly compare protein expression across hundreds of samples. However scoring tissue microarrays with a conventional microscope is a laborious task which is prone to error. Virtual slides are an excellent tool for capturing TMA images for later analysis as they allow manual scoring of TMAs at a computer console. Furthermore they introduce the possibility of rapid automatic scoring of entire tissue microarrays using image analysis. We describe a system developed to automatically score immunohistochemical staining on tissue microarrays with virtual slides.

The system analyses the slide at low resolution to identify cores (and identifies damaged or missing cores). It then analyses each core individually to calculate the amount of positive staining in the tissue. The results are presented to the user together with the virtual slide image of the cores for quality control and further study. This system has been used to score a TMA series of over 3,000 cores in less than 24 hours, significantly faster than a human scorer would be able to achieve.

In the remaining 14 cases, ages ranged from 5 to 70 years with 8 females. Tumour sizes ranged between 11-110mm. All lesions showed ill-defined borders, with 8/14 showing extrapulmonary spread into either chest wall or mediastinal structures. 9/14 cases show atypical features, two with extrapulmonary extension.

P128

Frequency and significance of atypical histological features in pulmonary inflammatory myofibroblastic tumours

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Inflammatory myofibroblastic tumour (IMT) is a rare mesenchymal neoplasm which may present in many organs including lung. Tumour behaviour is unpredictable although the WHO states ‘intermediate biological potential’. However, some pulmonary cases are still being classified as inflammatory pseudotumour (IPT), a term that likely includes varying reactive mass lesions with similar morphology, confounding prognostic data. Furthermore, within IMTs overall, atypical features (high cellularity, rounded/large polygonal cells, abundant ganglion-like cells, necrosis and giant cells) and lack of ALK-1 expression have recently been suggested to be associated with more aggressive behaviour.

We have retrospectively reviewed 38 cases reported as IPT, plasma cell granuloma or IMT between 1992 and 2008. Of these, 24 cases were classified as lesions other than IMT. In the remaining 14 cases, ages ranged from 5 to 70 years with 8 females. Tumour sizes ranged between 11-110mm. All lesions showed ill-defined borders, with 8/14 showing extrapulmonary spread into either chest wall or mediastinal structures. 9/14 cases show atypical features, two with extrapulmonary extension.

P129

Secondary vascular changes in pulmonary sequestrations

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Pulmonary sequestrations, both intralobar and extralobar, are localised lesions comprising lung parenchyma receiving their blood supply via aberrant systemic arteries and lacking continuity with the upper respiratory tract. This study retrospectively reviews parenchymal changes within 27 resected cases, in particular concentrating on secondary vascular changes. All 27 cases (1982-2008) had H&E and EVG stains for review. There were 11 females and 16 males, with an age range of 2 months to 60 years (average = 13 years). There were 22 cases with intralobar and 5 cases with extralobar sequestration. A specific feeding vessel was identified in all but one extralobar case. 15 of 27 cases showed intimal fibrosis and/or medial hypertrophy characteristic of plexogenic changes in the pulmonary vasculature with additional plexiform changes seen in 6 cases. Vascular changes such as medial hypertrophy were also seen within otherwise normal lung adjacent to the mass lesions in 42 intralobar cases. In addition, one case each of dissection of systemic vessels and lymphangiomatosis were seen, both in extrapulmonary lesions. In terms of the parenchyma within the sequestrations, 17 showed features of type 2 congenital cystic adenomatoid lesions. Marked hypertensive vascular changes may be seen within the pulmonary vessels in sequestrations with lesser changes more rarely seen in adjacent lung, likely due to prolonged increased pressure from the systemic blood supply. In addition, dissection and coexistent lymphangiomatosis are reported in these lesions.

P130

Automated Scoring of Tissue Microarrays using Virtual Slides

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Tissue microarrays (TMAs) are a widely used tool in medical research to rapidly compare protein expression across hundreds of samples. However scoring tissue microarrays with a conventional microscope is a laborious task which is prone to error. Virtual slides are an excellent tool for capturing TMA images for later analysis as they allow manual scoring of TMAs at a computer console. Furthermore they introduce the possibility of rapid automatic scoring of entire tissue microarrays using image analysis. We describe a system developed to automatically score immunohistochemical staining on tissue microarrays with virtual slides.

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P131

Immunophenotype of Ductal Carcinoma in Situ in BRCA Germine Mutation Carriers

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1University Medical Centre Utrecht, *Dept of Pathology and #Division of Internal Medicine and Dermatology, The Netherlands

Background: Germline BRCA1 related breast cancers have a distinct characteristic phenotype is already present in the pre-invasive stage.

Material and Methods: DCIS of 6 proven BRCA1 and 4 BRCA2 germine mutation carriers were stained by immunohistochemistry for ER, PR, HER-2/neu, CK5/6 CK14, EGFR and Ki67.

Results: 4/11 cases (36%) were ER positive, 0/7 (0%) were PR positive, 0/10 (0%) were HER2 positive, 5/10 (50%) were CK5/6 positive, 1/9 (11%) were CK14 positive, and 6/10 (60%) were EGFR positive. Mean percentage Ki67 were HER2 positive, 5/10 (50%) were CK5/6 positive, 1/9 (11%) were CK14 positive, and 6/10 (60%) were EGFR positive. Mean percentage Ki67 nuclear staining was 30% (range 0-100). These percentages are similar to those that have been reported for invasive cancers in BRCA1/2 mutation carriers, except for ER that is generally even lower in BRCA1/2 related cancers.

Discussion: DCIS in BRCA1/2 germine mutation carriers shows a so called basal immunophenotype with high proliferation and EGFR positivity similar to that of invasive cancers in such patients. This may be useful to identify “BRCA-ness” in cases of DCIS in diagnostic pathology, and opens up new ways for targeted therapy against EGFR to prevent development of invasive cancer in case of a germine mutation.

P132

Hypoxia-Inducible Factor 1a is Essential for Hypoxic p27 Induction in Endometrioid Endometrial Carcinoma

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1University Medical Centre Utrecht, *Departments of Pathology and #Surgical Gynaecology and Oncology, The Netherlands

Hypoxia-inducible factor 1a (HIF-1α) plays an essential role in the cellular adaptive hypoxia response. The cyclin-dependent kinase inhibitor p27(Kip1) is highly expressed in the normal endometrium but is lost during endometrial carcinogenesis. However, in high-grade cancers, p27 re-expression is observed. We analysed the role of HIF-1α in hypoxia-induced expression of p27 in endometrial cancer. Paraffin-embedded specimens from 39 endometrioid endometrial carcinomas were immunohistochemically stained for HIF-1α, p27, and Ki67. HEC1B, an endometrial carcinoma cell line, was cultured under normoxic or hypoxic conditions in the presence or absence of transiently expressed shRNAs targeting HIF-1α. Protein expression of p27 and HIF-1α was assessed by western blotting. Immunohistochemical staining revealed perinuclear HIF-1α expression in 67% of the cases and p27 staining centrally in the tumour islands, mostly around necrosis, in 46% of the cases. In 50% of the tumours with perinuclear HIF-1α expression, p27 and HIF-1α perinuclear/central co-localization was observed. Hypoxia-associated p27 expression showed less proliferation around necrosis. In HECIB, p27 protein expression was induced by hypoxia. This induction was abrogated by transient knockdown of HIF-1α using RNAi. Furthermore, hypoxia induced cell cycle arrest in HEC1B cells. We conclude that, in endometrioid endometrial carcinoma, p27 re-expression by hypoxia is HIF-1α-dependent and leads to cell cycle arrest. This may contribute to the survival of cancer cells in hypoxic parts of the tumour.

P133

Perinecrotic HIF-1α Expression and Necrosis Predict Prognosis in Patients with Endometrioid Endometrial Carcinoma

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Background. Hypoxia-inducible factor 1α (HIF-1α) plays an essential role in the adaptive response of cells to hypoxia, triggering biologic events associated with aggressive tumour behaviour. Hypoxia and its key regulator HIF-1α play an important role in endometrial carcinogenesis, but contradictory results have been published as to the prognostic value of HIF-1α expression in endometrial carcinoma. We therefore re-evaluated the prognostic value of HIF-1α expression in a large representative group of endometrioid endometrial cancer using well-established methodology.

Methods. In 98 patients with endometrioid endometrial cancer, expression levels of HIF-1α and p27 were analyzed by immunohistochemistry. Presence of necrosis, and type of HIF-1α expression (perinuclear, diffuse, or mixed) were noted.

Results. Stage, grade and depth of invasion showed prognostic value as expected. Indicators of poor prognosis were presence of necrosis (p=0.05) and perinuclear type of HIF-1α expression (p=0.03). In patients with perinuclear type of HIF-1α expression, high p27 expression was an additional prognostic factor. In Cox regression, HIF-1α was an additional prognostic factor to stage. Conclusion. In patients with endometrioid endometrial cancer, necrosis and necrosis related expression of HIF-1α are important prognostic factors. In view of the proposed role of hypoxia and HIF-1α in endometrial cancer, HIF-1α is thereby an attractive therapeutic target.

P134

Nitric oxide down-regulates expression of the haemoglobin-haptoglobin scavenger receptor (CD163) on human monocyte / macrophages

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Nitric oxide (NO) mediates many effects on immune system function. Although exaggerated NO production is well-characterised in many pathological states, it’s effect on the expression and function of the haemoglobin-haptoglobin scavenger receptor (CD163) is unknown.

Human monocytes were isolated by density centrifugation and subsequently exposed in 18-24 hour cultures to the NO generator DETA-NONOate. Co-incubation with factors known to promote CD163 expression was also performed. Metalloproteinase inhibitors were utilised to assess shedding as possible regulatory mechanism. CD163 expression was quantified by flow cytometry with supernatant soluble CD163 concentrations determined by ELISA. Post-incubatory cell viability was confirmed by metabolic capacity and CD14 expression. CD163 expression was also evaluated following exposure to the guanylate cyclase activator 8-Bromo-cGMP.

Nitric oxide downregulated monocyte CD163 expression by upto 70% at maximal concentrations. Similar attenuation was observed following co-exposure to both NO and interleukin-10 or dexamethasone. CD163 expression was downregulated by 24% through NO exposure following super-induction of CD163 expression by co-incubation with IL-10 and dexamethasone. Nitric oxide had no effect on cell viability but did induce a reduction in soluble CD163 detected in the culture supernatants relative to controls, thus excluding shedding as a downregulatory mechanism. The guanylate cyclase activator, 8-Br-cGMP, also induced downregulation of CD163, indicating a possible role of guanylyl cyclase in the downregulatory process.

This study has established a role of nitric oxide in regulating expression of CD163, possibly through activation of guanylate cyclase.
**P135**

Clinical significance of miR-21 and miR-145 expression in Colorectal Cancer

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Colorectal cancer (CRC) is the third most common cancer worldwide. The pathogenesis of CRC may involve aberrant expression of microRNA's (miRNAs) which are endogenously expressed short non-coding ~23nt regulatory RNAs that control the translation of many genes. Previous studies have shown that several miRNAs have altered expression in CRC including miR21 and miR145. In this study, the expression of these two miRNAs was quantified relative to 18s rRNA by real time RT-PCR in primary CRC. Total RNA was extracted from paraffin embedded formalin fixed sections of 30 primary CRCs, their flanking non-tumour tissues and 6 cases of adenoma by manual microdissection. The relative level of expression of both miRNAs was correlated to clinicopathological features including; tumour size, Duke's stage, differentiation and lymph node metastasis. miR21 and miR145 were significantly over-expressed in tumours; miR21 (p=0.001) and miR145 (p=0.004). Both microRNAs also showed a significant association with Duke's stage, miR21 (p=0.018) and miR145 (p=0.029), and lymph node metastasis, miR21 (p=0.017) and miR145 (p=0.029). Adenomas showed higher expression of miR21 than normal tissue suggesting that miR21 amplification is an early event in cancer development. Recent studies have shown that miR21 targets important tumour suppressor genes including Pdcd4, tropomyosin1, Pten and maspain thus increasing the ability of the cancer to invade. The target for miR145 is currently not known. Our results support the view that miR21 and miR145 may have a role in the pathogenesis of CRC.

**P136**

CSMD1, a novel tumour suppressor gene in breast cancer

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We have identified a large candidate tumour suppressor gene with CUB and sushi domains (CSMD1) on chromosome 8p23, a region frequently deleted in many tumours including 50% of breast cancers. CSMD1 has homologies to proteins implicated in cancer and cell adhesion. We studied CSMD1 expression in breast cancer samples (n = 50) by immunohistochemistry. CSMD1 was silenced using siRNA to investigate the biological consequences of reduced CSMD1 expression in 4 breast cancer cell lines. Down regulation of CSMD1 expression was identified in 26/52 (50%) of breast cancers. Down regulation of CSMD1 expression was more frequent in ducal cancers (P < 0.05) and in poorly differentiated tumours (P < 0.0007). Similarly CSMD1 expression was less frequent in large tumours compared to small tumours. Reduced CSMD1 expression in the cell lines BT20 and T47D decreased adhesion to fibronectin and/or vitronectin. No change was detected in either the proliferation or the invasiveness of these cells. However, there was a 15% increase in the proliferation of the benign MCF-10A cells, while the invasive MDA-MB-435 cells showed little change. We conclude that CSMD1 is an adhesion molecule due to its protein domain homology, cell surface localization and effect on adhesion. Moreover, like integrins, CSMD1 has the ability to influence cell proliferation.

**P137**

Expression array analysis of RPL19 gene silencing in prostate cancer

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¹University of Liverpool

Expression Array Analysis of RPL19 Gene Silencing in Prostate Cancer. Ribosomal protein-19 (RPL19) mRNA is differentially expressed in benign and malignant prostatic cell lines and tissues. In-situ hybridization confirmed it to be a powerful biomarker of prostatic malignancy and as accurate as Gleason score in predicting patient outcome. As part of the ribosomal protein complex, RPL19 modulates the synthesis of cellular proteins, hence contributing to the malignant phenotype. RNAi silencing directed against exon 11 of RPL19 variant “c” inhibited expression of the gene in PC3M prostate cancer cells. Exon 11 was chosen as the target for suppression since it is in seven of eight potential RPL19 splice variants. Stable RPL19-silenced transfectants were constructed and cloned. Quantitative PCR of the transfectants confirmed a 70% reduction in expression in the malignant cells to levels at, or below, those of benign prostatic PNT2 cells. Transfected RPL19 cells remained viable but were less adhesive than their parental cells. Invasion and collagen assay assays were performed on the RPL19 silenced clones. Transfected RPL19 RNA expression was analysed by two-colour Human Genome DNA Expression Microarray (Agilent Technologies) against control PC3M cells. GO term enrichment analysis was performed separately with lists of significantly up- and down-regulated genes to identify significant functional terms. RPL19 suppression in malignant PC3M cells had greatest effect on depleting the expression of groups of genes within pathways, particularly collagenases and the Rho pathway, indicating possible genetic mechanisms responsible for prostate cancer dissemination and metastasis.

**P138**

Expression array analysis of RPL19 gene silencing in prostate cancer

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Expression Array Analysis of RPL19 Gene Silencing in Prostate Cancer. Ribosomal protein-19 (RPL19) mRNA is differentially expressed in benign and malignant prostatic cell lines and tissues. In-situ hybridization confirmed it to be a powerful biomarker of prostatic malignancy and as accurate as Gleason score in predicting patient outcome. As part of the ribosomal protein complex, RPL19 modulates the synthesis of cellular proteins, hence contributing to the malignant phenotype. RNAi silencing directed against exon 11 of RPL19 variant “c” inhibited expression of the gene in PC3M prostate cancer cells. Exon 11 was chosen as the target for suppression since it is in seven of eight potential RPL19 splice variants. Stable RPL19-silenced transfectants were constructed and cloned. Quantitative PCR of the transfectants confirmed a 70% reduction in expression in the malignant cells to levels at, or below, those of benign prostatic PNT2 cells. Transfected RPL19 cells remained viable but were less adhesive than their parental cells. Invasion and collagen assay assays were performed on the RPL19 silenced clones. Transfected RPL19 RNA expression was analysed by two-colour Human Genome DNA Expression Microarray (Agilent Technologies) against control PC3M cells. GO term enrichment analysis was performed separately with lists of significantly up- and down-regulated genes to identify significant functional terms. RPL19 suppression in malignant PC3M cells had greatest effect on depleting the expression of groups of genes within pathways, particularly collagenases and the Rho pathway, indicating possible genetic mechanisms responsible for prostate cancer dissemination and metastasis.
P139
Expression of Pim Kinases in Non-Hodgkin’s Lymphomas: Evidence For a Role in the Inactivation of Wild Type p53
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1 Ninewells Hospital and Medical School

Two murine models of cancer development are associated with a striking propensity to develop lymphomas. Homozygous deletion of the p53 gene in mice is associated with an increased risk of developing lymphoma and in another murine model it has been shown that overexpression of the Pim-1 kinase is associated with development of lymphomas of B and T cell type.

However, inactivating mutation of the p53 gene is uncommon in cases of lymphoma in man, despite p53 mutation being a frequent molecular event in the pathogenesis of many other forms of malignant disease. Inactivation of p53 may be achieved by other means, for example through interaction with cellular proteins such as MDM2, the activity of which has been found to be enhanced in the presence of Pim-1. Pim-1 overexpression and consequent increase in MDM2 activity and/or levels could provide an alternative mechanism of p53 inactivation and therefore reconcile the experimental and clinical data with regard to the role of p53 in the pathogenesis of lymphoma. In this study immunohistochemical analysis of a series of 35 mantle cell lymphomas found Pim-1 expression to be elevated in 46% of cases. In addition there was a significant association between Pim kinase overexpression and elevated levels of MDM2 (p = 0.0031), which would support the theory that Pim may play a role in the inactivation of p53 through MDM2 activation.

P141
The Value of the Black Box Meeting
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1 University College London Hospital

The “black box” meeting is a common training tool in histopathology departments. Trainees view pre-selected cases, getting a chance to see rarer entities and broaden their diagnostic experience. Despite its widespread use there is little literature on the content and overall relevance of these meetings.

We have audited the black box meetings held in our teaching hospital department between November 2005 and November 2007, with the aim of quantifying the contribution that the meetings make to SpR training. Over the audit period we recorded the number of meetings, the number of cases presented per meeting and the diagnosis and speciality of each case. The gold standard was set at one meeting per week, at least four cases per meeting, and for all specialities listed in the RCPath curriculum for specialist training in histopathology 2007 to be represented.

There were 65 meetings (0.6 per week) with 242 cases (3.7 per meeting) over 2 years. The number of meetings and cases per meeting declined in the second year. All the specialities in the curriculum were represented. Gastrointestinal (19%) and skin cases (16%) were the most frequent. Malignant tumours were the commonest diagnostic category (40%) followed by non-tumour pathology (31%). The most frequent individual case type was malignant melanoma.

We concluded that the black box does make a significant contribution to SpR training and provides a sufficiently wide range of specialities. Following this audit the department has implemented measures to counteract the declining frequency of meetings.

P140
National E-learning Survey Among Histopathology ST1 Trainees
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Electronic learning or e-learning is an all-encompassing term to describe learning supported by the use of information and communication technology. Some emerging e-learning projects in pathology are already delivering high-quality learning solutions on a national scale, and are driving up standards by providing greater consistency and reliability in terms of quality learning and experience. The RCPath is hoping to work with DfI to develop a comprehensive e-learning training application along the lines of that already developed for radiology.

On behalf of the Histopathology training school board a survey was carried out among the ST1 trainees in the histopathology in the UK. The survey mainly focused on the views of the trainees on Histopathnet (the current ST1 e-learning resource) and the upcoming RCPath developments in e-learning.

Responses were received from 51/84 (61%) trainees. 57% of trainees used on-line education facilities on a daily basis, with a further 24% weekly. 82% reported on-line study was mainly at the workplace. Popular sites included Histopathnet and RCPath. Online facilities were used mostly for literature reviews, case reviews and text book access. 84% rated computer facilities at the workplace as excellent or satisfactory. Within Histopathnet, the ‘Cases’ section was most popular with 69% rating this excellent or satisfactory. There was support (75%) for development of virtual microscopy images to within the RCPath development.

ST1 trainees are clearly IT literate and actively using e-learning resources. This should encourage the further development of high quality resources.

P142
Lymph node yields in colorectal cancer – pathologists, patients or procedures?
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Variations in lymph node yields in colorectal cancer might be dependent on pathologists, patients or surgical procedure. Low yields could reflect diligence in finding small lymph nodes. This audit, therefore, assesses lymph node numbers and size in relation to grade of pathologist, patient age and surgical procedure. One hundred consecutive colorectal cancer resections were identified. Cases having neo-adjuvant treatment, concomitant inflammatory bowel disease or synchronous tumours were excluded leaving 81 cases. Small lymph nodes were defined as <5mm diameter. Mean (median) yield for trainees was 16.6 (15.0) and for consultants 14.2 (14.0). Mean (median) proportion of small lymph nodes was 74.0% (77.4%) for trainees and 72.7% (75.0%) for consultants. Mean (median) yields for procedures were: anterior resection 13.9 (13.5); right hemicolectomy 13.3 (14.4); sigmoid colectomy 14.6 (14.5). Mean (median) yields by age were: up to 60 years 17.6 (17); 61-70 years 16.4 (13); 71-80 years 15.8 (15); 81+ years 11.5 (11.5). Mean (median) proportion of small lymph nodes by age was: up to 60 years 68.1% (70.0%); 61-70 years 64.4% (68.0%); 71-80 years 70.6% (73.3%); 81+ years 89.4% (92.9%). These results suggest that older patients have fewer and smaller lymph nodes and this should be taken into account when comparing lymph node yields for different pathologists.
**P143**

**Streamed Internet Video for Pathology Research and Education: The Pathology Video Journal www.PathLab.org**

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Introduction: The amount of internet information available in video format is expanding rapidly. Most content is not peer reviewed or assessed for quality or veracity. No other pathology website currently publishes in pure video format.

Methods: User generated content is submitted to the website moderator/editor and assessed with direct feedback to the author requesting video edits, or amendments. After approval by the website editor/peer reviewer each video clip has a written abstract posted on the website which can then be retrieved by searching Google. The video clip is uploaded onto the Google Video server.

Results: The 5 videos posted have already received a total of 468 viewings and 81 downloads with very positive user feedback. A single hour-long video describing how to take a FNA received 358 viewings and 76 downloads. www.PathLab.org is now hyperlinked to RCSEngland, BSCC and BASO websites as the FNA video is also of interest to surgeons and radiologists.

Discussion: Internet video-on-demand will be an increasingly important means of teaching and training in biomedicine and science, particularly when describing a practical technique which is complex, difficult to apply or to replicate, and which would traditionally be taught ‘hands-on’ in the laboratory or clinic or by tutorials or seminars involving small groups of students or other professionals. Caveats include suitability for public display, patient informed consent, and a requirement to limit access via password protection for certain video footage.

**P144**

**Prostate biopsy workload: are Histopathologists working harder?**

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1University Hospitals of Leicester

**Background:** Extended prostate biopsy strategies have been shown to enhance diagnostic sensitivity for malignancy, compared with the classical sextant approach, and have been incorporated into current guidelines for biopsy sampling. Few studies to date have examined the workload implications of these changes in biopsy practice on Histopathology services.

**Materials and Methods:** All needle core prostate biopsies submitted for histological examination to Leicester University Hospitals NHS Trust over a ten-year period from Jan 1998 - Dec 2007 were identified from the APEX computer system, using standard SNOMED codes. Chi-square and linear regression analyses were performed to examine temporal trends in study variables.

**Results:** Results of preliminary analyses demonstrate positive linear trends in number of biopsies reported (+272%; P < 0.001), paraffin blocks per case (+46%; P < 0.001) and mean cores per case (+63%; P < 0.001). The malignant diagnosis rate has shown no significant change over this time.

**Conclusions:** Prostate biopsy workload for the Histopathologist (total number of biopsies, blocks and cores per case, and additional work performed) have all increased significantly over the study period. A substantial proportion of this increase reflects changes in clinical biopsy practice. These trends are likely to have major resource implications for Histopathology services in the future.

**P145**

**Gynecological malignancy referrals within the Yorkshire Cancer Network: An audit of diagnostic discrepancies**

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**Background.** Yorkshire Cancer Network (YCN) Standard Operating Procedures dictate most gynecological malignancies encountered by peripheral Cancer Units should be referred to the Leeds Cancer Centre gynaecological MDT for specialist management. As part of the referral process, histological diagnoses are reviewed by specialist gynecological pathologists to ensure diagnostic integrity. To date, the degree of diagnostic correlation between the pathology departments of the Cancer Units and the Cancer Centre is unknown.

**Methods.** Histopathology reports of 534 gynaecological malignancies of Cancer Unit origin were compared against corresponding review reports issued by the Cancer Centre gynaecology MDT over a 5 year period (2002–2006). Diagnostic discrepancies were classified according to RCP path guidelines: C1–Diagnostic error with major clinical impact, C2–Diagnostic error with minor clinical impact, C3–Diagnostic error with no clinical impact, N–No discrepancies.

Results. Of the 534 reports assessed, 230 (43.1%) contained diagnostic errors. 36 (6.7%) were classified as C1, 71 (13.3%) were classified as C2 and 123 (23%) were classified as C3. Complete agreement was noted in 304 (56.9%) cases. Of the 230 cases with diagnostic errors (C1,2,3), 63% occurred within cases of uterine malignancy (cervix / uterus).

Conclusions. This audit highlights a significant level of diagnostic error within Cancer Unit reporting of gynaecological malignancies. In the majority of such cases, errors were of a minor nature. Only a very small minority of cases revealed errors of potentially major clinical impact. In such cases the need for specialist review of referred gynaecological malignancies remains important for adequate patient care.

**P146**

**Accuracy in Death Certification – An Audit of Current Practice**

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**Background:** Current legislation on death certification in England and Wales requires that a doctor who has attended a deceased person must issue a medical certificate of cause of death (MCCD). Accurate certification of death allows statistical information to be gathered and used for health care monitoring, planning and provision as well as epidemiological research. Advisory notes for doctors are provided in the front of all blank books of death certificates together with an expanded form published by the Office for National Statistic’s Death Certification Advisory Group.

**Aims:** The purpose of this audit was to establish whether death certificates are being completed to a minimally acceptable standard in accordance with published guidelines.

**Methods:** Counterfoils from death certificates completed in a district general hospital over a three month period were analysed retrospectively for completion errors and logical sequencing of cause of death.

**Results and Conclusions:** A total of 306 certificates were completed during this time period. Of these 47% were completed to a minimally acceptable standard in accordance with published advisory notes. This figure increased to 76% if errors due to incomplete information and use of abbreviations were removed since these were felt to be spuriously high due to the use of counterfoils in data gathering. The findings are comparable to those of similar studies.

**Accuracy of death certification may be increased with greater education of junior doctors and greater trust emphasis on following published advisory notes to doctors.**
Patient Understanding of Hospital Pathology Services: A Questionnaire Based Audit

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Pathologists traditionally carry out much of their work behind closed doors and out of the public eye. We aimed to determine the current level of patient understanding of hospital pathology services.

Forty semi-qualitative questionnaires were completed by patients admitted to a hepatology unit between January and March 2008. The study group consisted of 23 males and 17 females with a mean age of 46.6 years (range 16-71 years). 22 patients were admitted for post-transplantation issues, 12 for pre-transplantation liver biopsy and 6 for transplantation. 31 patients had undergone at least one previous tissue biopsy.

80% of respondents had previously heard of a pathologist but only 38% recognised that they analysed their biopsy or explant. 60% thought pathologists were somehow involved in the diagnosis of liver disorders but only 50% thought they could influence treatment. An additional 15% believed that pathologists were only involved in the examination of dead bodies. 13% recognised that disciplines such as haematology and microbiology also fell under ‘pathology services’. When asked to rate the importance in their care, pathologists fared the worst behind surgeons, physicians and radiologists. 95% had no concerns about tissue retention and 78% were happy for their tissue to be used for research purposes.

This study highlights the current lack of patient understanding of hospital pathology services, even in those who have undergone previous tissue biopsies. We believe this re-enforces the need for education and interaction through events such as the forthcoming Royal College of Pathologists’ Pathology Week.

An Audit of Colorectal Cancer Specimens – What is the Best Measure for the Adequate Numbers of Lymph Nodes Examined?

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1Dewsbury & District Hospital

Aim:
To perform an audit on colorectal cancer specimens for the 3 main standards as recommended in the Royal College of Pathologists’ Minimum Dataset, 2nd edition, September 2007.

Methods:
The reports of 120 consecutive colorectal specimens between December 2006 - August 2007 were analysed.

Results:
• frequency of serosal involvement was 26.9% for colonic tumours and 25% for rectal tumours.
• frequency of extramural venous invasion was 26.7%.
• mean number of lymph nodes examined was 12.75.

All of these results are within the range recommended by the Royal College.

Observations:
In regards to the lymph node yield, is the calculation of the mean the best value for assessing adequacy?
Our results showed the range of lymph nodes examined was 0 – 40. the data is positively skewed, with 58.3% of the cases having lymph node numbers less than the mean.
The median may be a better central tendency measurement as it is used for asymmetrically distributed data. In our audit the median was 11.5, the value at which 50% of the cases have lower values.
It may be prudent to calculate the median as well as (or instead of) the mean in future audits, to remove the false assurance that achieving a mean number of lymph nodes above 12 is adequate, when more than half the cases may fall below this value.

Scottish Histopathology Specialty Training Recruitment 2008: Evaluation of Process

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The Scottish Histopathology recruitment process has evolved over three years, offering 8 ST1 posts in 2008. The person specification and application form were developed from templates. The application required factual information and evidence of reflector learning with eligibility criteria and 9 scoring fields.

The forms were scored by 8 paired, trained selectors over one day. The interview was structured in advance, mixing behavioural and scenario questions that assessed understanding of a histopathology report, clinical prioritisation, dealing with an error, interpreting a picture, preparing a presentation and evidence of reflective learning with eligibility criteria and 9 scoring fields.

The reports of 120 consecutive colorectal specimens between December 2006 - August 2007 were analysed.

Reliability of the shortlisting and interview tools was tested (Cronbach’s). An anonymous exit questionnaire was administered to interviewed candidates. Focus groups provided insight to assessors’ views of shortlisting and interview.

The 41 from 88 applicants who scored well at shortlisting were invited to interview. Interview candidates (n = 40) were assessed by two of four panels of two selectors providing 20 “appointable” individuals. Shortlisters’ scores correlated well (0.964, p<0.01). The shortlisting and interview tools were reliable (Cronbach’s alpha 0.859, 0.815). There was no correlation between shortlisting and interview scores (0.158). Candidates were positive about the interviews, considering the process fair, providing opportunities to display relevant attributes. Assessors highlighted shortlisting as better than 2007 and aspired to develop interviews towards a more sophisticated selection centre.

The evidence suggests a successful recruitment episode that has the confidence of assessors and is acceptable to candidates.
The impact of the European working time directives on modern surgical trainees

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Introduction

The European working time directive (EWTD) was introduced to establish minimum safety and health requirements for employment. The effects of EWTD will have on surgeons in training are unknown. The aim of this study was to evaluate the effects of EWTD implementation on the quality of life and training of surgical specialty trainees.

Materials and Methods

Questionnaires were posted to all 250 surgical trainees in Yorkshire. Subjective evaluation of training and theatre exposure in the three months before and the three months after enforcement of the EWTD were investigated, substantiated by objective logbook records. Groups were compared using the Wilcoxon signed rank test.

Results

50 responses were received. 30 trainees (60%) were working more hours than permitted, with 19 claiming to working >6 hours per week extra. EWTD did not appear to affect overall patient management (p=0.423), continuity of care (p=0.954), teamwork (p=0.647) or theatre exposure (p=0.677) as subjectively assessed by objective logbook records. Groups were compared using the Wilcoxon signed rank test.

Conclusions

Of increased job dissatisfaction and stress, along with poorer training opportunities. Assessments were hampered because logbooks are no longer mandatory for specialty membership examinations.