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ORAL PRESENTATIONS

Alternative Splicing of the Human α7 Neuronal Nicotinic Acetylcholine Receptor Gene (CHRNA7) -Novel Isoforms and Potential Implications

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Background: Splicing is a highly dynamic process in which non-essential introns are removed and essential exons are ligated. Alternative splicing is the phenomenon by which multiple different mRNA transcripts may be formed from the same pre-mRNA; allowing the formation of different protein isoforms which may have varying functional effects. Alternative splicing is the main cause of proteomic diversity in multicellular eukaryotes. This project looked at the α7 gene, as it has been associated with Alzheimer's disease and schizophrenia. In total, nine alternatively spliced isoforms of the α7 gene have been previously discovered, though their tissue distribution and function is currently unknown.

Objectives: This project investigated the different transcripts of the Human α7 Neuronal Nicotinic Acetylcholine Receptor Gene (CHRNA7/α7) produced from a panel of cell lines, including those derived from brain, lung and kidney tissue.

Methods: Three primer pairs were used to investigate the whole length of the CHRNA7 gene in the three different cell lines. Polymerase Chain Reaction products were visualised using electrophoresis on agarose gel and then sequenced.

Results: This study confirmed some previously denoted transcripts of the α7 gene and identified a novel transcript in the brain, lung and kidney cell line where exon 9 is completely spliced out.

Discussion/Summary: Bioinformatics predicted that this novel transcript yields 380 amino acids, as opposed to 520 amino acids seen with the full length α7 gene and that the subunit will span the cell membrane three times, as opposed to four times like with the full length gene. This means the C-terminus of the novel transcript will be intracellular instead of extracellular; so this may affect the internal signalling cascade. The next step is to investigate if the protein produced from the novel transcript, where exon 9 is spliced out, has any functional effects.

The Role and Regulation of Transcription Factor erm as Part of the Epigenetic Machinery in the Developing Zebrafish Hindbrain

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Background: Histone deacetylases are fundamental components of transcriptional silencing mechanisms and are required to promote specification of neurons and myelinating glia in the developing zebrafish central nervous system. The transcription factor erm was identified as hdac1 regulated from microarray based expressing profiling of zebrafish hdac1 mutant embryos.

Methods: Using whole-mount in situ hybridisation, analysis was carried out to determine the abundance and distribution of expression of erm in hdac1 mutant embryos, and also mind bomb mutant embryos, in which the neuronal progenitors prematurely and excessively commit to a programme of neuronal differentiation. Furthermore the phenotype resulting from the absence of erm in development was analysed using morphalino injection, designed to block the translation of erm.

Results: erm is a rhombomere centre marker in the hindbrain. Notch signalling demonstrated inhibition of erm. erm is a marker of the ventricular zone where progenitors lie, however it is expressed by cells that have just initiated the process of commitment to a programme of differentiation. Loss of function analysis of erm demonstrated its requirement for the formation of the midbrain hindbrain boundary as well as normal growth rate of the embryo.

Conclusion: erm is a marker of cells initiating the process of commitment to a programme of differentiation in the hindbrain and is a vital component of the epigenetic machinery required for growth of the embryo and midbrain-hindbrain boundary formation. This provides insight into the epigenetic regulation in the developing central nervous system increasing the potential for new therapeutic strategies of neurodevelopmental disorders caused by aberrant epigenetic regulation.

Identifying protein-protein interactions in the E.coli periplasm and the protection they confer against colicin E9

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ColicinE9 is a plasmid-encoded protein antibiotic produced by Escherichia coli that binds to BtuB and OmpF receptors and uses the Tol-system to translocate across the outer-membrane and periplasm of susceptible cells and kills them by degrading their DNA. Here we over-expressed TolAIII domain in the periplasm of E.coli DPD1718 cells and monitored DNA damage caused by ColE9 using a sensitive lux-reporter assay to investigate the possible roles of TolA in ColE9 translocation. Cells over-expressing TolAIII showed 53% periplasmic-protection against ColE9. This suggests that TolAIII over-expression can disrupt the normal Tol-system and reduces ColE9 translocation, possibly by altering the TolA-TolB interaction which is essential in the translocation of ColE9. Site-directed mutagenesis was used to mutate five residues 'Leu-Leu-Asp-Ile-Pro' in TolAIII which was found to be important in its interaction with the TolA-box of ColA. Cells over-expressing mutant TolAIII showed similar level of periplasmic-protection to that with TolAIII. This suggests that these residues are not important in the interaction between TolAIII and the TolA box of TolB. This study suggests that TolAIII plays an important role in ColE9 translocation by its indirect- interaction with TolB and TolA is important in energy dependent removal of Im9 from ColE9/Im9 complex. The identification of possible binding partner of TolAIII in periplasm and key residues in TolAIII will provide insights into the normal cellular role of the Tol-proteins that are important virulence determinants in Gram negative bacteria and may identify a novel antibiotic target for these important pathogens where the current therapeutic options are very limited.

New Resolution Recovery algorithms improve Cardiac Single Photon Emission Computed Tomography (SPECT) image quality and allow for image acquisition time to be halved

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New Resolution Recovery (RR) algorithms (Hermes Medical Solutions) may be implemented during cardiac SPECT image reconstruction and are proposed to improve image quality and allow for a reduction in image acquisition time. We aimed to investigate the effect of RR algorithms on image quality for full time and simulated half time acquired images. 40 patients underwent a one day stress-rest protocol for Tc-99m Myocardial Perfusion SPECT for the evaluation or diagnosis of coronary artery disease. Alternate bins were then removed from gated stress and rest raw data of 20 patients to simulate half time acquired images to which RR algorithms were applied. Differences in image quality between RR and Non-Resolution Recovery (NR) images were evaluated by a blinded clinician using a four point quality scoring system. RR algorithms significantly increased image quality scores compared with NR images when applied to rest full time images (2.55±0.76 and 2.35±0.81 respectively, $p = 0.04$) but not when applied to stress full time images (2.4±0.6 and 2.3±0.71 respectively, $p = 0.541$). When RR was applied to half time images there was no difference in image quality scores when compared with full time NR images at stress or rest ($p=0.75$ and $p=0.42$). Furthermore there was no difference in diagnostic classification ($\kappa = 0.871$) or diagnostic confidence ($p= 0.397$). Therefore implementation of RR algorithms during cardiac SPECT image reconstruction improves rest image quality and allow for SPECT image acquisition time to be halved. These findings also favour a reduction in radiopharmaceutical dose and patient radiation exposure.

The Effects of Ischaemic Reperfusion on Platelet Monocyte Binding in Man

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Background: Myocardial infarction is a major cause of morbidity and mortality in the UK. Arterial occlusion causes tissue ischaemia and, if prolonged leads to end organ damage. Early reperfusion improves outcome but experimental data suggest that restoration of blood flow may trigger additional injury beyond that induced by the ischaemia alone. However, the mechanism by which reperfusion injury occurs remains unclear. Platelets are known to have a fundamental role in the pathophysiology so we studied the effects of ischaemic reperfusion injury on platelet monocyte binding.

Methods: Twelve healthy subjects were randomised to upper limb ischaemia (200 mmHg) or sham (10 mmHg) for 20 minutes. Blood samples were collected at baseline, 5 and 45 minutes following reperfusion; immunolabelled with IgG1/CD14 and CD14/ CD42a and analysed using flow cytometry where at least 2500 cells were measured. Data collected were anaylsed using GraphPad Prism.

Results: Baseline platelet monocyte aggregations were similar in both groups (p=0.79). In the ischaemic group, platelet monocyte binding was increased at 5 and 45 minutes post-reperfusion (31% and 36% respectively, p=0.03 for both) while there was no significant increase in the sham group (29% and 28% respectively, p=0.80 for both).

Conclusion: Ischaemic reperfusion injury activates platelet monocyte binding in man. This may lead to thrombosis, myocardial stunning and microvascular dysfunction which may impair the benefits of early reperfusion. Further studies are required to consolidate our understanding of ischaemic reperfusion injury.

Is the transcription factor Engrailed 2 a good target for monoclonal antibody therapy for pancreatic cancer?

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Pancreatic cancer is the fifth most common cause of cancer death in the UK. Prognosis for pancreatic cancer patients is extremely poor, with conventional treatments for cancer being largely ineffective. Recent research has found that the transcription factor Engrailed 2 (EN2) is expressed ectopically in some forms of breast, lung, prostate and bladder cancers. It is predicted that EN2 is ectopically expressed in pancreatic cancer, which would allow tumour cells to be specifically targeted by antibody therapy.

Using polyclonal EN2 antisera this paper firstly investigates surface expression of EN2 on pancreatic tumour cell lines using FACS analysis. Then a tissue microarray of 220 pancreatic tumour samples was stained by immunohistochemistry to assess EN2 expression across a range of pancreatic malignancies. Normal pancreatic tissue was also surveyed for expression. 97.7% of the malignant pancreatic tumour samples were positive for EN2. However, 98% of normal samples of pancreas also stained positive for EN2, with similar cytoplasmic distribution of staining to the tumour tissue. No clear membranous staining was observed in the tissue.

Further research with monoclonal antibodies against native EN2 is needed to provide further data on the character of EN2 expression in pancreatic cancer, allowing it to be evaluated as a therapeutic target.

Relative Genetic Imbalance between chromosome 8 and c-Myc copy number as an indication of survival in uveal melanoma

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Amplification of the long arm of chromosome 8 has been strongly correlated with metastatic death in uveal melanoma; with patients with only one additional copy of 8q having a better prognosis than those with higher levels of amplification. The most commonly identified shortest region of overlap (SRO) within this region is 8q21-qter; within which can be found the locus of the oncogene MYC at 8q24.1. MYC amplification is of interest, as deregulation of the nuclear transcription factor has been correlated with increased cellular growth, proliferation and self-renewal, in addition to a poor level of differentiation. Accordingly, the objective of the study was to use MYC copy number to quantify the amplification of the long arm of 8q and correlate this with patient survival.

Fluorescence in situ hybridisation (FISH) was performed on 76 archival primary uveal melanoma samples to determine the presence of Relative Genetic Imbalance (RGI) between chromosome 8 and MYC copy number (more signals for the MYC gene compared to those for centromeric 8). FISH was performed using a Vysis CEP8 probe targeting centromeric 8 and a probe for the MYC gene, at 8q24.1. 60% of samples showed a RGI, confirming MYC amplification and indicating that high levels of amplification for 8q will be missed using CEP 8 alone. RGI for MYC was found not to correlate with patient survival, in the absence of monosomy 3. However, where a RGI was already present between chromosomes 3 and 8, amplification of MYC further worsened prognosis.

High-throughput Screening for the JAK2 V617F Mutation in Colorectal Tumours using High Resolution Melting Analysis

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A recurrent somatic activating mutation, V617F, in the pseudokinase domain of Janus Kinase 2 (JAK2), has been recently described in BCR/ABL negative myeloproliferative disorders. JAK2 is a cytoplasmic tyrosine kinase and a key mediator of cytokine signalling. The V617F mutation leads to stimulation of downstream signalling pathways involving signal transducer and activator of transcription (STAT) proteins which have a putative role in colorectal cancer (CRC) tumourigenesis and metastasis. Here we sought to evaluate the frequency of the mutation in a series of primary tumours and their corresponding metastatic deposits.

Quick-multiplex-consensus (QMC)-PCR followed by high resolution melting (HRM) analysis was used to screen for JAK2 V617F in DNA derived from formalin-fixed paraffin-embedded (FFPE) CRC tumours. We screened 118 tumours of which 63 were primary and 55 were subsequent metastases. Twenty-two CRC cell lines were additionally screened.

Ninety-four of the 118 tumours (80%) were found to have a wild-type melting profile on first screening. Twenty-four of the 118 tumours (20%) displayed aberrant melting of which 5 were identified as being of low quality and excluded from further analysis. After re-melting and correcting for inter-well variations, all samples were deemed wild-type.

This is the first study of JAK2 V617F in both primary and metastatic CRC. Mutations were not found and thus it is unlikely that this genetic alteration plays a part in either CRC development or metastasis.

KATP Channels- Blood Marker for Endothelial Function?

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Background: ATP-sensitive potassium (KATP) channels are found in vascular smooth muscle cells and play an important role in controlling vascular function. They are also detectable in blood but their relationship with vascular function is unknown.

Objective: To investigate the previously unknown relationship between levels of KATP channels in blood and vascular function in normal healthy subjects.

Methods: Blood samples were obtained and vascular function was assessed by carrying out three non-invasive tests in 25 normal healthy subjects. The levels of KATP channels were determined by measuring levels of mRNA subunits, Kir6.1/SUR2B, using real time RT-PCR test while vascular function are assessed using (i) iontophoresis with laser Doppler imaging, (ii) post-occlusive reactive hyperaemia test (PORH).

Results: This study showed that the Kir6.1 pore-forming subunit was expressed in human blood. Subjects were divided into 3 groups based on levels of Kir6.1 expression. Subjects in the group showing highest expression (n=7) had a significantly greater PORH recovery compared with subjects with the lowest expression (85.48571 arbitrary units versus 54.45 arbitrary units) (p= 0.045)

Conclusion: The mRNA Kir6.1subunit levels in blood showed a positive, significant relationship with endothelial function. Levels of KATP in blood could potentially be used as blood marker for endothelial function in vivo.

An Intronic SNP in the Alpha-1-Antitrypsin Gene May Confer Protection to Chronic Obstructive Pulmonary Disease

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Chronic obstructive pulmonary disease (COPD) results from complex interactions between both environmental and genetic factors. This is evidenced by the considerable variation found in the risk of developing COPD despite the established dose-response relationship from the biggest known risk factor, tobacco smoking. Thus, genetic susceptibility remains poorly understood given the best-characterised genetic determinant of COPD, severe alpha-1-antitrypsin (AAT) deficiency, only affects 1-2% of all COPD patients.

Following an unpublished genome-wide association study implicating the AAT gene as the strongest locus associated with lung function (a heritable surrogate predictor of COPD), one such reported intronic single nucleotide polymorphism (SNP) rs3748312 was investigated as part of a larger research project aimed at identifying rare sequence variants of the AAT gene that may be associated with COPD.

A sample of 230 COPD patients of European descent either predicted to carry one of six haplotypes conferring COPD risk, or who presented with severe early-onset COPD were genotyped for SNP rs3748312 within the AAT gene utilising TaqMan® assay with >5% of samples sequenced for concordance. The data was compared against control data of 60 patients of European ancestry from dbSNP.

Upon examination for differences between cases and controls, borderline significance was observed for the allelic distribution (p=0.049, OR 0.57 95% CI: 0.323 – 1.003), whilst the genotype distribution exhibited a non-significant difference (p=0.096 OR 0.583, 95% CI 0.308 – 1.106).

This preliminary study suggests the SNP merits further work in a more adequately powered investigation with adjustment for covariates given the borderline nature of the findings indicative of a protective effect for developing COPD with the minor allele (A). It is feasible that associated functional SNPs in linkage disequilibrium reflect the true association.

Mutant isoforms of the egg activation factor, phospholipase C zeta: the key to male infertility and future therapy?

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The function of sperm is twofold: to deliver paternal genes to the oocyte, while reactivating the oocyte from cell cycle arrest. The most popular reactivation theory is the sperm-factor model, whereby a soluble sperm protein enters the egg. Strong evidence suggests that the molecule responsible is phospholipase C zeta (PLCζ), a sperm-specific protein. It is likely that a functionally impaired version of PLCζ could be a cause of male-factor infertility. We sought information on sequencing and localization to understand the mechanism of PLCζ; information necessary to develop a targeted therapeutic.

We used PCR to screen for PLCζ abnormalities in three new infertile males, with history of intracytoplasmic sperm injection (ICSI) failure. We transfected HEK293T cells with three PLCζ isoforms: wild type (PLCζWT), a published Histidine-Proline translocation (PLCζH398P) and a newly identified frameshift (PLCζF1267).

Upon sequencing, exons appear normal. However all patients display an intronic sequence discrepancy between exon 8-9, for which functional and regulatory impact remains unknown. Mutant PLCζ has significantly reduced levels of expression, with temporal differences suggestive of delayed expression. Additionally, there are spatial localisation differences, with PLCζF1267 exhibiting some nuclear localisation, while both PLCζH398P and PLCζWT exhibit cytoplasmic localisation.

This highlights a potential role of PLCζ in infertility, since out of three screened infertile patients, all have intronic abnormalities. Cellular localisation of PLCζ appears to be cytoplasmic, indicating the need for re-evaluation of previous localisation hypotheses. Mutants demonstrate aberrant localisation and expression, suggesting a basis for functional impairment, providing evidence for the role of a new therapeutic.

Translational Regulation of Pro-Survival Factors in Oesophageal Adenocarcinoma (OA)

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Background: Accumulating evidence suggests that environmental pressures that invade the oesophagus during reflux, such as bile and hypoxia may aid the progression of Barrett's Oesophagus to Oesophageal Adenocarcinoma. Once exposed to these stresses, cells may respond by up-regulating certain growth factors such as VEGF and COX-2, which will enhance tumour angiogenesis and survival. Factors, such as HIFα have been well reported to increase expression of VEGF both transcriptionally and by acting on the 3'UTRs, stabilising the mRNA for translation. Both these stages of gene up-regulation were investigated in VEGF and COX-2.

Aims: To investigate the expression of VEGF and COX-2 and their regulatory mechanisms in a panel of oesophageal cancer cell lines in response to hypoxia, acid and bile salts.

Methods: Cell lines were exposed to the test conditions for varying time periods to assess cell viability. Once sub-lethal doses were determined, certain cell lines were analysed for changes in VEGF and COX-2 gene expression using qRT-PCR post treatment. Reporter constructs were then used to investigate regulation of VEGF and COX-2 expression through their promoters and 3'UTRS.

Results: Up-regulation of VEGF and COX-2 gene expression was observed post bile salt ($p<0.05$) and hypoxia treatment in certain cell lines. Increases in VEGF and COX-2 promoter and 3'UTR reporter activity were observed with bile salt and hypoxia treatment with particular reference to a 15-fold increase ($p<0.0001$) in COX-2 promoter activity with bile salts and a 4.6-fold increase ($p<0.01$) in VEGF promoter activity with hypoxia.

Conclusion: The results from this study may help us to appreciate that these conditions may not only up-regulate VEGF and COX-2 gene expression, but also play a role in stabilising mRNA through binding of proteins to their 3'UTRs, facilitating translation and ultimately increasing protein production.

The Role Of Toll-Like Receptor 6 in Critical Limb Ischaemia

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Critical limb ischaemia (CLI) is the most severe form of peripheral arterial disease. Despite advances in treatments, more than 30% of patients with CLI undergo major amputation. The pathophysiology underlying ischaemia-induced damage in skeletal muscle is poorly understood. Recent evidence suggests Toll-like receptors (TLRs) may play a role in the pathological response to endogenous ligands released in response to tissue injury. In ischaemic muscle, TLRs have been observed to be upregulated. This study investigated the role of TLR6 in ischaemic muscle.

TLR6 expression, distribution and co-localization with TLR2 were studied in ischaemic human muscle biopsies and in vitro using C2C12 myotubes cultured in ischaemic conditions by Western blot and immunofluorescence. TLR6 ligand Pam2CSK4 and a neutralising-TLR6 antibody were used to investigate downstream signaling pathways, Interleukin-6 release and apoptosis in vitro by Western blotting and ELISA.

TLR6 protein expression was significantly upregulated in critically ischaemic muscle and in C2C12 myotubes cultured in ischaemic conditions, TLR6 was shown to co-localize with TLR2. In our in vitro model, TLR6 activation by simulated ischaemia contributed to increased apoptosis and Interleukin-6 release. Neutralising-TLR6 antibody significantly reduced ischaemia-induced apoptosis and cytokine release.

TLR6 stimulation in ischaemic muscle leads to activation of downstream signaling pathways that results in cytokine release and apoptosis contributing to inflammation and muscle damage. TLR6 and TLR2 co-localization suggests that both these receptors are critical in this pathophysiological process. TLR6 antagonism attenuated ischaemia-induced apoptosis and inflammation. Therefore TLR6 inhibition may be a potential target in reducing skeletal muscle damage in CLI.

Antigen Microarrays For Rapid Screening of Rheumatoid Arthritis and Other Autoimmune Diseases

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Rheumatoid Arthritis is the most common autoimmune disease worldwide. Medical advances have led to the evolution of novel techniques that can considerably improve early diagnosis and management of Rheumatoid Arthritis, an importance advocated by 2009 NICE guidelines[1]. Of these, anti- citrullinated protein assays and protein microarrays are at the forefront[2,3]. This research aimed to analyse the potential of microassay techniques in the diagnosis, treatment and classification of Rheumatoid Arthritis and other autoimmune diseases.

PVDF-coated slides were manufactured using spin-coating techniques, onto which a range of autoantigens were printed using microarray technology. Preliminary tests assessed qualities of PVDF-coated slides and microassay methods. 30 donated serum samples, encompassing 7 different autoimmune diseases, were tested and analysed for presence and titre of autoantibodies to specific autoantigens using comparative methods.

Comparative analyses highlighted diverse differences and strong similarities between and within autoimmune states, with unique autoantibody profiles observable. Hierarchical Clustering Analysis using Pearson's Correlation demonstrated a potential for diagnosis and subgroup identification.

A proof of purpose was clearly demonstrated for microarrays, with huge potential to simultaneously screen for wide ranges of autoantibodies to unprecedented levels in clinical settings worldwide. As a result, protein microarray techniques have pivotal future roles in many aspects of immunology.

NICE Guidelines: Rheumatoid Arthritis. 2009 [10/01/11]; Available from: http://www.nice.org.uk/nicemedia/pdf/CG79FullGuideline.pdf.

Wegner, N., et al., Autoimmunity to specific citrullinated proteins gives the first clues to the etiology of rheumatoid arthritis. Immunol Rev, 2010. 233(1): p. 34-54.

Balboni, I., et al., Multiplexed protein array platforms for analysis of autoimmune diseases. Annu Rev Immunol, 2006. 24: p. 391-418.

Age and Gender Affects Proliferation Rate and Cell Surface Marker Expression of Human Infrapatellar Fat Pad-Derived Stem Cells

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Cell based therapies are being investigated for biological repair of a variety of disorders. Previous work has shown that mesenchymal stem cells (MSCs) from older patients have reduced proliferation rates. As age is associated with greater musculoskeletal (e.g. osteoarthritis) and cardiovascular (e.g. coronary artery disease) morbidity, an optimal expansion strategy is required for these older patients. This in vitro study investigates how age and gender affect MSC proliferation rate and cell surface characterisation.

Infrapatellar fat pad derived MSCs were isolated and expanded from 14 patients undergoing total knee replacements. Cells were seeded at densities between 50 and 10,000 cells/cm2 and cell proliferation studies, flow cytometry and cell surface staining were performed.

A statistically significant relationship showing lower seeding densities are associated with higher cell proliferation rates was found. Regression analysis showed that as age increases, cell proliferation rates become less responsive to changes in seeding density. Cell surface marker, CD105, had a constant expression irrespective of age. Females were found to have consistently higher cell proliferation and cell surface marker expression.

Our study has shown that patient characteristics do effect cell proliferation rate and cell surface characterisation, but as seeding density has such a significant relationship with proliferation rate, it can be altered, possibly along with other cell culturing strategies, to compensate for the effects of patient factors on MSCs. We have also shown that gender affects cell proliferation and cell surface characterisation, something most previous studies may have failed to identify as they group male and female patients together.

The Use of Chick Cardiomyocytes Micromass Culture to Investigate Sodium Valproate Teratogenicity at Different Times and Durations of Exposure

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Background: Maternal exposure to sodium valproate (SVA) at a specific time during gestation has been associated with serious congenital malformations including heart defects. This study was aimed to investigate the effect of different times and durations of exposure to SVA on chick cardiomyocytes.

Methods:Chick embryo hearts were harvested and the cardiomyocytes micromass was treated with a series of SVA concentrations (25µM, 100µM, 400µM and 800µM). The starting day of culture was denoted as day 0 and on day 6, the resazurin assay was performed to measure the cell viability therefore detecting for cytotoxicity, followed by the kenacid blue assay to quantify the protein production. The cells were morphologically scored throughout the experiment for any change in the number of contractile foci and their pace that indicates teratogenic effects.

Results: In Experiment 1, where the cells were given SVA on day 1 only, significant ($P<0.05$) reduction in the number of contractile foci was observed in 400µM and 800µM. Exposure on day 1 and day 3 in Experiment 3 produced a more dramatic effect demonstrated by reduced number in contractile foci ($P<0.05$ in 400µM and 800µM) and a reduction in the pace of contraction ($P<0.01$ in 800µM). Cytotoxicity was also demonstrated in concentration as low as 100µM ($P<0.05$). In Experiment 4 where the drug was given on day 1 and removed on day 2, the beating returned to the level comparable to that of the control.

Conclusion: This study demonstrated the teratogenicity of SVA. Furthermore, it suggests that sodium valproate can be toxic to cells upon repeated exposure. Most importantly, it points to the possibility for cells to recover from a teratogen if the drug is cleared from the system soon enough.

Balboni, I., et al., Multiplexed protein array platforms for analysis of autoimmune diseases. Annu Rev Immunol, 2006. 24: p. 391-418.

Live three dimensional mouse gut imaging to investigate the migration of intestinal epithelial cells

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Mutations in the Adenomatous polyposis coli (APC) gene are found in 80 percent of sporadic colorectal cancer tumours. The APC gene is known to have multiple functions including roles in differentiation, proliferation, cell migration and apoptosis. For the first time we carried out live 3D time-lapse movie analysis of whole mouse gut tissue to quantitate the migration patterns of gut epithelial cells. We measured the contribution of APC to productive cell migration. We also investigated the contribution of apoptosis to productive cell migration by inhibiting the anti-apoptotic protein Bcl-2. Our results showed that a mutation in APC does not alter productive cell migration, although the high variance indicated the need for a larger sample size to confirm this. We found that in both normal (wild type) and APC mutant mice, the use of the anti-apoptotic drug ABT-737 caused a loss of productive cell migration. This finding raises questions of how apoptosis is linked to cell migration in the gut epithelium and also a possible undiscovered role of Bcl-2 in cell migration.

The development of in vitro human bronchial epithelial cell models in studies of barrier formation

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Introduction: In vitro models of human bronchial epithelial cells are widely used in studies of permeability of the cell monolayer to investigate drug transport and susceptibility to allergen exposure in airway epithelium. However, less evidence are published on utility of these models in barrier formation. Therefore, we assessed the utility of bronchial epithelium models by: (1)measuring trans-epithelial resistance (TEER) across cell monolayer and (2)analyzing mRNA expression of tight junction proteins (TJP) i.e. zona -occluden 1 (ZO1), both representing tightness of cell monolayer.

Method: Cells types used were: (1) normal human bronchial epithelial cells (NHBEC) from two different donors, (2) BEAS-2B TGFβ -sensitive (BEAS-2BS), (3) BEAS-2B TGFβ-resistant (BEAS-2BR) and (4) Calu-3. Cells were seeded on Transwell® polyester inserts, raised to air-liquid interface (ALI) culture after 2 days and maintained on ALI for 21-28 days. TEER measurements were taken from day 2 on ALI. Then, cells were fixed and immunofluorescence-labeled with primary mouse antibody anti-ZO1, counter-stained with 0.01% propidium iodide and visualized under confocal microscopy. RNA samples of the cells were collected every 7 days of ALI to quantify ZO1 mRNA expression level. Experiment was repeated three times (n=3).

Result: Calu-3 had the highest TEER followed by NHBEC, BEAS-2BS and BEAS-2BR. NHBEC have the highest ZO1 mRNA expression while Calu-3 had the lowest ZO1 mRNA expression. No significant change in ZO1 mRNA expression in all cells during the ALI period. From immunohistochemistry, NHBEC had the most substantial ZO1 network while BEAS-2Bs' ZO1 distribution are nil/ sparse.

Conclusion: NHBEC is the most reproducible barrier-forming model, with careful considerations on variability of different donors, passage number, temperature, cell culture technique and mucus production. BEAS-2B cells are the least reliable model due to its very low TJP formation i.e. ZO1.

Differential sensitivity and response of monocytes to Clostridium Difficile toxin A and toxin B

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Host immune cells are believed to orchestrate the colonic inflammatory response during Clostridium difficile infection, mediated by two enterotoxins: toxin A and toxin B. Following disruption of the intestinal barrier, the toxins can exert their cytotoxicity upon peripheral blood monocytes, lymphocytes and neutrophils recruited into the lamina propria. Accordingly, susceptibilities of these immune cells to the toxins may determine the severity of the disease.

To investigate the response of these cells to the toxins, we exposed human peripheral blood monocytes, lymphocytes and neutrophils from whole blood to various concentrations of toxin A and B (8.5 - 8500ng/ml) at different time intervals. We also purified monocytes by plastic adherence in order to determine whether susceptibility of monocytes was independent of other mononuclear cells.

After exposing whole blood to either toxin for 3h, in contrast to lymphocytes and neutrophils, we found that CD14-positive events (specific for monocytes) reduced to < 5% of the control ($P < 0.02$) and cell size about 50% of control ($P < 0.03$) in a time- and dose-dependent fashion. Unexpectedly, when monocytes were adhered before exposure to 1700ng/ml of either toxin for 24h, no significant differences were found compared with control.

We conclude that while lymphocytes and neutrophils are resistant, monocytes from whole blood are exquisitely sensitive to the cytotoxic effects of both toxins. The effects of the toxins may not only be specific to cell type but also to the nature of the cell, as indicated by the lack of response of adherent monocytes to the toxins.

Expression of ion channels in the atrioventricular ring tissue in the rat heart

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Introduction: The cardiac conduction system (CCS) consists of the sinus node(SN), atrioventricular node(AVN), His bundle and Purkinje fibres. Further areas of specialised tissue - atrioventricular ring tissue(AVRT) also exists around the tricuspid, mitral and aortic valves forming the left, right and aortic rings(LR/RR/AR), which unite to form the retroaortic node(RAN). The function of the AVRT is not known, but catheter ablation of these areas has been shown to terminate atrial tachycardias(Kistler et al 2004). Therefore the aim of this study was to investigate the expression of ion channels in the AVRT and compare their expression to that in the CCS/working myocardium(WM).

Methods: 12 hearts from rats were frozen and cryosectioned. Immunohistochemistry was used to label serial sections to visualise the: atrial muscle(AM), ventricular muscle(VM), SN, AVN, RR and RAN which were then collected via laser assisted microdissection. qPCR using 18 ion channels and markers was used to analyse the level of mRNAs in the tissue samples.

Results: As expected, there was a classical distribution of ion channels in the AM/VM/SN/AVN tissues. In the RR/RAN, there was significantly lower expression of Tbx3(positive CCS marker) and HCN4(responsible for the pacemaker current If) than in the CCS and when compared to the WM, there was lower expression of Kir2.1(responsible for resting potential IK1) but higher expression of HCN4.

Conclusion: The RR/RAN have a unique profile in the expression of ion channels, but more importantly the molecular properties of this tissue are pacemaker like and therefore could in fact contribute to ectopic pacemaker activity.

Synergistic effects of carbon nanotubes and POSS-PCU: Applications of Nanotechnology in Surgical Oncology

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The advent of nanotechnology heralds a new paradigm in experimental biology and clinical medicine. Carbon nanotubes (CNTs) are nanoscale semiconductors with novel physical attributes. Recent evidence suggests that exposing CNTs to near infrared (NIR) laser would cause them to dissipate substantial amounts of heat energy, which can be exploited to thermally ablate cancer cells. Functionalizing CNTs with a nanocomposite polymer, polyhedral oligomeric silsesquioxane poly(carbonate-urea) urethane (POSS-PCU) would enhance dispersion and augment the rate of temperature increase as well as achieving a higher maximum temperature. Here we demonstrate that NIR irradiated POSS-PCU-CNTs appear to act synergistically in terms of temperature profiles, and are able to thermally ablate cancer cells in vitro. NIR irradiation of CNTs were conducted using an 808 nm diode laser at 0.5 watt and 1 watt. Temperature profile was recorded using a thermal camera. A colorectal cancer cell line, HT-29, was used as a model for photothermal ablation. Cell count was done using a haemocytometer and fluorescence-activated cell sorting (FACS). Graph plotting and statistical analysis was conducted using MATLAB®. Maximum final temperature of CNTs was statistically significant at both 0.5W ($p=0.0003$) and 1W ($p=0.001$), compared to control. Maximum final temperature of POSS-PCU-CNT was statistically significant at both wattages ($p=0.0325$, $p=0.0479$), compared to pristine CNTs. Cell kill of NIR irradiated pristine CNT ($p=0.000107$) and POSS-PCU-CNT ($p=0.0000842$) was statistically significant compared to control. POSS-PCU and CNTs act synergistically to achieve higher temperature profiles, and are able to thermally ablate HT-29 colorectal cancer cells in vitro when exposed to NIR laser.

The Action of Phytochemicals on Lipid Accumulation and Lipotoxicity in HepG2 Cultured Cells

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Non-alcoholic fatty liver disease (NAFLD) is becoming prevalent in developed countries, due to increasing incidence of risk factors. Steatosis (hepatic lipid accumulation) is benign NAFLD and, under certain exposures, can progress along the NAFLD severity spectrum to non-alcoholic steatohepatitis (NASH). A primary intermediary is fatty acid-mediated oxidative stress (lipotoxicity). Treatments are currently limited. Due to presence of lipid accumulation in developing steatosis and oxidative stress in progressing to NASH, anti-steatotic or antioxidant compounds could offer preventative/treatment measures. Therefore, the aim was to determine protective actions of phytochemicals (quercetin dihydrate, (-)-epigallocatechin gallate, L-sulforaphane and indole-3-carbinol) against lipid accumulation or oxidative stress, as potential NAFLD therapy.

Endogenous oleate causes lipid accumulation developing steatosis whereas endogenous palmitate causes lipotoxicity leading to NASH. HepG2 cells were exposed to oleate (steatosis model) or palmitate (NASH model) alongside one phytochemical for 24 hours. Nile Red measured changes in lipid accumulation and Neutral Red measured viability changes.

Significance ($P<0.0001$) was shown for oleate causing lipid accumulation and palmitate causing lipotoxicity. None of the phytochemicals caused significant decreases in lipid content or increases in cell viability.

Despite the phytochemicals having established anti-steatotic and antioxidant properties, none exhibited a significant protective effect against oleate-mediated lipid accumulation or palmitate-mediated lipotoxicity and therefore could not be suggested to protect against steatosis and NASH in vivo as potential treatments. It was concluded that further research was required using alternative phytochemicals. However, statistical significance for the effects of oleate and palmitate highlighted that the model works and could be used in future experiments.

Understanding the molecular mechanisms of liver fibrosis provides insight into novel biomarkers of disease

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Introduction: Liver fibrosis is a major cause of morbidity and mortality and is characterised by excessive extracellular matrix (ECM) deposition from activated hepatic stellate cells (HSC). Although potentially reversible, current methods of diagnosis are invasive. There is a critical need for non-invasive (i.e. not liver biopsy) markers of fibrotic activity and disease progression. We identified ectopic expression of the Sry-box transcription factor, SOX9, in as a novel mechanism to explain aspects of liver fibrosis. The aim of this project was to identify novel Sox9 targets in fibrosis and assess their suitability as biomarkers

Methods: Rat HSCs were isolated using established perfusion techniques and cultured activated on plastic. Sox9 was abrogated using siRNA. Livers were collected from carbon tetrachloride induced fibrotic and control rats and processed for fixed tissue. Expression was analysed by western, qPCR and immunohistochemistry.

Results: From a cohort of 20 genes, vimentin, osteonectin, osteoactivin and enolase-1 were verified by qPCR from Sox9 knockdown HSCs as potential downstream targets. In silico analysis revealed Sox9 binding sites in potential regulatory regions of all 4 genes. Western blotting showed protein expression changes in enolase-1. Immunohistochemistry detected vimentin and osteoactivin in fibrotic tissue and surrounding nuclear Sox9 in activated HSCs.

Conclusion: These data suggest vimentin, osteonectin, osteoactivin and enolase-1 are novel Sox9 targets. The protein expression of Vimentin and GPNMB suggests they are present in activated HSCs and contribute to scar formation in liver fibrosis and, as circulating proteins, have the potential as biomarkers for liver fibrosis.

Superantigen stimulation induces T cells to express a regulatory phenotype that produce the anti-inflammatory cytokine IL10

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Background: The bacterial superantigen exotoxins are best known for the role they play in toxic-shock syndrome (TSS), where they induce massive TCR Vβ-specific T cell proliferation and pro-inflammatory cytokine production. However, the activation of excessive immune responses is unlikely to confer any evolutionary advantage to superantigens. Previous work has shown that superantigen stimulation can convert naïve CD4+ T cells into regulatory T cells. Therefore, 'activation-induced regulatory T cells' could represent a novel immune evasion strategy. Whether superantigen stimulation induces similar changes in CD8+ T cells has yet to be identified.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from healthy human volunteer blood samples and stimulated with toxic shock syndrome toxin 1 (TSST-1), at a range of concentrations for three days. The cells were stained with antibodies to cell surface and intracellular regulatory markers before acquisition and analysis using flow cytometry.

Results: Superantigen stimulation resulted in the conversion of peripheral blood CD4+ and CD8+ T cells to T cells bearing the regulatory phenotype, CD25+FoxP3+. Expression of CD25+FoxP3+ was TCR Vβ2-specific. Superantigen-stimulated CD4+ and CD8+ T cells produced the anti-inflammatory cytokine, IL10, in a dose-dependent manner, suggesting a regulatory function for these cells.

Discussion: This work has shown that TSST-1 stimulated CD4+ and CD8+ T cells are converted into cells with a regulatory phenotype that produce IL10. Superantigens may provide an evolutionary advantage to the bacteria that produce them by suppressing host immune responses locally in the nasopharynx, their ecological niche, therefore prolonging infection and increasing the probability of transmission.

Epigenetic Regulation of Epithelial-Mesenchymal Transition in Idiopathic Pulmonary Fibrosis

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Idiopathic Pulmonary Fibrosis (IPF) is a chronic fibrotic lung disease, for which the exact cause is still unknown. Myofibroblasts are key effector cells in the fibrotic process contributing to IPF pathogenesis. Current evidence points to alveolar epithelial cells (AEC) as a source of myofibroblasts in the lung, via the process of Epithelial-Mesenchymal Transition (EMT). EMT causes the transdifferentiation of epithelial cells to mesenchymal cells and is induced by the cytokine, Transforming Growth Factor-β (TGFβ). As EMT progresses, epithelial cells lose characteristic cell markers, such as E-cadherin, and acquire those of myofibroblasts, such as alpha-Smooth-Muscle Actin (α-SMA) and Fibroblast-Specific Protein-1 (FSP-1). This study aims to explore the epigenetic regulation of EMT in IPF, with special interest in histone acetylation and methylation. Human Bronchial Epithelial Cells and A549 cells were cultured to 100% confluence and stimulated with TGFβ for 10 days. Flow cytometry, quantitative PCR (QPCR) and Chromatin Immunoprecipitation (ChIP) techniques were then carried out to analyse the expression of cell markers and the underlying epigenetic modifications. We found that E-cadherin expression decreases with TGFß, with a concomitant increase in α-SMA and FSP-1. Furthermore, E-cadherin gene silencing was associated the repressive chromatin mark histone H3 lysine 9 trimethylation (H3K9me3) at its promoter, whereas increased expression of mesenchymal markers α-SMA and FSP-1 may be related to the active chromatin mark histones H3 and H4 acetylation. Our findings strongly suggest that epigenetic regulation is critically involved in myofibroblast differentiation through EMT and provide the basis for further studies on the epigenetic mechanisms of EMT, which may lead to better understanding of IPF pathogenesis and identification of novel therapeutic targets.

The role for Gli3 in cortical neuronal differentiation

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The formation of cortical neurons during development is essential in maintaining functional connectivity. To function correctly, cortical neurons must outgrow axons that make connections to appropriate targets, both within and outwith of the cortex. Mutations in Gli3, a zinc-finger transcription factor, has been implicated in several human developmental disorders that are characterized by brain deformities. In order to study the role of Gli3 in axonal outgrowth, I performed immunohistochemistry and analyzed two different Gli3 mutants. For the first mutant, Gli3XtJ/Pdn/Golli tau-GFP, my results demonstrated a defect in axon outgrowth, and a deformity of the subplate. I also studied a conditional mutant Emx1 Cre;Gli3Pdn/fl;Golli tau-GFP, in which Gli3 is reduced specifically in the cortex from when Emx1 Cre is expressed, around E9.5. This was carried out to determine a time period for when Gli3 indirectly regulates axon outgrowth, and to elucidate which aspect of axon outgrowth is indirectly controlled by Gli3. Conditional mutants did not have a defect in axon outgrowth, which suggests that axon outgrowth defects in other Gli3 mutants are due to processes occurring in the earlier stages of cortical development, such as patterning of the forebrain. It is therefore vital to determine precisely when recombination occurs. It will then be possible to study forebrain patterning in Gli3XtJ/Pdn mutants at this specific time point to determine the molecular mechanisms downstream of Gli3 which contribute to the axon outgrowth defect. This will help to increase our understanding of the pathophysiology of the human developmental disorders associated with defects in Gli3.

Development of a Bilayered Dermal Scaffold Using New Generation Nanocomposite Materials

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Background: Despite the myriad of skin substitutes, current gold standard treatment of full-thickness burns remains split-thickness autografts. However, their use cannot be extended to patients with a large %total body surface affected. The objective was to develop a porous bilayered scaffold for dermal replacement from a novel nanocomposite-polymer, polyhedral-oligomeric-silsesquioxane poly(caprolactone-urea)urethane (POSS-PCL) and to seed adipose-tissue-derived stem cells (ADSC's) which enhance wound healing and angiogenesis.

Methods: The inner-layer was produced via phase separation for a highly porous morphology. A removable outer-layer incorporated silver nanoparticles to impart antimicrobial properties. Effect of different pore sizes on physicochemical properties was established by tensile testing, contact angle, permeability, FTIR and scanning electron microscopy(SEM) analysis. Optimal pore morphology for cell proliferation was elucidated through ADSC culture. Cell viability and apoptosis were tested using an Alamar Blue™(AB) and LDH assay. All tests were repeated on Integra®.

Results: The physical construct was easy to handle and clinically applicable. Macroporosity and permeability of scaffolds was demonstrated, which were up to 72% porous; confirmed by SEM. Outer-layer contact angle was >100°, indicating hydrophobicity and the inner-layer was <70° indicating hydrophilicity of the scaffold. Young's moduli ranged from 0.406-0.492 MPa. Both results are comparable to skin. AB assay showed cell proliferation onto the scaffold, comparable to that on Integra®.

Conclusions: In vitro assessment of the dermal scaffold suggests it is a promising alternative to the current industry leader, Integra® and has many desirable properties that could successfully mimic human skin. Future directions involve covalently-bonding bioactive molecules(i.e.cyclic-RGD) to further enhance cell proliferation.

Assessment of a DNA-Protein Kinase Inhibitor as a chemo-and/or Radiotherapy Potentiating Agent in Medulloblastoma

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Medulloblastomas are paediatric malignant tumours of the cerebellum; accounting for 10% of all paediatric cancer deaths. Ionizing radiation (IR) and Etoposide have been shown to have anti-tumour activity in medulloblastoma by causing DNA double-strand breaks (DBSs). These DSBs can be repaired by the cell, leading to treatment resistance. Inhibition of DNA-Protein Kinase (DNA-PK) has been shown to enhance Etoposide and IR toxicity in adult tumours by blocking DSB repair. This study investigates the use of the novel DNA-PK Inhibitor, NU7441, as a chemo-and/or radiotherapy potentiating agent in medulloblastoma.

Two human medulloblastoma cell lines were used (D425 and D283) to investigate the potentiating effect of NU7441 (1µM) on differing doses of Etoposide and IR. This was investigated in vitro using an XTT cell proliferation assay. Growth inhibition was expressed in relation to NU7441 untreated control.

NU7441 was shown to potentiate the effect of IR in D425/D283 ($P<0.0001$ and $P<002$ respectively). D425 showed a 2.23 fold reduction in GI50 ($P = 0.002$) and D283 showed a 4.5 fold reduction in GI50 ($P=0.002$). The effect of NU7441 was abolished past 4 Grays in D283.

The effect of Etoposide was not statistically significantly potentiated in D425/ D283 using NU7441 ($p>0.05$ for both cell lines). However, both cell lines gained a 2 fold GI50 reduction. Any effect of NU7441 was abolished at 3µM.

NU7441 was shown, in vitro, to further sensitize medulloblastoma cell lines to IR; showing proof of principle for continuing development. NU7441 was not shown to significantly further sensitize medulloblastoma cell lines to Etoposide.

Validation of a biomarker for therapy with histone deacetylase inhibitors

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Aberrant epigenetics play an important role in tumourigenesis and has driven the search for mechanism-based drugs to regulate chromatin. One novel group of drugs is histone deacetylase inhibitors (HDACi). These target both transcriptional and non-transcriptional pathways to elicit apoptosis in cancer cells via a mechanism that has yet to be fully characterised. A recent genome -wide loss of function screen to identify genes that govern sensitivity to HDACi has implicated the importance of HR23B. This has a key role in targeting ubiquitinated cargo proteins to the proteosome. The aim of this project was to validate HR23B as a biomarker in cancer using U2OS cells treated with two HDACi, a novel drug, CXD101, and the FDA approved, suberoylanilide hydroxamic acid (SAHA). Both drugs were found to have a similar potency in inducing apoptosis, eliciting PARP cleavage and increasing levels of acetylated histone H3 in cells. siRNA knock-down of HR23B reduced HDACi-induced apoptosis whereas doxycycline-induced overexpression of HR23B increased apoptosis. Immunohistochemistry was used to stain for HR23B in sixty normal and sixty malignant colon biopsies. It was found that a significantly higher intensity and frequency of HR23B staining correlated with colon tumour malignancy. Thus, results showed that higher HR23B levels indicate tumours that are potentially more sensitive to HDACi treatment and that these increased levels are found in malignant colon tumours. This provides a rationale for using HR23B as a biomarker for future stratification of patients according to tumour HR23B levels.

A Novel Method for the Measurement of VASP-phosphorylation by Cytometric Bead Array

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Introduction: Vasodilator-stimulated phosphoprotein (VASP) is a microfilament-associated focal adhesion protein which is a major substrate for cAMP-dependent protein kinase . As such, VASP phosphorylation has been used as a surrogate measure for platelet cAMP. Here we describe a novel method for the sensitive and reproducible measurement of VASP-phosphorylation using a cytometric bead array (CBA). We also demonstrate its use as a means of detecting the effects of various Gs-coupled agonists and antagonists on platelets, and of assessing inhibition of the platelet P2Y12 receptor in vitro.

Methods: Lysed platelet samples prepared from hirudin platelet-rich plasma were incubated with a proprietary bead (Functional Bead Conjugation Buffer Set, Becton Dickenson) which was conjugated according to instructions with a monoclonal antibody to VASP (mAb IE273 anti-VASP). Bead-bound phosphorylated VASP (VASP-P) was detected by flow cytometry following addition of a fluorescent second antibody (FITC-conjugated antibody 5C6 antiVASP pSer 157). Flow cytometry was performed on a Becton Dickenson LSRII flow cytometer using FACSDiva acquisition software. The results are expressed as median fluorescence (mf).

Results: The assay performed well, giving reproducible results over a wide range of concentrations of VASP-P with little variation in performance between different batches of beads. The methodology was successfully used to detect concentration-dependent increases in platelet VASP phosphorylation in response to iloprost, PGE1, PGE2, ONO-AE1-329 (an EP4 receptor agonist), adenosine and a cAMP analogue. These increases in VASP-phosphorylation were prevented in the presence of the appropriate specific antagonist. The assay was also used successfully to demonstrate the ability of the P2Y12 antagonists cangrelor, ticagrelor and prasugrel active metabolite to prevent the reduction in VASP-phosphorylation brought about by addition of ADP to platelets in which VASP-phosphorylation had been elevated by PGE1.

Conclusion: This novel assay provides a simple, sensitive, reproducible and flexible method for determination of VASP-phosphorylation in platelets.

Atypical pneumonia – a confusing case?

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A 53-year-old man was admitted to hospital with a 4-day history of lethargy, headache, nausea, vomiting, diarrhoea, fevers and rigors. He worked in developing disused properties and had returned from holiday in Turkey three weeks previously. On examination, he was febrile, tachycardic and tachypnoeic with saturations of 100% on air. There were right basal crepitations and a chest radiograph demonstrated right mid-zone shadowing. White cell count was 9.8 x 109/l with a lymphopenia. He was initiated on intravenous co-amoxiclav and clarithromycin. Legionella urinary antigen was detected on day 2 and co-amoxiclav was replaced by rifampicin. Later that day, he became confused, looking 'vague' and his Glasgow Coma Score dropped to 9. He was intubated and transferred to the Intensive Care Unit. CT brain scan and lumbar puncture were normal. A working diagnosis of Legionella Encephalitis was made. His condition improved and he was extubated after 24 hours. He remained ataxic with difficulty in feeding and swallowing. He was discharged 12 days later with resolution of symptoms and completed a 3-week course of antibiotics.

Legionnaire's disease is a serious cause of atypical pneumonia which may progress to life-threatening multi-organ failure with a mortality of 10%. Neurological manifestations, seen in 40%, range from acute confusion, hallucinations, stupor, coma, cerebellar disturbances, and isolated nerve lesions. Our case demonstrates the rapid clinical deterioration of a patient with Legionella Encephalitis and highlights the need for accurate interpretation of clinical features, appropriate investigations, early initiation of empirical antibiotics and supportive therapy.

Facial emotional recognition in Parkinson's disease with apathy

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Aims: To compare emotional processing in Parkinson's disease (PD) sufferers with apathy (PD+A), to those without apathy (PD-A) and healthy controls, (HC)

Methods: PD sufferers (n=96) without cognitive impairment and 32 HC (n=32) were included in the study. Of those with PD, n=23 met criteria for apathy on the Apathy Evaluation Scale (AES). Assessments included the ability to recognise expressed emotion, (happy; sad; fear; anger; surprise; disgust; neutral) using a facial expression recognition task, (FERT). Each participant was asked to recognize both composite and gradations (30/50/70/100%) of each emotion. Those with PD were either assessed in their, 'on' dopaminergic medication state, (n = 48) or 12 hours 'off' medication, (n = 48).

Results: The PD+A group was found to be significantly impaired in the recognition of happiness, (p = .002) and disgust, (p = .008) in comparison to those without apathy (PD-A). Such findings were consistent with gradations of emotion (happiness, p = .03; disgust p = .024). Emotional recognition did not differ significantly between Pd+A and HC.

For those PD participants who were "on" medication during the FERT, those with apathy (PD+A) remained significantly impaired in the recognition of happiness, (p = .055) compared to the PD-A group. However, for those who were 'off' medication during the FERT, those with apathy (PD+A) were found to be significantly impaired in the recognition of disgust, (.014), surprise, (p = .018), as well as happiness (p = .011), compared to the PD-A group.

No significant differences in the 'on' state were seen between PD+A and PD-A on recognition of gradations of emotion, whilst 'off' medication the PD+A group, but not the PD-A group, were impaired in their recognition of happiness, (p = .017); disgust, (p = .014) and surprise, (p = .018).

Conclusions: The presence of apathy as well as dopaminergic state influences emotional processing in PD. In particular, recognition of the emotions of disgust and surprise may be dopamine dependent.

Pituitary Tumour Apoplexy in a patient with sinusitis

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Pituitary tumour apoplexy (PTA) is a rare clinical syndrome characterized by hemorrhage or infarction into a pituitary adenoma, resulting in a rapid rise in intrasellar pressure. It is a neurosurgical emergency, and most commonly presents with a constellation of symptoms including retro-orbital headache, visual symptoms and nerve palsies. Pituitary dysfunction can lead to endocrine deficits, the most lethal of which is adrenal insufficiency. Diagnosis is made by MR scanning, and treatment, while controversial, usually involves surgery in unstable patients. Here, we describe a case of a 44-year-old man presenting with headache, sinusitis and bilateral blindness. MR scans were consistent with a diagnosis of PTA, and trans-sphenoidal decompression by removal of the macroadenoma was carried out. Sinus mucosal examination showed thick inflamed mucosa, consistent with sinusitis. In regards to this case, we reviewed the literature on PTA, with a special consideration to its pathology. We also investigate the literature reporting an association between sphenoid sinus mucosal thickening and PTA, and speculate whether an underlying sinusitis process may predispose a pituitary tumour to undergo apoplexy.

Endoscopic Transnasal Transphenoidal Resection Of Pituitary Adenomas: Initial Results

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Background: Surgical approaches to the pituitary fossa have evolved, from the transcranial and microscopic transphenoidal till the latest endoscopic transphenoidal approach. Our aim is to analyze our initial experience resecting pituitary adenomas with a pure endoscopic endonasal transphenoidal approach.

Materials and Methods: Last year we operated on 16 patients with pituitary adenomas using the endoscopic transphenoidal approach. Eight were men (50%) and 8 women (50%) with average age 52.66 years (range 23-72). Nine adenomas were non-functioning (56.25%), 2 secreted GH (12.5%)-one of which presented as pituitary apoplexy, 2 ACTH (12.5%) and 3 PRL (18.75%). Eight adenomas had suprasellar extension (50%) and 14 patients presented with visual disorders (87.5%). The degree of resection was monitored with pituitary-MRI and both visual and pituitary functions were followed.

Results: We achieved total resection in 14 patients (87.5%) and subtotal in 2 (12.5%). Intraoperative one patient presented rhinorrhea (6.25%), succesfully treated with fat, tachosil and lumbar puncture, while 2 other patients with possible post-operative rhinorrhea were preventively controlled with transient lumbar puncture. One patient developed diabetes insipidus (6.25%) and one hypocortisolaemia (6.25%). Significant improvement in both visual and hormonal disorders was observed in all patients.

Conclusion: A purely endoscopic endonasal transphenoidal approach is a safe and effective method, well tolerated by patients. Compared to the microscopic transphenoidal technique, it has a wider visual field, greater brightness and proximity to the tumor. Furthermore, the absence of dilators and the simultaneous access of both nasal chambers, offers more flexibility while handling the surgical instruments. However, it requires specialized equipment and proper training.

Can nurse-led oxygen management improve the delivery of oxygen therapy in the Acute Medical Admission Unit?

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Background: The NPSA outlined 281 incidents (2004-2009) relating to inappropriate oxygen management including 9 directly-related patient deaths and a further 35 probable deaths. This project aims to improve nurses' oxygen delivery knowledge and skills thereby facilitating compliance with BTS guidelines in ≥95% of cases.

Methodology: In 2011 two students audited oxygen management methods over 4 weeks. Using baseline data, errors were identified and improvement strategies adopted including bundles as well as design and distribution of an oxygen flowchart and the use of stickers to correct misleading SEWS charts. Due to difficulties encountered with clinical staff, we approached the Medical and Nursing Directors of NHS Tayside who fully endorsed such changes. For each test of change (8 in total), a full PDSA cycle was performed.

Discussion: Post-intervention data highlighted problems in introducing extra paperwork such that nursing workload was increased to beyond an acceptable level. Other barriers encountered were a high staff turnover rate, lack of resources needed to appropriately educate staff, out-of-date charts that fail to comply with recent modifications in BTS guidelines and lack of funds available to implement such changes.

Conclusions: Our methods have not made any improvements to ensuring correct oxygen management. However it is still thought that this can be improved to 100% compliance with further research, education of relevant staff members in tackling ward 'culture' and widespread implementation of the methods described above. NHS Tayside has agreed to alter the SEWS charts in line with our recommendations and will implement the flowchart later this year.

Childhood Obesity In The West Bank

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Introduction: The prevalence of childhood obesity worldwide is increasing rapidly and its well established association with cardiovascular disease means it cannot be ignored. Despite the fact that childhood obesity is likely to be high in Palestine, with adult obesity up to 54%, cardiovascular disease causing 45% of deaths, and a culture of no exercise, poor diet and cultural acceptance of obesity, there are no data on childhood prevalence within the West Bank.

Methods: We measured height, weight and blood pressure in 160 randomly selected children from 3 schools in Abu Dis, West Bank. Obesity was defined by BMI corresponding to gender and age percentiles linked to adult values of 30kg/m2 and 25kg/m2 for obesity and overweight. Hypertension was defined as pressure >95th percentile for gender, age and height.

Results: Results showed that obesity prevalence was 3.8% (95%CI 0.8 – 6.7) (higher in girls, p=0.06), overweight prevalence was 23.8% (17.2 – 30.3) and hypertension prevalence was 6.3% (2.5 – 10.0) (higher in girls, p=0.004).

Discussion: There is a high prevalence of cardiovascular risk factors in the Palestinian 6-11 year old population which will lead to high rates of disease if interventions are not made. This is likely to be due, at least in part, to low levels of exercise, a high energy diet and a high rate of undernutrition in infancy. The higher rate of obesity and hypertension in girls is likely to be due to lower levels of exercise compared to boys. Further, larger studies must be conducted to confirm these findings before interventions are implemented.

Case Series - Catch Up Growth of 10 Very Low Birthweight Extreme Preterm Neonates to Two Years of Age

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The first two years of life is critical for catch up growth in very low birthweight (VLBW) extreme preterm neonates. This pilot case series aims to observe and identify factors influencing growth, especially catch up growth of VLBW extreme preterm neonates.

Ten consecutive neonates delivered at <31 weeks' gestation and birthweight <1500g who were admitted into NICU in Queens Medical Centre from January to February 2008 were recruited. 1 case was excluded as follow up was done in another hospital. Retrospective review of case notes was performed. Catch up growth was defined as Z score of >-1.28 (10th percentile) at 2 years of age. Z score was calculated using reference value from the UK-WHO low birthweight growth chart.

Five of the nine neonates showed evidence of catch up growth. In comparison to neonates without catch up growth, these five neonates had longer duration of NICU stay (105.8 days vs 67.5 days) and parenteral feed (20.25 days vs 10.25 days). On discharge, three of these five infants with catch up growth were given very high energy formula while all the infants without catch up growth had only preterm formula. No major differences in birthweight, gestational and maternal age were noted.

Excessive and low catch up growth predispose to metabolic syndrome and suboptimal cognitive development respectively. However, there is lack of consensus in defining optimum catch up growth in VLBW preterm neonates. More studies are needed to investigate the optimum rate of catch up growth and its effect in later life.

To treat or not to treat? Vitamin D treatment in primary hyperthyroidism

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Primary hyperparathyroidism (PHP) is one of the most common endocrine disorders. It leads to increased catabolism of vitamin D and hence vitamin D deficiency and PHP frequently co-exist. There has been clinical hesitation to replace vitamin D in PHP for fear that this may lead to further increase in plasma calcium concentration. Short term studies have suggested that this may not be the case and we now report the long term safety of vitamin D replacement in patients with PHP and vitamin D deficiency.

Nineteen patients (1 male) with PHP diagnosed on standard biochemical bases were studied. All had been found to have vitamin D deficiency (serum 25OHD <10ng/ml; n=8) or markedly insufficient (<20ng/ml) and were treated with 1.25mg (50 000iu) ergocalciferol daily for 10 days and then once a month thereafter. Six of the patient had previously been treated with bisphosphonates. Blood samples were obtained before treatment and after 12 months.

Before treatment mean 25OHD was 10.9 (SE 1.1) ng/ml; this increased to 32.6 (4.2) ng/ml after 1 year of ergocalciferol ($p<0.001$). Over the same period plasma calcium remained stable at 2.77 mmol/l before treatment and 2.72 afterwards. Plasma PTH fell non-significantly with the greatest fall in PTH occurring with the greatest change in 25OHD. No adverse events were recorded in relation to treatment.

We conclude that restoration of 25OHD to the normal range in patients with PHP is safe and ought to be undertaken as part of routine clinical management.

The Subjective Experience of Post Psychotic Depression: a Photo-Elicitation Study

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Post Psychotic Depression (PPD) occurs frequently in individuals following recovery from an acute episode of schizophrenia. It is associated with impaired quality of life, increased rates of relapse or rehospitalisation, deliberate self harm and suicide. However, little research has focused on the subjective experience. This is the first study to use a qualitative descriptive approach alongside a photo-elicitation method to explore individuals' experiences of PPD. Eight individuals first took photographs that they believed represented aspects of, or provoked emotions related to, their depressive experiences and then participated in in-depth interviews. Individuals described their depression as a trajectory starting from reflecting on their psychosis to becoming depressed, being depressed and finally wanting to get better. The psychotic episode was seen as a highly traumatic event which triggered negative appraisals of shame, embarrassment and a devastating fear of relapse. A loss of cognitive and emotional functioning and social isolation were underpinned by periods of low and flat moods. Family often showed a lack of empathy and depressive symptoms were sometimes ignored by healthcare providers. Knowledge of the subjective experience of PPD might improve providers' communication with their patients and allow for the development of appropriately targeted interventions, such as psychological therapies aimed at minimising the negative appraisals made by patients while recovering from an acute episode of schizophrenia. Additionally, photo-elicitation proved an achievable and effective method, and could now potentially be used to address other qualitative research questions within this population where experience is hard to convey.

Pyoderma gangrenosum: A report of a rare complication after knee arthroplasty requiring muscle flap cover supplemented by negative pressure therapy and hyperbaric oxygen

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Pyoderma gangrenosum (PG) is rare ulcerating skin condition easily confused with wound infection following surgery. We report a complicated case of PG following knee arthroplasty where delayed diagnosis and repeated debridements lead to significant tissue loss. Successful reconstruction was achieved with a muscle flap, but subsequent reactivation of PG and superadded infection placed both the reconstruction and patient's life at risk. Prolonged combined use of negative pressure therapy (NPT), immunosuppression and hyperbaric oxygen (HBO) was successfully used to reduce the wound size, enhance wound granulation, promote re-epithelialisation, and provide pain relief. There is little or no published literature on these treatment modalities for the management of PG, with only one reported case using both NPT and HBO for PG (not following knee arthroplasty). More studies are necessary to determine the role of both modalities in the management of pathergy in large and complex wounds and the rare nature of this complication following knee arthroplasty explains the lack of evidence-based guidance. In conclusion, we suggest a surgical algorithm. This is the first report of PG following knee arthroplasty with the use of both NPT and HBO in order to achieve soft tissue coverage.

Intracytoplasmic Sperm Injection - A Case of Dandy Walker Syndrome

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Background: Intracytoplasmic sperm injection (ICSI) is one of the most widely used of the assisted reproductive techniques (ART). It describes the microsurgical injection of one spermatozoon head into the ooplasm through the zona pellucida of an oocyte to stimulate fertilisation. As only one spermatozoon is required it is recommended for male factor subfertility.

The very nature of artificially injecting a spermatozoon head or nucleus into the oocyte bypasses many evolutionary barriers allowing for fertilisation with suboptimal spermatozoa. Thus, despite its widespread use there are still concerns to its safety and the long term complications in children conceived this way.

Methodology: Case study was performed using patient history and data from Royal Blackburn Hospital with patient's oral permission. Literature review and discussion were based on papers indexed by PubMed using the search terms: 'intracytoplasmic sperm injection' and 'genetic malformation'.

Discussion: It is unclear as to whether ICSI was the cause of the primary infant's Dandy Walker Syndrome. There are various paternal and maternal factors implicated as well as the process of ICSI itself that could have explained this incidence.

Case Summary: A couple with male and female factor subfertility (underwent ICSI, giving birth to a child with Dandy Walker Syndrome in the first attempt and a healthy baby girl in the second. In light of this there will be further discussion into possible complications and future improvements in ICSI.

Periodontal disease, cardiovascular disease and all-cause mortality. A prospective study in the Belfast PRIME Study cohort.

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Background: Periodontal disease is one of the most prevalent diseases and has been reported to affect up to 90% of the worldwide population. Periodontal disease is a chronic inflammatory condition, which includes gingivitis (inflammation of the gum) and periodontitis (inflammation of the periodontal tissues). Recently there has been interest in the possibility of an association of periodontal disease with cardiovascular disease (CVD) and mortality. It is believed that systemic inflammation, which influences each stage of atherosclerosis, may be the link.

Materials and Methods: 1,346 men aged 60 to 69, recruited into the Belfast cohort of the Prospective Epidemiological Study of Myocardial Infarction (PRIME), who had no history of CVD were included in the current study. Clinical events reported by the men in postal questionnaires were presented to a validation committee who agreed a diagnosis. Deaths were directly notified to the PRIME team by the Central Services Agency in Northern Ireland. Cox proportional hazards model was used to test for associations.

Results: All-cause mortality was found to be associated with periodontal attachment loss (PAL) and the adjusted hazard ratio for this association was 1.75 (95% c.i. 1.03-2.97). The severity of PAL was found to be related to the risk of all-cause mortality in a dose-dependent manner. There was no significant association found between CVD and periodontal disease.

Conclusion: High levels of periodontal damage as measured by PAL were found to increase the risk of all-cause mortality by 75%. Periodontal disease was not found to be associated with CVD events.

Lung cancer risk of indoor air pollution from solid fuel: a systematic review and meta-analysis

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About 70% of people from developing countries are exposed to solid fuel smoke. The International Agency for Research on Cancer have classified smoke from in-home burning of coal as a Group 1 carcinogen and biomass smoke as Group 2A. The aim of this systematic review was to quantify the impact of biomass fuel and coal on lung cancer and explore reasons for heterogeneity in the reported effect sizes.

A systematic review of primary studies reporting the relationship between solid fuel use and lung cancer was carried out. The review was based on pre-defined criteria and studies that dealt with confounding factors were used in the meta-analysis. Sub-group analyses considered fuel types, smoking, country, cancer cell type and gender. Publication bias and heterogeneity were also estimated.

The pooled effect estimate for coal smoke as a lung carcinogen (OR=1.82, 95% CI 1.60 to 2.06) was greater than biomass smoke (OR=1.50, 95% CI 1.17 to 1.94). The risk of lung cancer for combined fuel was greater in women (OR=1.81, 95% CI 1.54 to 2.12) compared to men (OR=1.16, 95% CI 0.79 to 1.69). The pooled effect estimates were 2.33 (95% CI=1.72, 3.17) for adenocarcinoma, 3.58 (1.58, 8.12) for squamous cell carcinoma, and 1.57 (1.38, 1.80) for tumors of unspecified cell type.

These findings suggest that in-home burning of coal and biomass is associated with an increased risk of lung cancer. The review defined inadequate assessment of smoking in many studies (excluded from review) and recommends factors which must be included in future studies.

Exploring the extent of communication surrounding the transition to palliative care in patients with heart failure.

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Background: The End of Life Care Strategy for England recognises the importance of a timely transition to palliative care (PC) within the context of heart failure (HF). There is evidence that communication around this issue is poor, limiting the capacity of patients and their families to make fully-informed care choices.

Method: The three phases of the study constituted 1) a literature review; 2) interviews (n = 7) and focus groups (n = 3) with 24 HCPs specialising in cardiology and PC; and 3) quantitative questionnaires completed by hospital in-patients with HF (n = 8), and various HCPs involved in their care. The qualitative data were analysed using the principles of thematic analysis. Quantitative data are presented descriptively and comparisons are drawn between data sources.

Results: The literature review identified 19 relevant papers, from which a number of barriers to effective communication about transitions emerged: 1) the unpredictable trajectory of heart failure and resultant prognostic ambiguity; 2) the uncertainty of HCPs regarding patient preferences; and 3) low levels of confidence in dealing with end of life issues due to inadequate education. The data obtained from HCPs supported these findings, and a limited concurrence between palliative medicine and cardiology specialists regarding the communication of prognosis and access to PC services for HF patients was also identified.

Conclusion: There is currently no consensus outlining an ideal format for end of life communication within the context of HF. In addition, there is a need for both established prognostic guidelines and further education to develop communication skills.

Case report on a child with Noonan Syndrome and a previous history of Myelodysplasia presenting with lymphoedema

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Noonan Syndrome (NS) is an autosomal dominant disorder that could be inherited or arise de novo and is caused by dysregulation of the RAS-MAPK pathway. The most common mutation in this pathway is of the PTPN11 gene. NS is associated with a distinct facial dysmorphology, congenital cardiac defects and delayed developmental milestones. Complications that are linked with NS include myelodysplasia and lymphatic dysplasia. This case report presents a 4-year-old female Caucasian patient with a history of myelodysplasia and a current presentation of unilateral lower limb lymphoedema. Her history and facial features were consistent with a diagnosis of NS, a diagnosis which was not considered previously. The probability of this diagnosis being due to a PTPN11 gene mutation in light of her past medical history and the implications of living with a confirmed diagnosis of NS for the patient and her family is discussed in this report.

Investigation of Veins Hypothesis in Multiple Sclerosis

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Introduction: MS is an autoimmune-related disorder but with unclear pathogenesis. A recent study by using high-field susceptibility weighted images (SWI) at 3.0 Tesla (T) has reported a significant reduction in visibility of periventricular white matter veins in MS compared to healthy individuals. However, decreased venous visibility in MS could possibly due to cerebral atrophy. This pilot study compares effects of brain atrophy to veins visibility in MS to vascular patients and healthy individuals by using SWI at 7.0 T.

Methods: Region of interest (ROI) analysis was used to investigate the difference between veins volume in MS and vascular/ healthy individuals. 11 MS, 8 vascular and 2 healthy individuals were participated. ROI analysis was conducted on SWI at 7.0 Tesla to detect veins volume at 3 slices of every patient. Brain volume of every slice was also calculated to normalise the segmented veins.

Results: ROI analysis found lower mean of veins volume in both MS (mean±SED, 3462±221.7mm^3) and vascular patients (mean±SED, 3827±264.6mm^3) compared to healthy individuals (mean±4272mm3). In a subgroup analysis the mean volume of veins in vascular patients that had brain volumes in the MS range, was approximately similar to MS patients. When the veins volume was normalised, no difference between means of the three groups was observed.

Conclusion: Our findings support the previous study of reduced veins visibility in MS patients compared to healthy individuals. Our study also suggests the contribution of cerebral atrophy to decreased veins visibility as we found insignificant difference of median veins volume between MS and vascular disease patients. Further research with larger sample size is proposed to prove the higher parenchymal veins volume in MS patients compared to the other groups.

Mentalizing-related computations during strategic interactions in people with autistic-spectrum disorders

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Background: Successful social interaction requires an ability to generate an internal model of others' thoughts and intentions: a process known as 'mentalising'. This is necessary for negotiating a variety of situations in daily life and difficulties in doing so are believed to underpin the deficits seen in individuals with Autistm Spectrum Disorders (ASD). Little is currently known about how these difficulties influence decision-making in an interactive context.

Methods: We used a recently developed experimental paradigm [Hampton 2008] to assess the contribution of mentalising in 16 ASD and 16 control individuals' performance of a competitive, interactive two-player strategic task known as the 'Inspection game'. 3 mathematical models were compared to subject behaviour- 'influence model' (IM) taking 'mentalising' into account and simpler 'reinforcement learning' (RL) and 'fictitious play' (FP) strategies. Skin conductance was recorded throughout and intelligence and autistic traits were indexed using questionnaires.

Results: Individuals' without ASD behaviour against other humans was better predicted with the IM than simpler RL and FP models with significant differences ($p<0.05$) than those with ASD who were predicted by both models. Moreover, the groups maintained this difference for computer interactions. Prediction by IM/RL ratio showed linear correlations with questionnaires measuring autistic traits.

Conclusion: There are objective differences to suggest that interactive behaviour of individuals with ASD is different to that of individuals without ASD which suggest deficits in 'theory of mind'.

Incarcerated for Illness; Prostitution, Venereal Disease and Lock Hospitals in British India

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Background: New documents recently became available at the National Library of Scotland about Lock hospitals in British India. These hospitals were created following the introduction of the Contagious Diseases Act of 1864 and were designed to stop the rapid spread of venereal disease, such as syphilis and gonorrhoea, by legalising prostitution. Venereal disease affected 20 to 30% of the British army in the late nineteenth century, and therefore had a large impact on how well it could function. Prostitutes were made to register themselves and undergo weekly examinations with a speculum and, if found diseased, were incarcerated and forced to undergo an often lethal mercury treatment.

Discussion: This project has collated historical documents that have not previously been examined to show recurrent themes from the army hospital reports between 1873 and 1890. Eight themes have been identified showing a variety of things, such as reasons why the Lock Hospital system failed to control venereal disease, attitudes towards race and gender in British India and beliefs in science that existed at the time.

Conclusion: The Contagious Diseases Acts were unsuccessful at controlling venereal disease, and the question as to whether this was their full function arises. The Lock Hospital army reports illustrate the utter disregard that the British Empire felt for native Indian people and women at this time, and show that at least part of their purpose was to control both of these groups.

Peptidomic and proteomic analysis of saliva reveals potential biomarkers for predicting oral cancer progression and relapse

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The majority of oral cancer is diagnosed at an advanced stage, with poor prognosis due to high risk of relapse. A protein biomarker in saliva could allow for frequent and non-invasive monitoring to permit earlier diagnosis by predicting malignant progression from oral dysplasia and indication of relapse.

A comparison of the salivary peptidome and proteome of oral cancer, oral dysplasia and control patients was undertaken for discovering differentially expressed proteins.

Pooled saliva samples were combined from 4 oral cancer, 6 mild oral dysplasia, 5 severe dysplasia and 8 healthy control patients.

Comparing the endogenous peptidomes was achieved using liquid chromatography and tandem MALDI mass spectrometry (LC-MALDI MS/MS) of non-trypsinised salivary peptides.

Quantitative shotgun proteomics of salivary proteins was obtained through iTRAQ labelling of trypsinised peptides, mixed-mode fractionation and LC-MALDI MS/MS.

Peptidomic analysis revealed the cancer pool had 4 times the number of peptides from the Proline-Rich Proteins (PRPs), than control and mild dysplasia, whereas the severe dysplasia pool had 3 times the number. This step wise elevation suggests differences in the production or proteolytic activity of these proteins during oral cancer progression.

Shotgun proteomics discovered 9 differentially expressed proteins between cancer and control pools; with Protein S100-A8 in particular, having a 2.4 fold increase in the cancer pool.

This proof-of-principle study indicates there are peptidomics and proteomic differences between saliva of oral cancer, dysplasia and control patients which, after further validation, could be translated for use as salivary biomarkers in the clinical setting.

A cross sectional study investigating the prevalence and associated risk factors of postnatal depression in west rural Kenya

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This study aims to investigate the prevalence of Postnatal Depression (PND) and its associated risk factors in the rural community of Muhoroni in Western Kenya.

Cases of PND were identified using the Edinburgh Postnatal Depression Scale (EPDS). Although the EPDS remains un-validated for women in Western Kenya it has been validated in a number of similar Sub-Saharan African countries. Data were collected in the form of a questionnaire which was delivered by interview. Mothers with a child aged 6-52 weeks were recruited at the local missionary hospital and within the community.

Of the 275 women invited to take part 258 were interviewed (93.82%), and the proportion of women screening positive for PND was 53.5% +/- 6.09% C.I. Women with PND were more likely to have been worried during their pregnancy, to have experienced excessive pain in the first 6 weeks after giving birth and to have suffered recent personal illness or the death of a relative.

The estimate of prevalence for PND was very high in comparison to similar African studies. Besides being a true representation of prevalence, these levels could either be attributable to high existing levels of depression, or because the EPDS is culturally unsuitable for screening for PND in this population. Some risk factors are amenable to interventions which may reduce the risk of women developing PND. Further research should confirm the suitability of the EPDS in Kenya and the prevalence of PND in other parts of the country.

Evaluation of repeated enzyme immunoassay testing in Clostridium difficile infection

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Enzyme immunoassays (EIAs) are the most widely employed test in diagnosing Clostridium difficile infection (CDI). The test is limited by its low sensitivity (63-99%). This has led to repeat testing following an initial negative result. We investigated the value of repeat stool testing.

A database of all stool EIAs ordered for a suspected CDI between January 2007 and September 2008 at University Hospitals Bristol was examined. The areas of emphasis were repeat EIA testing and physicians' patterns of ordering tests.

A total 5031 patients contributed to 11,118 samples. 11% of samples were positive for CDI and 88% were negative. Of those positive, 69% were over the age of 65. 56% had a single test and 44% underwent repeat testing. Of those having 1 or more test 11% were positive, those having 2 or more tests 13% were positive, 3 or more 11% were positive. Those negative on the first test (1483/4519) were more likely to get re-tested than those with a positive result (80/465) (OR 2.36 [95% CI 1.85-3.02]). The proportion of positive tests fell over time (13% in January-November 2007 versus 10% in December 2007-September 2008, $p<0.001$). The rate of re-testing increased over time (26% versus 36% respectively, $p <0.001$).

The study suggests that re-testing following an initial negative result may be beneficial, but the data is inconclusive. Results demonstrate clinicians' lack of confidence in EIA to rule out CDI. The prevalence of CDI has fallen over time. This may have led to the increased rate of re-testing observed.

The Prevalence and Topography of Cerebral Microbleeds in Alzheimer's Disease Patients and Elderly Healthy Volunteers on Ultra-High Field 7 Tesla MRI

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Introduction: The study aimed to evaluate the clinical utility of newly advanced Ultra-High Field 7 Tesla MRI in cerebral microbleed (CMB) study. CMBs are old and asymptomatic haemorrhages and observed as hemosiderin-laden macrophages under microscope. In MRI term, CMB is a focal signal loss (diameter ≤10mm) observed on T2*Gradient Recalled Echo MRI. The study focused on prevalence, topography and cellular location of CMB with associated risk factors of Alzheimer's disease (AD), age and male gender.

Methods: 10 AD patients and 45 healthy controls (mean age=58.9±9.6; 51% male) were recruited in this study. An optimised MRI protocol for CMB detection was used (3D T2*w MRI, 7 Tesla, TE=20ms, TR=50ms, Spatial Resolution=5mm. CMBs were characterised by black, round and atleast half-bound by parenchyma using manual FSL images' detection. The statistical tests used in this study were the Crosstabulation Chi-Square and Logistic Regression Analysis.

Results: The prevalence of CMBs was more than 50% higher than low field MRI study. 70% AD patients and 71.4% healthy controls over 60 years old had atleast one CMB. There was significant association between CMB prevalence and presence of AD, age and male gender ($p<0.05$). CMBs were significantly distributed in temporal lobe in AD patients and frontal lobe in healthy controls ($p<0.05$). Cellular location results showed that AD patients significantly preferred CMB distribution in superficial cortex while age-matched healthy controls preferred subcortical white matter ($p<0.0001$). The Volume-Based Analysis confirmed significant distribution of CMB in temporal lobe for AD patients ($p<0.05$) and white matter region for healthy controls. ($p<0.0001$)

Conclusion: The significant results were robust and coherent with hypotheses and literature background. These paramount findings suggested Ultra-High Field 7 Tesla MRI as important breakthrough in CMB study.

An Unusual Case of Intracaval Leiomyomatosis

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A 42-year old female presented with a six week history of lower abdominal pain, a lower abdominal mass and nausea. The patient was initially operated on for a massive tumour of uterus (8.4cm). The histology gave a diagnosis of intravenous leiomyomatosis. This is a progressive invasion of a leiomyoma (also known as fibroids – benign smooth muscle neoplasm) from the uterus into a vein, which, while "metastasising", is considered benign.

However, the patient developed further symptoms of difficulty in breathing when asleep, chest pain and dizziness. Therefore, due to the histology and the further symptoms, the patient had a series of more detailed investigations to explore the extent of the spread. The investigations included echocardiography, coronary angiography, and contrast MRI.

It was shown that the leiomyoma extended from the pelvis, through the iliac veins, through the left common iliac vein, into the inferior vena cava and then into the right atrium and ending at the A-V junction. The diagnosis of an intracaval leiomyomatosis was then made. Intracaval leiomyomatosis is a rare disease and extension into the right heart is exceptional.

The tumour crossed the drainage angle of the hepatic and renal veins and completely filled the caval lumen. Consequently, there was renal and hepatic dysfunction due to poor drainage of the respective veins. The pulmonary artery however, was not involved. Complete excision of the tumour was achieved under extracorporeal circulation, with subsequent reconstruction of the IVC. The patient went on to make a full recovery after a stay on ITU.

Livedoid vasculopathy associated with a raised factor VIII level; case report and review of the literature related to coagulation disorders

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Livedoid vasculopathy (LV) is a chronic idiopathic disease characterised by painful purpuric lesions and ulceration of the lower extremities. Originally described as a vasculitis, more recently, the main aetiopathology is considered to be vaso-occlusive thrombosis of dermal venules.

We report a case of LV in a 34-year female presenting with extensive ulceration of her feet and ankles. The pain from the lesions was uncontrolled with opiate analgesia and impaired walking. Previous treatment with courses of oral prednisolone with aspirin and pentoxyphylline failed to control the disease.

Biopsy taken from an ulcer edge revealed fibrin deposition within the lumen of dermal blood vessels with an absence of any significant perivascular inflammatory infiltrate, supporting the diagnosis of LV. Screening blood tests for underlying vasculitis were negative. Thrombophilia screen was normal apart from a raised Factor VIII level.

Treatment was started with LMWH at anticoagulant dose and oral dipyridamole. Within ten days there was a 40% improvement in ulceration and she was able to halve her analgesia. After 4 weeks there was an 80% improvement in ulceration and opiate analgesia was discontinued.

This is the first reported case to date of LV associated with a raised factor VIII level; a recognised risk factor for venous thromboembolism. It emphasises the importance of histopathological confirmation of diagnosis, undertaking a comprehensive thrombophilia screen and the therapeutic use of anticoagulant drugs.

A literature review was also carried out of cases of LV associated with coagulation disorders published from 1980-2010; a total of 132 reported cases were found.

We present a case of LV associated with a raised Factor VIII level.

Back Pain as a Presentation of Osteoporotic Vertebral Fractures Secondary to Testicular Involvement in Leprosy

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We present an unusual case of a patient presenting with a common symptom, which was a poorly-recognised complication of his chronic condition.

A 34 year-old man with known lepromatous leprosy presented with a two-week history of severe back pain. Spinal MRI showed multiple compression fractures of T11/12 and L2/4 vertebrae, with vertebral osteoporosis confirmed on DEXA scan. Examination revealed reduced body hair and small testes. Hormone profiling demonstrated reduced testosterone and raised LH/FSH levels, consistent with primary hypogonadism. Testicular involvement of lepromatous leprosy had led to secondary osteoporosis and its resultant clinical sequelae.

Although leprosy classically manifests as skin and nerve destruction, testicular involvement has been reported in up to 80% of patients[1]. Acute lepromatous orchitis or chronic infiltration can lead to primary hypogonadism and reduced testosterone levels in a significant proportion of cases[2]. Most patients present with local testicular symptoms (pain, swelling, reduction in size) or gynaecomastia[3]. This case is unusual in highlighting osteoporotic vertebral compression fractures as the initial presentation of lepromatous testicular involvement.

Osteoporosis is a relatively common complication of leprosy[4], but may be under-diagnosed due to limited awareness of the sequelae of this tropical condition. This case emphasises the need for greater awareness of manifestations of tropical diseases in patients presenting in the UK, and the importance of diagnosing secondary causes of osteoporosis in patients presenting with compression fractures. It also demonstrates that a full clinical assessment should include examination of the endocrinological system, in order to elicit further information in patients with unusual presentations.

Creating A Novel Electronic Resource to Teach the Anatomy of the Hand

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Introduction: We rely on our hands for virtually everything that we do, but despite this many of us will experience a hand condition during our lives. One in five hundred children are born with a congenital abnormality, one in thirty develop a nerve compression problem, and one in five A+E presentations are for a hand related injury. This requires surgical trainees with a sound knowledge of the anatomy of the hand, but evidence suggests that in some cases this is lacking. For example, not all junior doctors are confident in testing muscular function, or diagnosing hand related abnormalities on plain film X-ray.

Aim: The aim of this study was to address these gaps in knowledge with the creation of an innovative electronic educational resource on the anatomy of the hand.

Method: Product development was informed through an appraisal of the pedagogical approaches used for teaching anatomy, a systematic search and appraisal of high quality electronic resources, and a questionnaire completed by 16 clinical staff and 12 medical students. The resource was then created on Camtasia v.7.1 software, using cadaveric photographs produced in the anatomy laboratory, alongside a range of other media types, and the final package reviewed by 11 respondents of the original questionnaire.

Results: Feedback was overwhelmingly positive, with 91% of those reviewing the software believing that it had contributed to their understanding of the anatomy of the hand.

Conclusion: Clinical staff and others may benefit from the creation of innovative electronic teaching resources in anatomy.

Infantile Hypertrophic Pyloric Stenosis and Gestational Age: A 12 month Retrospective Study on Paediatric Surgical Patients at St George's Hospital

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Kumar & Abels report the yearly incidence of infantile hypertrophic pyloric stenosis (IHPS) in the UK around 3 per 1000 live births[1]. Characterised by projectile vomiting few weeks after birth[2]. Treatment involves appropriate resuscitation, followed by pyloromyotomy[3]. Physical examination has shown to detect about 90% cases in experienced hands[4]. This rate is reported as declining due to the dependence on ultrasound scans, which have shown a sensitivity of 97% and specificity of 99% in diagnosing IHPS[5]. A 12month retrospective study conducted collecting data from paediatric surgical patient notes to determine whether a new criterion was needed to help identify at risk patients.

15% (9/59) IHPS were female, and 85% (50/59) were male. The mean age of 38days old (range 12days to 118days). 86% (51/59) infants were correctly shown to have IHPS on examination. 12% (7/59) reported as IHPS on examination but shown to have reflux on ultrasound. 88% (52/59) had IHPS which were classified as 8% (5/59) small IHPS, 41% (24/59) moderate IHPS and 39% (23/59) severe IHPS. Ultrasound measurements reported the mean length of the pylorus was 20.4mm (34/40). The transverse diameter was 11.8mm (17/40). The mean muscle thickness was 4.5mm (34/40).

This study found that there is a correlation between gestational age and increasing size of pyloric length, transverse measurements and muscle thickness[6]. Males were at a greater risk[7]. There is a need to find universal criteria to use alongside ultrasound to help identify those at risk. These patients can be followed up to ensure their well being[1,5,8,9].

The Assessment of Psychotic-Like Experiences in Childhood and Adolescence

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Introduction: The study of psychotic-like experiences (PLEs) in adolescence offers valuable insight into the development of psychotic disorder. Semi-structured interviews are the 'gold standard' for their assessment but are more time consuming and expensive than self-reports. The evidence regarding their validity of self-reports is equivocal.

Methods: Semi-structured interviews were performed at ages 12+ (n=6467) and 17+ (n=3477), using the ALSPAC cohort. Positive responses to stem questions triggered further questioning, following which the interviewer assessed symptom presence. Questionnaires were performed at ages 13 (n=7129) and 16 (n=5126). PPVs and sensitivities were calculated, before and after cut -offs suing additional information were included.

Results: The PPVs for interview stem questions were higher than for questionnaires. Most symptoms had poor PPVs, except for auditory and visual hallucinations. PPVs improved when excluding 'maybe' responses or 'suspected' ratings by the interviewers. PPVs could be improved by using cut offs based on frequency, distress, duration, or symptom number, but this caused sensitivity to fall.

Discussion: The questionnaire PPVs were probably underestimated because they were performed at different times to the interviews. However, the low PPVs for stem questions suggests a ceiling effect. Improvements were possible but the reduced sensitivity indicates this approach would be of little worth for screening. Ultimately the PPVs and sensitivities are likely to have been constrained by the low prevalence of PLEs. Future research should focus on utilising questionnaires as an initial screen, with follow up interviews. This could this save on resources, and provide additional insight into the development of psychotic disorder.

Immature Teratoma of the Omentum

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Germ cell tumours are an uncommon but well-documented malignancy of the ovary that account for 1-2% of ovarian malignant disease. Germ cell tumours of the omentum are extremely rare; a literature search reveals only 30 reports of omental teratomas since the first case in 1734, of these reports only two describe immature teratomas.

We would like to describe a case of an immature teratoma of the greater omentum. This subtype of germ cell tumour has only been documented twice in medical literature and it is therefore important to describe the patient's presentation and management to promote a better understanding of the disease course and outcome.

A 27 year old woman was seen in gynaecology clinic for investigation of her primary subfertility. History and examination identified a pelvic mass which was confirmed with MRI investigation. At laparotomy a mass was removed from the greater omentum and sent for histology. The mass was confirmed as an immature teratoma and it was decided that chemotherapy should be commenced after egg-harvesting for fertility preservation had been undertaken.

Unfortunately the patient developed a recurrence after completion of her chemotherapy and underwent further surgery. She continues to be followed-up in clinic.

We review the relevant literature to discuss the etiology of this rare tumor and our management strategy.

This case report is a chance to discuss the impact of an aggressive tumor in a young woman trying for children and we aim to consider the significant social issues along with the unusual histological findings.

Orlistat Prescription Outcomes in Primary Care Weight Management: From Drop-Out Rates to Weight Gain

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The NICE obesity guidelines recommend Orlistat use in weight management programmes if lifestyle changes have limited benefit. Discontinuation of prescriptions is suggested if patients fail to reach recommended weight loss targets (5% and 10% total weight reductions by 3 and 6 months respectively)(1).

The aim of the audit was to assess Orlistat prescription in the GP weight management programme. A retrospective case review was undertaken using electronic records. Data was standardised as percentage weight change from baseline. Mean BMI for the 107 patients identified was 38.4kg/m2 (29 – 69.34).

Drop-out rate before first FU appointment was 19%. Combined drop-out/discontinuation rates by 3 month FU was 60%. Only 40% of patients continuing treatment at 3 months reached recommended weight loss, with a significant reduction of 4.63% (85–102%, $p<0.05$). 24% continuing treatment at 6 months achieved 10% loss, with average 6.38% reduction (80–105%). Six month weight change was not statistically different from 3 month FU ($p>0.05$). Of those patients not achieving 3 and 6 month target weights, the percentage continuing beyond those points was 85% and 77% respectively. Patients continuing treatment past 3 months despite not hitting targets still failed to lose 5% by 6 months (16/22). 19% of end-point weights showed no change/increased weight from baseline.

Orlistat treatment showed high drop-out rates and modest achievement of recommended weight loss targets. Unless patients show a good initial response, weight loss generally remains minimal throughout. Strict prescription protocols (similar to NICE guidelines) could reduce prescription costs and improve outcomes.

Reference: NICE clinical guideline 43, issue December 2006

A study of potential additional benefits of GLP-1 agonism with liraglutide in type 2 diabetes

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Objective: To assess the clinical outcomes of liraglutide administration in subjects with type 2 diabetes in Tayside region, with emphasis on HbA1c, blood pressure and body weight, hence the potential benefits in the management of diabetes and its associated complications.

Methodology: Anonymised data on type 2 diabetic patients who had been started on liraglutide (n=99) were extracted from Health Informatics Centre (HIC). Parameters analysed were HbA1c, body weight, body mass index, systolic and diastolic blood pressure, total cholesterol, HDL cholesterol and triglycerides. Baseline and results after 44.00 - 52.75 weeks were compared using paired t-test for statistical significance.

Results: Mean baseline HbA1c for the study population was 81.53 mmol/mol (9.62%). A mean reduction in HbA1c of 12.21 mmol/mol (1.12%) (n=62, p<0.00001) was observed with liraglutide after a median follow-up of 44 weeks. Use of liraglutide had also resulted in a mean reduction in SBP of 6.45 mmHg (n=54, p=0.0055), DBP 0.92 mmHg (n=55, p=0.42), weight 3.61 kg (n=44, p<0.0001), BMI 1.27 kg/m2 (n=41, p<0.0001), triglyceride 1.22 mmol/L (n=5, p=0.38), total cholesterol 0.07 mmol/L (n=6, p=0.068) and HDL 0.00 mmol/L (n=5, p=0.90).

Conclusions: Liraglutide produces additional non-glycaemic benefits on top of glycaemic control in type 2 diabetes and has the potential to limit associated complications. These beneficial effects include weight reduction and improvements in systolic and diastolic blood pressure. It could be a promising regimen in the clinical management of diabetes mellitus.

Audit of practice of oesophageal endoscopy: How accurate is our diagnosis and should oesophagitis be biopsied?

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Gastroesophageal reflux disease can lead to Barrett's oesophagus (BO). These patients are at higher risk of developing high grade dysplasia and oesophageal adenocarcinoma (OAC). In some cases, BO and cancer are diagnosed by biopsying oesophagitis (OS). The Royal College of Pathologist's (RCPath) guidelines advise against biopsying oesophagitis but not BO.

Patients were identified from electronic histopathology and Barrett's databases. Clinical data was collected from NotIS and WebHISS covering the period 2003-2009.

Among 42 patients diagnosed with HGD or T1 OAC, 4 (9.5%) were diagnosed due to biopsying OS and 15 (35.7%) by biopsying BO, the remainder being diagnosed based on normal biopsies or biopsies of suspected lesions. A total of 140 patients had a new diagnosis of BO. 6/140 (4.2%) were diagnosed based on biopsies for OS with no endoscopic features of BO.

Among 58 patients with OAC who did not receive a previous endoscopy, 36 (62%) had stage ≥3 OAC, while 8/58 (14%) had stage 1 OAC. Of 20 patients who had previous endoscopies within 5 years, 11/20 (55%) had stage ≥3 OAC and 8 (40%) had stage 1. All but one Barrett's surveillance patient had a stage 1 OAC. Out of 245 endoscopies performed in November 2009, 12/26 patients with OS had biopsies taken.

Biopsying of OS within the NUH trust is not in agreement with current RCPath guidelines. However, a significant proportion of patients with cancer and BO were diagnosed based on this practice. The cost-effectiveness of routine biopsies needs to be weighed against clinical judgement.

Does atopic disease have an impact on the association between giardiasis and post-infectious chronic fatigue and irritable bowel syndrome?

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Background: Bergen, Norway, was exposed to an outbreak of Giardia lamblia caused by contamination of the city centre's main water supply in 2004. A historic cohort study was initiated.

Methods: Three years after the outbreak, a questionnaire was sent to all laboratory confirmed cases of giardiasis (n=1262). 817 (response rate 64.7%) were included in the exposed group. 1128 controls (response rate 31.4%), matched for age and sex, were included in the study. Crosstables were used to analyse prevalence. Confounding and effect modifiers were evaluated by use of logistic regression analyses, which was also used to adjust for confounders.

Results: In the exposed group, 47.8% of those with asthma had IBS, in controls with asthma 23.9% had IBS ($p<0.05$ for the difference between the groups). In the exposed group without asthma, 45.3% had IBS, in controls without asthma 12.2% had IBS ($p<0.05$). Looking at chronic fatigue, in the exposed group with asthma, 51.5% had CF and in controls with asthma, 19.3% had CF ($p<0.05$). In the exposed group without asthma, 44.9% had CF, in controls without asthma 10.7% had CF ($p<0.05$). Allergy followed the same pattern as asthma regarding the prevalence of IBS and CF.

Conclusions: Having asthma or allergy increases the risk of IBS and CF in the control group. In the group exposed to giardiasis 3 years previously, atopic disease status was not associated with higher prevalence of IBS and CF. However, this group has a very high prevalence of the outcome measures irrespective of the atopic status.

Ponseti Technique Achilles Tenotomy: Can the feel of the tenotomy predict problems?

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Introduction: Ponseti clubfoot treatment has gained popularity over the last decade. The infant is likely to undergo an Achilles tenotomy as part of their treatment. It is well recognised amongst practitioners performing this procedure that there is usually a satisfying give with the tenotomy but in a minority there is a slow gradual release. To the authors knowledge we are not aware of any studies looking at ease of tenotomy to predict problems.

Method: We reviewed the medical records of 69 infants who had visited the Ponseti Clinic and underwent tendo Achillis tenotomy (20 female, 49 male).

Results: The number of pre-tenotomy casts averaged at 3.6 (min 2 – max 11). There were a total of 104 tenotomies (right 20, left 14, bilateral 35). 27 had a gradual release of which 26 required longer treatments in cast or re-tenotomies (4). 4 patients had bilateral tenotomies of which one side was a good release and the other was gradual. In all of these patients the side with a gradual release required longer in cast post-tenotomy.

Conclusions: Our study shows that patients with a gradual release are more likely to stay in a cast for longer post-tenotomy or require re-tenotomy. We recommend that these patients are reviewed more closely to ensure they do not run into any problems. We also recommend an ultrasound scan three weeks post tenotomy

Will I live? An assessment of the accuracy of prognostic tools used to predict the survival of young women with breast cancer

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Background: How long will I live, is a question many ask when diagnosed with breast cancer. This is difficult to answer in young patients (<40 years) since the literature suggests they have higher mortality and the prognostic tools are considered less accurate. We considered two prognostic tools: Nottingham Prognostic Index (NPI) and Adjuvant Online (AOL), in a group of young patients, comparing their predicted prognosis with their actual survival.

Methods: Data was collected from the breast unit at the DPOW Hospital, Grimsby between January 1998 and December 2006. A cohort of 90 young primary breast cancer patients was created and actual survival data was recorded. The NPI and AOL scores were calculated and used to estimate 10-year survival probabilities. Pearson's correlation coefficient was used to demonstrate the association between the NPI and AOL scores. A constant yearly hazard rate was assumed to generate 10-year cumulative survival curves using the NPI and AOL predictions.

Results: Actual 10-year survival for the 81 patients who underwent potentially curative surgery was 76.6% (CI:68.0-86.2%). No significant difference existed between the actual survival and the NPI and AOL 10-year estimated survival, which was 76.6% and 81.9% respectively. The NPI and AOL results demonstrated strong correlation. Pearson's correlation coefficient was 0.927 ($p<0.01$). Overall the NPI cumulative survival curve more accurately reflected the actual survival in young patients.

Conclusions: The tools used to predict survival for young breast cancer patients have been shown to be statistically robust with the NPI possibly being a stronger predictor of patient survival.

CSF leaks and their repair following transsphenoidal pituitary surgery for tumour resection

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Background - Following hormone insufficiency, CSF leaks are the most common complication of transsphenoidal pituitary surgery for tumour resection. Several repair methods exist, information regarding their use is however limited. This study aims to identify the frequency and extent of CSF leaks following such surgery, and to determine the success of the repair methods commonly employed.

Methods - Operative reports and discharge summaries of the 255 patients that underwent pituitary surgery, performed by one neurosurgery consultant, over a 5 year period, were retrospectively reviewed. Noted were the number of CSF leaks, graded as small, moderate or large, the repair method employed in each case, its outcome, and any resulting complications.

Results - 38% (97/255) of patients experienced a CSF leak during their initial surgery, 76.3% (74/97) of which were graded "small". 73.2% (71/97) of initial repairs were carried out using spongostan and duraseal, more extensive methods were employed for the remainder. 3.1% (8/255) of patients developed a post-operative leak, 50% (4/8) of which were the result of initial repair with spongostan and duraseal. 37.5% (3/8) of post-operative leaks were treated conservatively with the remainder requiring surgical repair. No cases of meningitis occurred.

Conclusions - CSF leaks present a meningitis risk making their recognition and repair essential. Most leaks were successfully repaired using spongostan and duraseal with other methods having lower success levels. Extensive repairs were however more common with larger leaks and may be equally successful at treating small leaks as simpler methods, increased complication risk however precludes such use.

Audit of adherence to MRSA screening protocol

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Introduction: MRSA (Meticillin Resistant Staphylococcus Aureus) is a major cause of morbidity and mortality. The authors undertook an audit in October 2008 assessing adherence to MRSA screening protocol in Mayday Healthcare NHS Trust on the Care of the Elderly wards. The audit was presented to the department and actions were implemented to improve practice. A re-audit was then performed in October 2009.

Method: Data was obtained in retrospect from patient notes and electronic records of all inpatients on the Elderly Care wards in Mayday Hospital during October 2008 and October 2009. 114 and 124 patients were included in the audit and re-audit respectively.

Results: "All patients >65 years old admitted through A&E should be screened for MRSA colonisation on admission" was the first standard assessed. Compliance with this standard was 46.4% in 2008, compared with 86.3% in 2009.

"All MRSA negative patients at risk of MRSA infection (invasive devices, open wounds, new-onset sepsis, critical care) should be re-screened for MRSA weekly" was the second standard assessed. Compliance with this standard was 10.7% in 2008, compared with 47.4% in 2009.

Discussion and recommendations: There has been a marked improvement in the number of patients receiving an MRSA screen on admission. However, re-screening protocol of MRSA-negative patients remains poor. The authors recommend:

1. All nursing staff should be granted authorisation to complete the electronic MRSA screening forms
2. MRSA protocol should be clearly published on the wards
3. A MRSA screening checklist should be incorporated into the patient drug charts

Laparoscopic cholecystectomy without intra-operative cholangiography

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The routine, selective and non-use of intra-operative cholangiography (IOC) during laparoscopic cholecystectomy (LC) is the subject of a worldwide debate. This study evaluates the management of patients with gallstones without the use of IOC during LC. Patients who presented with gallstones from 2002 to 2011 were selected and data were prospectively collected including demographics, clinical presentation and the results of abdominal ultrasound (US) and liver function tests (LFTs). Patients were classified according to the risk of common bile duct (CBD) stones and received Magnetic Resonance Cholangiopancreatography (MRCP) or Endoscopic Retrograde Cholangiopancreatography (ERCP) accordingly. The incidence of CBD injury was recorded and re-admissions following LC and subsequent interventions documented. Seven hundred and seventeen patients were identified, 549 (76.6%) of whom were classified as low risk and did not receive MRCP or ERCP. Out of the low risk group, there were only 19 re-admissions following LC and stones were confirmed on ERCP in three patients. The remaining 169 patients (23.6%) were classified as medium or high risk and underwent MRCP or ERCP with the identification of stones in 57 cases. During LC, minor injury of the CBD occurred in three patients. One patient suffered an unrecognised ischaemic injury following open conversion and received reconstructive biliary surgery seven months later successfully. Laparoscopic cholecystectomy can be performed safely without the use of IOC. The selective use of MRCP and ERCP is an adequate protocol for pre-operative investigation, identification and management of stones within the CBD.

Quality of Life After Total or Subtotal Gastrectomy for Gastric Carcinoma

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Background: There remains some debate as to whether there is a better quality of life (QOL) for patients following total gastrectomy (TG) and subtotal gastrectomy (SG) for cancer. At present it would appear that although TG has a higher post-operative mortality and morbidity than SG, both have similar survival rates provided an R0 resection is performed. The aim of this study is to evaluate and compare the quality of life in patients after TG and SG.

Methodology: Ninety-four surviving patients out of a total of 231 who had undergone TG or SG between 1994 and 2009 were identified from a prospectively collected database. All patients were sent out the European Organisation for Research and Treatment of Cancer (EORTC) core questionnaire (QLQ-C30 v.3) and the gastric module (QLQ-STO22). 53 patients responded, with a mean age of 73 years, 25 had TG and 28 SG. Results from the TG and SG group were compared using the independent samples t test with the aid of PASW.

Results: There was no significant difference between the quality of life between TG and SG based on functional scales and global health status. However dysphagia and eating restrictions, which are part of the gastric cancer-specific module (QLQ-STO22), were shown to be significantly worse in the TG group than the SG group (p=0.04 and p=0.023 respectively).

Conclusion: This study has demonstrated that there is no difference in overall quality of life in patients with TG or SG, although dysphagia and eating restrictions are worse after TG.

Audit of the Management of Urinary Incontinence in Women over 75 years: A Retrospective Review of 50 Case Notes

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Background: The prevalence of Urinary Incontinence (UI) increases with age, and is associated with significant co-morbidities as well as considerable negative impact on quality of life. A growing population of older people means it is a rising problem in this already vulnerable population. The prevalence in older adults in 24 hour care is 60% and 35% in older hospitalised patients. UI is often disregarded as a normal part of aging by health professionals, resulting in improper investigation and management. This highlights the necessity of this Audit.

Method: Following a review of current National Guidelines for the management of UI in elderly women, a simple pro forma was derived outlining six key components of assessment and treatment. The pro forma created was used to Audit the management of 50 patients on care of the elderly wards in the hospital using their case notes.

Summary: 88% of incontinent patients were asked about symptoms. Only 10% received appropriate examination. 76% and 80% had urinalysis and blood glucose/calcium performed respectively. Alarmingly, 0% of patients had the type of UI classified as stress, urge or mixed. Subsequently, 0% received appropriate treatment.

Conclusion: Knowledge of current guidelines amongst healthcare professionals is sub-standard. No element of assessment or management is entirely fulfilled. Classification of incontinence and initiating of treatment were particularly inadequate areas. Therefore, it is crucial that the current guidelines are reinforced through teaching programmes for foundation doctors and through appointment of link nurses on wards to provide advice on basic continence assessment.

Validation of a new index to predict mortality from community-acquired pneumonia in Malawi; the SWAT-Bp score

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Community-acquired pneumonia (CAP) is prevalent in Malawi, in part due to HIV co-infection, and currently there is no rapid method of assessment for use on admission to hospital. In developed countries, severity scores are accurate methods by which to stratify patients according to their risk of mortality, but these scores exclude patients with HIV infection. The aim of this study is to validate the accuracy of the SWAT-Bp score in predicting the mortality risk from CAP in patients admitted to hospital in Malawi.

The five variables constituting the SWAT-Bp score (male **S**ex, muscle **W**asting, non-**A**mbulatory, **T**emperature (>38^{o}C or <35^{o}C) and **B**lood pressure (SP<100 and/or DP<60)) were recorded for all patients presenting with CAP in the Queen Elizabeth Central Hospital, Blantyre, Malawi, over a period of six weeks (n=115). The sensitivity and specificity of the score were calculated to determine the accuracy at predicting mortality risk.

Median age was 35 years, HIV prevalence 88.2% and mortality rate 9.6%. The SWAT-Bp cut-off point of 2 is most sensitive (90.9%) and specific (70.2%) for predicting the mortality risk, with high accuracy (AUC 0.852). A SWAT-Bp score of ≤2 indicates a low risk of mortality (1.4%) and a score of >2 indicates more severe pneumonia with higher mortality risk (24.4%).

The SWAT-Bp score is a valid tool for rapid assessment of pneumonia severity on admission to hospital in Malawi, thereby assisting in effective management of patients. Further validation following the imminent introduction of the score in Malawi is required.

An Audit Analyzing Care of Children and Adolescents with Type 1 Diabetes Mellitus Before and After Treatment with Subcutaneous Insulin Infusion Pumps

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Objective: To analyze the care of children with Type 1 Diabetes Mellitus before and after treatment with subcutaneous insulin infusion (CSII), by means of measuring the HbA1c trend, insulin requirements, admissions to hospital and episodes of diabetic ketoacidosis (DKA).

Background: Injections constitute the commonest method of insulin administration. However, meals and physical activity need to be adapted to the injection regimens. CSII pumps allow flexibility in both timing and amount of meals and physical exercise, with greater resemblance to physiological insulin function. Several studies have shown an improvement in glycaemic control and reduction in the frequency of hypoglycaemia following treatment with insulin pumps.

Method: Data was collected from the notes and Electronic Patient Records of 15 patients treated with insulin pumps. Data was collected on HbA1c levels, insulin requirements, admissions to hospital and episodes of DKA before and after treatment with insulin pumps. The total daily insulin dose per kilogram of body weight and the HbA1c trend were calculated. The data was analyzed and results from before and after initiation of treatment with an insulin pump were compared.

Result: HbA1c levels and insulin requirements were shown to decrease on pump therapy. Hospital admissions were also shown to decrease by 73.3% and the incidence of DKA declined by 49.9%.

Conclusion: Treatment of diabetic children with insulin infusion pumps in Wrightington, Wigan and Leigh was shown to be effective and lead to an improvement in glycaemic control. Despite a significant reduction, HbA1c levels however remained above target range for most patients.

Estimation of goiter endemic severity and iron deficiency prevalence in adolescent girls living in the region of Tyumen

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Iron and iodine deficiency are among the most common pathological conditions that affect physical and mental development. Here, we investigate the prevalence of goiter and iron deficiency in adolescent girls of Tyumen region, and evaluate to which extent this is linked to iron deficiency in mothers.

The study was conducted in a population of adolescent girls aged 13-18 (n=152). Thyroid gland volume was measured by ultrasound to evaluate goiter prevalence (M. Zimmermann, WHO, 2003). Iron deficiency was diagnosed by iron concentration (immunoturbidimetry) and ferritin levels (colorimetric method). Thyroid function was monitored by hormones levels. Additionally, frequency of thyroid diseases, anemiaand use of iron/iodine drugs among the subjects' mothers were collected.

In examined groups, goiter frequency and reduced thyroid function were found in 15% and 3.2% of cases, respectively. Noticeably, 28% of subjects presented latent iron deficiency (LID) and 8% anemia. Investigating this high LID frequency in adolescents, we found a negative correlation between mother's anemia duringpregnancy and the serum iron (SI) levels of their girls ($r = -0.19$; $p=0.028$). Thyroidpathologies contracted during pregnancy negatively correlated with SI levels in girls($r=-0.44$; $p=0.035$).

Importantly, we found a strong correlation between iron drug usage during pregnancy and the serum ferritin level of girl ($r=0.51$; $p=0.013$). These results suggest that Tyumen region has a mild goiter epidemic. Interestingly, the treatment of LID and anemia during pregnancy diminish the susceptibility for iron deficiency in girls. This also highlights the need for additional therapeutic and diagnostic programs to reduce LID prevalence.

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The Use of Anti-epileptic Drugs in People with Profound Intellectual and Multiple Disabilities with Epilepsy

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Epilepsy has been found to be more prevalent in those with learning disabilities (LD) than in the general population. Seizures in this population are associated with higher mortality and morbidity and are refractory to treatment. Little is known about treating epilepsy in these patients because of the lack of quality research. They remain on more old-fashioned anti-epileptic drugs (AEDs) due to the lack of evidence on the efficacy, tolerability and safety of newer AEDs in this population.

The clinical notes of all 300 patients with profound LD in the catchment area were analyzed for details of any epileptic seizures and subsequent management. Of the 300, 95 (31%) have epilepsy and 75 were eligible for the study. Of these 75, 24% were defined as seizure free and they were treated with 11 different therapy regimens, with 56% achieving seizure control with only one AED. The three particularly promising regimens were sodium valproate, carbamazepine and lamotrigine monotherapy. At least 36% of patients on each of these therapies were seizure free. Suprisingly, 48% of patients were taking a newer AED and, of these, 25% were seizure free. On the other hand, 50% of the seizure free patients were taking at least one newer AED, although 78% of seizure free patients were taking a classical AED.

In conclusion, epilepsy is more prevalent and intractable to treatment in patients with LD. Several therapies could offer seizure control; and that newer AEDs can be effective at controlling seizures but their safety needs to be established.

Management of Neonatal Umbilical Cord Gas Results – An Evaluation of the Efficacy of Current Local Guidance

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With respect to disability-adjusted-life-years, intrapartum asphyxia (IA) is the eighth leading cause of health burden in the world1. Sustained IA can result not only in early neonatal morbidity2, but can also impact significantly on a child's life3 4. For this reason, obstetric care is often scrutinised in retrospect, with particular emphasis placed on objective measures of foetal intrapartum oxygenation. Umbilical cord sampling (UCS) is one such objective measure, which can be invaluable in the assessment and management of the newborn.

This project aimed to address several areas of the UCS guidance at a Lancashire teaching hospital. Compliance with the clinical indication/s to take a sample, as well the management of neonates with abnormal UCS results, was audited by considering 1,460 births between 01/01/2010 and 31/04/2010. The accuracy of the samples taken was also considered, according to the arterio-venous pH and pCO2 differences, and demographical details including birth-weight and delivery method were collected.

Overall, 39.4% of the neonates with an indication for UCS had an accurate paired sample taken, and management of neonates with an abnormal UCS was poor, with 16.7% having their oxygen saturation measured. The accuracy of results was significantly worse in operative compared to vaginal deliveries [U=1697, p< 0.001]. In addition, significantly more babies with an abnormal UCS had meconium stained liquor [c2=11.31, df=2, p=.003].

Discordance between the guidance from the Women's, and Child Health directorates may account for the poor compliance demonstrated. The absence of information on the UCS procedural technique could be related to the inaccuracy observed, perhaps more so in operative deliveries due to differing priorities of care. A revised collaborative guideline incorporating recommendations on several areas of clinical practice relating to UCS has been produced; it is hoped that this will aid in improving the local care of all neonates at risk of IA.

The Potential of Oral Iron Supplements to Decrease Blood Transfusion in Elective AAA Surgery

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Background: Elective AAA surgery is associated with blood loss and resulting intra/post-operative transfusion.

Blood transfusions are financially costly and strain a reducing donor base. They are also correlated with post-op wound & chest infections, prolong admissions and risk transfusion reactions & infection transmission.

Haemoglobin levels have been shown to increase by 1.73 g/dL with a 3-4 week oral course of ferrous sulphate.

Pre-operative iron supplementation could reduce the percentage of patients transfused, total units used, complication rates and admission duration

Study: Retrospective case notes analysis of 50 elective open AAA repairs determining:

1. Blood transfusion rates, pre- & post-op Hb
2. Potential benefit of pre-op ferrous sulphate to patient, blood-bank resources and NHS cost

Summary of Results:

50 patients. Mean age 73.4 (59-88).

Mean Hb pre-op 14.0 & post op 9.9.

56% of patients requiring blood transfusion: 21/50 intra-op & 14/50 post-op.

Overall, average transfusion rate was 2.22 units per patient.

11 patients had 2 units or less transfused

Conclusion: In this study, giving a 2-3 week course of ferrous sulphate prior to elective AAA surgery could reduce the percentage of patients requiring blood transfusion from 56% to 34%; save 42 units of packed red cells, over £10,000; or £200 per patient.
The limits of any retrospective study are apparent. However this research has served to determine the potential of a larger prospective RCT which, as a direct result of these findings, will be starting shortly.

Audit of the use of Non-Invasive Ventilation in patients with chronic obstructive pulmonary disease

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Non-invasive ventilation (NIV) has been shown to reduce intubation rates, length of stay and mortality in patients with chronic obstructive pulmonary disease (COPD) in decompensated type two respiratory acidosis. National guidelines state in the absence of contraindications, NIV should be considered within sixty minutes of hospital arrival when medical treatment fails. The efficacy of treatment should then be closely monitored and plans documented in the event of failure.

We aimed to determine whether NIV was being used when indicated and assess adherence to national guidelines once initiated.

Patients were identified through medical coding and laboratory blood gas records. Case note review and completion of the standardised BTS proforma were used to assess the completeness and appropriateness of intervention.

Twenty-one patients fit the inclusion criteria. Of these, fifteen received NIV. In two patients valid reasons for not commencing NIV were documented. However in the remaining four cases there was no evidence of NIV being offered.

Documented evidence of one- and four-hourly blood gas monitoring was found in only six and four of cases respectively. There was no evidence of plans if NIV failed in three cases and target inspiratory pressures were only reached in two cases.

The audit concluded shortcomings in our delivery of NIV. Lack of knowledge among staff was identified in a subsequent questionnaire, as well as poor documentation and inappropriate oxygen therapy as key areas for improvement. We have subsequently developed a trust NIV training package, revised our NIV documentation and amended the drug charts to include oxygen.

Should certified practical skills courses be made available to all Foundation Year trainees?

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Competency in practical skills is an important aspect of training for the Foundation Year (FY) doctors. This questionnaire survey aimed to investigate if the current FY trainees have performed several practical procedures of importance and their level of confidence in carrying them out unsupervised.

A questionnaire on the number of times that the doctors have performed these skills and their level of confidence was distributed to FY trainees in six NHS hospitals in England.

88 FY trainees responded to the survey (58 FY1s; 30 FY2s). The percentage of trainees who have performed these skills and their average level of confidence (in a scale of 1 to 5) are as followed: intubation (32%,1); chest drain (33%,1); central line (26%,1); femoral line (23%,1); peripheral line (28%,1); lumbar puncture (64%,3); ascitic tap (57%,3). Only 25% of the trainees have attended certified training courses on these skills during their FY training (21% FY1s; 33% FY2s). More than half of these trainees (73%) found the courses very useful. 92% of trainees who did not attend practical skill courses are very interested to attend them. All the trainees agreed that these courses should be available for all the FY doctors. 92% believe that these courses are most beneficial during the FY1 training.

In conclusion, most FY trainees have low confidence and exposure to these important practical skills. Certified practical skills courses should be made available to the FY doctors for the benefit of their trainings and competencies. This will also increase the quality of patient care.

Metabolic outcomes following laparoscopic adjustable gastric banding and Roux-en Y Gastric bypass surgery in obese diabetic and non-diabetic individuals

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Background: Obesity and its complications, including type 2 diabetes mellitus are a global challenge. Diet, with or without pharmacological intervention fails to achieve significant weight loss in the majority of cases. Bariatric surgery is gaining popularity as a treatment option. This audit assesses the metabolic outcomes following laparoscopic adjustable gastric banding and Roux-en-Y gastric bypass surgery.

Methods: A retrospective study, which included all patients who underwent laparoscopic adjustable banding (n=241) and Roux-en -Y gastric bypass (n=41) at our centre between January 2009 – January 2010. Pre and post operative (up to 12 months following surgery) data, including weight, diabetic status (HbA1c and drug regimes), lipid profiles (total cholesterol, LDL, HDL cholesterol and triglyceride) and peri-operative insulin requirements were collected and analysed to assess weight loss, improvements in diabetes and co-morbidities.

Results: Mean preoperative BMI (kg/m2) of the bypass patients was 52.1±7 with a mean age of 42.9±9 years. At 6 weeks, 3, 6, 9 and 12 months postoperatively, percentage excess weight loss (%EWL) was 24.5±9.5, 36.0±11.7, 48.2±14.0, 60.1±13.8 and 59.0±17.9 respectively. Bypass achieved greater weight loss compared to gastric banding ($p<0.01$). No difference in weight loss between diabetics and non-diabetics was observed ($p>0.10$). There were significant improvements in HbA1c; decreasing by a mean (±SD) of 1.2±1.1% and all diabetic patients experienced reduction in diabetic medications at 12 months. Improvements in other risk factors were also observed following bypass surgery.

Conclusion: RYGB is highly effective in achieving weight loss in morbidly obese subjects. The procedure is also associated with dramatic improvements in diabetes and other risk factors.

TTAs vs. EDSs: A comparison of methods of providing primary care with a discharge summary

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Background: It is a compulsory requirement that a hospital produces a discharge summary. This provides a summary of the reasons for admission, diagnosis and consequent management plan. This is often the only documentation a GP receives in relation to a recent admission. In effect a discharge summary is a form of 'handover'. Producing a detailed and thorough discharge summary results in financial gains. Traditionally the discharge summary is hand-written and commonly referred to as the TTA ('to take away'). Recent years has seen the introduction of the EDS (electronic discharge summary). This audit provides a comparison of the TTA and EDS methods of producing a discharge summary.

Methods: This retrospective audit used a random sample of 50 TTAs and 50 EDSs were selected from one ward in a two-month period. Completion rates for criteria of the discharge summary were analysed.

Results: The EDS is a superior form of discharge summary, significantly for documenting diagnosis, co-morbidities, investigations, drug history and instructions for GP. One major concern highlighted in performing this audit is that many doctors were unaware of where and how to document co-morbidities due to inadequate training.

Conclusions: Junior doctors should be more aware of the importance of the discharge summary; they should be providing clear, complete and concise information. Documenting co-morbidities has implications on clinical coding, and in turn financial incentives, therefore training in the use of the EDS should be improved. There is a place for other healthcare professionals to contribute to the discharge summary.

The Utility of Ejection Fraction (EF) in an Elderly Heart Failure (HF) Population

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Background: Major differences in co-morbidities, age and gender have been identified between HF with preserved ejection fraction (HFpEF) and HF with reduced ejection fraction (HFrEF). However there is limited and conflicting data concerning outcomes between HFpEF and HFrEF. EF may have limited utility in predicting outcomes among HF patients, implying that it is becoming a redundant measure for the management of HF.

Methods: Retrospective cohort study of 514 hospitalised elderly HF patients (2005 - 2007). Covariates including Left ventricular ejection fraction (LVEF) were assessed against mortality to determine significance. The population was categorized by age to determine the relationship of LVEF to age.

Results: LVEF was not predictive of 30 ($p = 0.55$) or 360 day mortality ($p = 0.485$). LVEF lacked prognostic use for 30 and 360 day mortality among all three age categories, < 76 years ($p = 0.56$/ 0.638), 76 – 85 years ($p = 0.486$/ 0.169) and > 85 years ($p = 0.844$/ 0.035). Liver function tests (LFT) were predictive of 30 and 360 day mortality. This included creatinine ($p = 0.005$/ < 0.05), bilirubin ($p = 0.018$) and ALT ($p = 0.001$). Urea ($p = < 0.05$/ < 0.05) and frusemide/ thiazide (< 0.05/ <0.05) were also predictive.

Conclusions: EF lacks utility as a prognostic indicator at 30 and 360 days in elderly HF patients demonstrating limited use as a diagnostic, risk stratifying or prognostic tool in the management of HF patients. LFT's, urea and the presence of frusemide/ thiazide have greater use as predictors of outcomes in HF patients.

Clinical Audit of Paediatric Diabetic Retinal Screening

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NICE guidance recommends that any child aged 12 and over with diabetes should be offered annual retinopathy screening. In March 2009 retinopathy screening figures at Bristol Royal Hospital for Children (BCH) were only 4%. This audit set out to establish the current screening figures and whether results from the screening service were shared with secondary care.

Data was collected retrospectively for all children attending BCH with a diagnosis of diabetes aged 12 and over for the twelve months commencing 1st September 2009. The BCH Diabetes Database was used to extract demographic information. ORION, a database provided by the Bristol Digital Retinal Eye Screening Service, was used to collect information on eye screening invitations, attendance and results.

149 children were identified as eligible for screening, of which 77% were invited to attend annually. 85 of those children (74%) had a screening result within the last 15 months, of which 7% were found to have background diabetic retinopathy changes in one or both eyes.

The BCH Diabetes Database was found to have correct, current results recorded for only 24 children (21%). This highlighted that screening results were not being shared with secondary care and as a result insufficient results passed onto the National Diabetes Audit.

These results provided a platform for implementing service improvement. A multi-disciplinary team was assembled to realize changes. These included: development of a new operational policy for retinal screening, patient education leaflets, stream-lining of results to be shared with secondary care and passed onto National Audit.

Are we facing a new epidemic of coronary heart disease?

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Introduction: In the UK there are more than 110 000 myocardial infarctions, resulting in excess of 70 000 deaths per annum. The deaths from Coronary Heart Disease (CHD) between 1980 and 2000 fell by 50% and have continued to decrease. This is largely attributed to a reduction in risk factors, along with advances in treatment and management. There are emerging fears that successes in reducing mortality could be undermined by a rise in risk factors including obesity, physical inactivity and diabetes in the 35-54 age group.

Methods: Data from the Office of National Statistics obtained from death certificates and the British Heart Foundation Statistics database were analysed. Trends in mortality overall and for different age groups were analysed over time. The mortality rates from the catchment area of the Royal Sussex County Hospital, Brighton, were compared to national figures. Statistical analysis including JoinPoint regression were employed.

Results: The national trend for mortality in CHD has decreased. Local data suggests that there has been a significant decrease in the 55-64 and 65-74 age groups ($p<0.05$). The two youngest age groups analysed (35-44 and 45-54) showed small declines of 0.02% (SE ± 0.12) and 0.1% (SE ± 0.22) per annum respectively.

Discussion: The success in reducing mortality from CHD runs the risk of being reversed. Local data suggests there is no decrease in mortality in the 35-54 age group, supporting national trends. More effective reduction of risk factors is required in this age group.

Sexual Health Safeguarding in Teenagers presenting to the Emergency Department

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Background: Teenage sexual activity is extremely prevalent in the UK, and South London has the highest rate of teenage pregnancy in Europe. The GMC has published guidelines to help identify young people at risk of sexual abuse, and these are supported by legislation (Sexual Offences Act 2003, Children's Act 1989). We audited documentation of sexual health risk assessment and capacity in young people presenting to the Emergency Department(ED) of a London teaching hospital.

Methods: We identified all patients aged 13-18 years seen in ED over a 6 month period with sexual health complaints. We collected data on sexual health documentation using electronic and paper patient records and assessed current practices against the GMC recommendations.

Results: 41 patients were identified (7 were aged < 16 yrs). Presenting complaints included pregnancy issues, sexually transmitted infections and emergency contraception. Documentation for 16-17 year olds was generally inadequate, in particular relationship details. Documentation for <16 years olds was better, especially around partner details and sexual health education. Documentation of patient competence was generally poor. In patients where safeguarding issues were identified the majority were referred to child review meetings.

Conclusions: Current documentation of sexual health risk assessment needs to be improved. The lack of adequate documentation may be due to perceived lack of need for risk assessment in the ED or lack of knowledge of GMC guidelines. Using a multidisciplinary approach we have developed a proforma to be implemented in the ED to aid ED staff in sexual health risk assessment.

The Mights of Mitomycin (An Audit)

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Background: Bladder cancer is one of the most common urological malignancies. Following transurethral resection of the bladder tumour (TURBT), adjuvant chemotherapy is considered for all patients with superficial bladder cancer, as without this recurrence rates are about 70%.1 A single dose of Mitomycin (MMC) can reduce the 5 year recurrence to 45%.2

The current European guideline recommends one immediate post-TURBT instillation of chemotherapy (within 24 hours) for individuals with superficial transitional cell carcinoma (TCC).3

This audit aimed to investigate the current practice, establishing whether patients prescribed MMC post-operatively are receiving their treatment on time.

Method: All patients prescribed MMC post-TURBT between 1st July and 28th September 2009 were identified from the Royal Cornwall Hospital pharmacy department and the case notes reviewed.

Results

Table 1: When patients received their MMC

Time Lapse	Patients
<24hrs	9 (31%)
24-48hrs	9 (31%)
>48hrs	2 (7%)
not given	(14%)
uncertain	5 (17%)

Table 2: Break down of time lapse

Time Lapse (hours)	Mean	Median
Operation to Dispensing	11	4
Dispensing to Administration	13	5
Operation to Administration	23	27

Conclusion: Although the majority of patients do receive post-operative MMC this is not within the guideline period of 24 hours. Recommendations were made either for further staff training or intra-operative MMC administration.

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Scoliosis surgery at RMCH and SRFT

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This retrospective audit was done to collate data on all spinal deformity surgeries performed at the Royal Manchester Childrens Hospital and Salford Royal Foundation Trust in 2010. The aim was to establish baseline demographics, morbidity, mortality and compare the infection rates and post-operative complications in relation to the national data. The data was collected from the theatre log books at both sites and correlated with clinic letters. The audit shows that the biggest group receiving spinal surgery for scoliosis is within the 10-16 age group (63%) with the least being the over 30 (13%). The incidence of deep infection was 0.7% in comparison to the national rate of 3.31% which can be attributed to difference in sample size. 52% of the operations included patients with non-idiopathic and 48% with an idiopathic aetiology. There was no reported mortality in patients receiving spinal surgery with a 0.7% of incomplete neurological deficit which resolved in comparison to the national data (0.60%). The audit concludes that RMCH and SRFT have lower than average rates of post-operative complications with no reported mortality in 2010. In addition, more non-idiopathic than idiopathic cases (52:48%) were treated than the national average ratio of (45:55%). There is a need for regular re-audits to evaluate practice, maintain adequate infection control and fully inform patients for the purpose of consent.

Co-morbid conditions present in children and adolescents with Chronic Fatigue Syndrome

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Chronic fatigue syndrome (CFS) is not an uncommon disorder in young people which causes many disabling symptoms. There have been very few studies looking at the presence of co-morbid conditions in these patients, and this study aimed to fill that need by providing an information base-line for clinicians and researchers alike.

Data was collected from the hospital notes of 120 patients who had a confirmed diagnosis of CFS established whilst under the care of a Consultant Paediatrician.

The majority of patients in the cohort (n=67, 56%) had at least 1 distinct co-morbid condition. There were a total of 129 diagnoses of 51 different conditions. The largest number of co-morbid conditions any one patient had was 8, and the mean number of co-morbid conditions per patient was 1.96.

The most common sub-group of co-morbid conditions was psychiatric, with 28 patients having at least one psychiatric condition, most commonly anxiety (n=15) and depression (n=6). There were also a large number of patients with at least one gastrointestinal (n=19), respiratory (n=17) and musculoskeletal (n=14) condition. Patients with co-morbidities had a lower functional ability score at diagnosis than those with none.

This study has demonstrated that young people with CFS are likely to have co-morbid conditions that need to be dealt with alongside their CFS. This should be taken into account when caring for such a patient, particularly since the presence of co-morbid conditions appears to have a negative impact on the patient's functional ability level.

Study of the success rate of In-Vitro Fertilisation (IVF) according to treatment plan in women diagnosed with hydrosalpinx during ovarian stimulation in 2008

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Background: There is evidence that division of hydrosalpinx prior to IVF treatment may improve success rates; however, there is minimal research into its treatment when identified during an IVF cycle. The purpose of this study was to investigate whether freezing all embryos followed by salpingectomy and subsequent frozen embryo transfer conferred any benefit over initial fresh transfer with or without later salpingectomy and frozen transfer in patients diagnosed with hydrosalpinx during ovarian stimulation.

Method: The electronic database ACUBase was used to identify those patients undergoing IVF treatment during 2008. The follicular tracking ultrasound scans of these patients were then consulted to select those diagnosed with hydrosalpinx during ovarian stimulation. The electronic database URMIS and theatre diaries were used to identify which of these patients had undergone salpingectomy after this time. ACUBase was then used to obtain details and outcomes of these cycles.

Results: Two of 18 patients diagnosed with hydrosalpinx underwent freeze-all followed by salpingectomy and frozen transfer, none of which resulted in pregnancy. Of the 14 patients undergoing fresh transfer regardless of hydrosalpinx, one became pregnant (7.1%). One of the 14 undergoing fresh transfer followed this with salpingectomy and subsequent frozen transfer but did not achieve a pregnancy.

Conclusions: In patients undergoing salpingectomy the two different treatment plans showed no difference in pregnancy rate, and in fact division of hydrosalpinx appeared to confer no benefit at all. Although greater numbers are needed there is no evidence that freeze-all is superior to initial fresh transfer in this situation.

Quality Improvement and Clinical Effectiveness: Improving the prescribing of Gentamicin in NHS Tay-side

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Background: The use of gentamicin, in the treatment of infections, presents a significant risk both to patient safety and also to NHS Board Clinical Governance (1). Inaccurate dosing, sample time error and incorrect monitoring can lead to potentially harmful side effects of ototoxicity and nephrotoxicity (2). We aim to determine the errors encountered in gentamicin prescribing in NHS Tayside to help update the NHS Tayside Gentamicin Guideline currently used by medical staff in our hospitals (3).

Method: We audited 98 cohort cases of gentamicin prescribing over an 8-week period in the medical wards of Ninewells hospital. Patients were identified from an electronic list of gentamicin levels provided by the Tayside Biochemical Department and data was collected using a pro-form sheet.

Results: Inaccurate Dosing - Out of 98 cases only 10 received the correct dose of gentamicin. 47 received the correct dose + 20mg, 27 had a dose > 20mg out with the recommended dose and 14 did not have either their weight or height recorded to calculate the recommended dose (figure 1).

Incorrect Monitoring: Gentamicin blood levels post first dose ranged from 4.5 to 72 hours. The normal range is 6-14 hours (4). Out of 98 cases 68 did not complete a 72-hour course of gentamicin; 44 for valid reasons and 24 due to error (figure 2). Nephrotoxicity occurred in four patients and gentamicin was appropriately stopped in these cases.

Conclusion: This audit identified errors encountered in gentamicin prescribing. We have used the results to update the NHS Tayside Gentamicin Guideline to include stricter specifications around dosing and clearer instructions regarding monitoring, with the aim to help reduce error. We have used clinical audit to improve the quality of our guideline and raise clinical standards.

Line sepsis – don't blame your tools!

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Parenteral Nutrition (PN) is increasingly used to manage patients in whom enteral feeding is unfeasible. National guidelines highlight line sepsis as a major complication. We evaluated line complications in PN patients at GSTT, and compared with 2005 data.

Prospective dual-centre cohort study of patients started on PN over a 12-month period Clinical data collected via pro forma; microbiology data collected via Electronic Patient Records. Outcomes compared with historical data.

141 patients were recruited (61 females, 80 males). Mean age was 58 years. The commonest PN indication was gastrointestinal tract malfunction (77%) as opposed to inaccessibility (13%). Line complications occurred in 35 patients (25%), most commonly line sepsis. Line sepsis rate has significantly reduced since 2005 (11% vs. 31%; Fisher's test p=0.0002).

Line complications were significantly more likely to occur in ward-based patients versus ICU (34% vs. 2%; Fisher's exact test p<0.0001). By contrast, there was no significant difference between complication rates comparing central lines with PICC/ Hickman lines on wards or ICU (Fisher's test p=0.83). The mean duration of PN was similar across line types (PICC: 20 days, Hickmann: 21 days, CVC: 17 days).

This dual-centre audit demonstrates a significant reduction in line complications since 2005. However, line sepsis remains common in patients receiving PN. We found a significant difference in line complications between ICU and ward patients that cannot be explained by the use of PICC/Hickman lines vs. CVC lines. Training in line handling of PN patients on wards should therefore be re-evaluated.

Subclavian Deep Vein Thrombosis in an Otherwise Healthy 9-year-old Boy

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One in ten deep vein thromboses originate in the upper extremity, 80% of which are attributable to a secondary cause, such as a central venous catheter or cancer.

Master A was an otherwise fit and well nine-year-old boy who presented with a seven day history of spontaneous left arm swelling and superficial venous distension around the left shoulder. He had no significant past medical history, and was not on any medication. There was no family history of venous thromboembolism and no history of trauma or illness, but it was noted that Master A was a very keen showjumper.

A doppler ultrasound of the left subclavian vein demonstrated a venous thrombosis. Thoracic outlet syndrome was ruled out by imaging, and a thrombophillia screen was normal. By a process of exclusion, a diagnosis of Paget-Schroetter syndrome was made: thrombus formation caused by impact-related trauma to the vessel, as a consequence of his showjumping. Master A was managed as an inpatient for seven days where he received catheter directed thrombolysis and intravenous anticoagulation. He was then warfarinised for three months. Repeat imaging demonstrated recannalisation of the vessel.

Paget-Schroetter syndrome is rare. It is commonly associated with thoracic outlet syndrome, and patients with underlying thrombophillia are at an increased risk.

Here a case of primary upper extremity deep vein thrombosis in a nine-year-old boy is described. The diagnosis of Paget-Schroetter syndrome was made, in the absence of underlying thrombophillia or thoracic outlet syndrome, thought to be caused by trauma related to showjumping.

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