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ORAL PRESENTATIONS

Does cardiomyocyte-specific deletion of the Plasma Membrane Calcium ATPase (PMCA) pump alter micro-RNA expression in heart failure?

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Background: MicroRNAs are newly discovered small non-coding RNAs that can regulate hypertrophic gene expression at the post-transcriptional level through targeted mRNA 'silencing' in heart failure. Abnormal Ca^{2+} handling impairs cardiac function and our research group has shown that deletion of the calcium extrusion pump, plasma membrane Ca^{2+} ATPase1 (PMCA1), leads to dilated cardiomyopathy and heart failure. This study aims to determine whether deletion of PMCA1 leads to altered microRNA expression in heart failure.

Methods and Results: PMCA1 cardiomyocyte-specific knockout ($PMCA1^{cko}$) mice were generated using Cre/LoxP technology. A microarray plate revealed a number of microRNA changes in $PMCA1^{cko}$ mice (n=5) compared to $PMCA1^{loxp/loxp}$ (controls) (n=7) which, by reverse transcription and qPCR, confirmed a marked down-regulation ($p<0.05$) of miRNAs let7e (75%), let7i(50%), 101 (76%), 101a(61%), and 93(57%). $PMCA1^{cko}$ and $PMCA1^{loxp/loxp}$ mice were subjected to haemodynamic stress by transverse aortic constriction (TAC) inducing cardiac hypertrophy. After TAC, $PMCA1^{loxp/loxp}$ mice demonstrated a downregulation of mir-101a by 50% ($p=0.06$) compared to sham operated $PMCA1^{loxp/loxp}$ mice but there was an overexpression by 61% (<0.05) in the PMCA1cko mice (n=3). Rcan1.4, a marker of NFAT activity, was upregulated (>300%) in $PMCA1^{cko}$ mice (n=7) under basal conditions.

Conclusions: Deletion of PMCA1 has been shown to directly or indirectly regulate transcription of microRNAs let7e, 7i, 101, 101a and 93, whilst under pathological hypertrophic conditions, deletion of PMCA1 leads to upregulation of miR101 and 101a. Initial studies suggest MicroRNAs 101 and 101a may regulate pathological hypertrophy through suppression of the calcineurin-NFAT pathway, one of the most well characterised pathways in heart failure.

Pioglitazone acts on L-type calcium channels causing vasodilatation in porcine coronary arteries.

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Background: Pioglitazone is an oral hypoglycemic agent used to lower blood glucose in patients with type II diabetes. Pioglitazone activates PPARγ, a nuclear hormone receptor involved in DNA transcription regulation, enabling recovery of insulin sensitivity, particularly in adipose tissue. Moreover, pioglitazone cause vasodilatation which is desirable in diabetics due to their increased risk of atherosclerosis. This investigation looks into the mechanism of pioglitazone-mediated vasodilatation in porcine coronary arteries.

Methods: Coronary artery segments were contracted using a thromboxane mimetic and subsequently exposed to pioglitazone. Vasodilatation was measured using isometric tension recording.

To determine the mechanism behind the pioglitazone-mediated vasodilatation, pathways suspected of being involved were blocked to establish whether this inhibited relaxation. We inhibited PPARγ, potassium channels, NO synthase, AMP kinase, Rho kinase, L-type calcium channels, removed endothelium and removed extracellular calcium.

Results: Inhibition of PPARγ, potassium channels, NO synthase, AMP kinase, Rho kinase and removal of endothelium failed to significantly inhibit the vasodilatation, indicating that relaxation was independent of these pathways. A two-way ANOVA showed that depletion of extracellular calcium significantly inhibited vasodilatation by 36% when compared to a control ($p<0.001$). Moreover, exposure to 0.1µM nifedipine, an L-type calcium channel blocker significantly inhibited vasodilatation by 34% ($p<0.0001$).

Conclusion: Pioglitazone causes vasodilatation by blocking the influx of extracellular calcium through L-type calcium channels.34% of vasodilatation was inhibited indicating that pioglitazone must also act through other pathways. In addition to reducing the risk of atherosclerosis, "off-target" calcium channel blockade makes pioglitazone beneficial to hypertensive diabetic patients since it lowers blood pressure.

Assessment of arterial stiffness indices in stroke survivors

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Background: Arterial stiffness is an independent predictor of stroke and carotid-femoral pulse wave velocity (cfPWV) is considered the best measure of arterial stiffness. PWV can be estimated by simultaneous non-invasive assessment of the arterial pulse waveform at two sites using a cuff-based oscillometric device (Vicorder). PWV is an important determinant of cardiovascular risk. However, only a small number of studies have examined PWV in people with cerebrovascular disease (CVD).

Objectives: This study aimed to establish reference values for PWV in people with CVD, and to compare PWV in this group with a group of age-and sex- matched healthy volunteers (HV)

Methods: Patients with manifest CVD and HV were recruited from outpatient stroke clinics, rapid-access TIA clinics and Acute Stroke Units in Leicester, UK. Casual BP was estimated using the Omron BP monitor. cfPWV and brachio-femoral PWV (bfPWV) were estimated using a standardised protocol (Vicorder).

Results: PWV was measured in 33 CVD patients (mean age 64±8) and 42 HV (mean age 62±8). The mean resting BP was similar (CVD:132/78, ±21/14, HV:130/78, ±15/10). There was no significant difference in cfPWV (CVD:7.66, ±1.73, HV:7.44, ±1.52;p=0.77) or bfPWV (CVD:14.38, ±5.58, HV:11.98, ±3.24;p=0.18) between the two groups.

Conclusion: Although there was no statistically significant difference in PWV between CVD and HV groups, our study suggests that bfPWV may be higher in those with CVD, while the accepted gold standard "cfPWV" was similar in both groups. Further research is warranted to identify if bfPWV is increased in CVD and to clarify the prognostic value of PWV.

An explorative study into the role of midwives in future efforts to eradicate Female Genital Mutilation in Sudan

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Background: Female genital mutilation (FGM) refers to 'all procedures involving partial or total removal of the external female genitalia for non-medical reasons.'[1] It is considered a cultural tradition and in Sudan 69% of females are affected[2], with high complication rates. Midwives perform most FGMs in Sudan[3] and many past NGO and Governmental efforts were aimed at midwives. However, progress has slowed, and lack of direction has lead to the gradual abandonment of many of these initiatives.

Methodology: The study was set in Khartoum state, Sudan, May 2012.12 midwives and 6 relevant stakeholders were interviewed using semi-structured one-to-one interviews.

Findings: Knowledge of FGM complications among midwives was high, with most learning from midwifery school or an education programme. Main reasons to practice FGM included income, demand from society and tradition. Barriers to stopping practicing were subsequent lack of income, demand from society and confusion over the current law. Suggestions to support midwives in stopping FGM included changes to the law, provision of employment from the Government, as well as suggestions for NGOs such as micro-finance, and advocacy and raising awareness.

Conclusions: My findings revealed past efforts to educate midwives about FGM have been largely successful, but there are several other influential factors such as income which play an equally large role. Any change in the law is unlikely due to the current political situation. My suggestions are therefore aimed at National and International NGOs and include awareness raising and education of the public, and better support for midwives stopping FGM.

The concurrent association between mood disturbance and disease status in patients with Ankylosing Spondylitis (AS)

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Introduction: Depression and anxiety are recognised as common features in patients with chronic inflammatory conditions, such as Rheumatoid Arthritis. Few studies, however, have focussed on the prevalence and overall impacts of mood disturbance in AS. This study therefore aimed to investigate the combined effect of depression and anxiety on several aspects of AS severity.

Methods:605 participants in a UK cohort of patients with diagnosed AS (EASi-QoL) were included. Sociodemographic and disease-related variables were collected [pain (numerical rating scale), disease activity (Bath AS Disease Activity Index), and physical function (Bath AS Functional Index)]. Mood disturbance was measured by the Hospital Anxiety and Depression Scale.

Results: The majority of responders were males (72%), with a mean age 51 (SD 12). 298 patients (49%) reported mood disturbance. Among these, 166 (56%) demonstrated a co-existence of depressive and anxious symptoms; 27 (9%) had depressive symptoms only and 105 (35%) had anxious symptoms only. After controlling for sociodemographic factors, greater disease activity was most strongly associated with mixed anxiety and depression (OR 7.66, 95% CI 4.10-14.30). Similarly, there were significant independent associations of mixed depression and anxiety with poor function (OR 5.91, 95% CI 3.17-10.99) and increased pain (OR 4.76, 95% CI 2.56-8.86).

Conclusion: This study drew attention to the high prevalence and frequent co-occurrence of depression and anxiety in patients with AS. Findings suggested that AS patients with co-morbidity of depression and anxiety had poor disease status. Both anxiety and depression should be considered in planning care for AS patients in clinical practice.

Awareness of Breast Self Examination among Sudanese female medical students January-April 2012

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Together with cervical cancer; breast cancer represents fifty percent of cancer incidence in Sudan. It is detected in late stages due to lack of awareness and screening programs. Breast Self Examination (BSE) plays a major role in early detection of the disease, and hence increasing the chances for survival. Medical students should take part in breast health education in the society.
This study is aimed to explore knowledge, attitude, and practice among Sudanese female medical students towards BSE.

This is a cross-sectional, descriptive, analytical, institutional based study. A stratified random sample of 363 female students from faculties of medicine in Khartoum state were questioned regarding awareness of BSE via a pretested, pre-structured questionnaire by well trained volunteers. Questions related to BSE, breast cancer, and awareness about screening program were asked. Ethical clearance was obtained from the ethical committee of each faculty, and informed consent was taken from each student.

The mean score of knowledge is 6.9/11, (4.6 for juniors, and 8.9 for seniors).There is a significant effect of positive family history of breast cancer on knowledge score (P value =0.001). A number of 187 (49%) students perform BSE, but only 85(23.4%) of them perform it monthly. The vast majority (95.8%) rated BSE as important for early detection of breast cancer.

There is a strong effect of academic experience on knowledge, attitude and practice of BSE among Sudanese female medial students. Awareness about BSE is expected to increase by early introduction of health education in the curriculum.

Clinical and Biochemical features of Sporadic and Hereditary Phaeochromocytomas and Paragangliomas.

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Currently 33% of phaeochromocytoma and paraganglioma are reported to be hereditary .Though genetic testing enables the identification of hereditary patients, various issues have prompted the search for additional ways to help distinguish between hereditary and sporadic cases. In this study, the clinical and biochemical features of sporadic (44) and hereditary (33 mutations in SDHD, B, VHL, RET and NF-1) phaeochromocytoma and paraganglioma patients were compared .Patients were identified via multidisciplinary database searches and assigned to the hereditary group on the basis of a positive genetic test in any of the known susceptibility genes. Whilst, sporadic patients were classified on the basis of a negative family history, no clinical evidence of a hereditary syndrome and a negative genetic test if available. Findings of statistical significance included: a lower mean age of diagnosis (33.2± 18.1 vs 45.1± 19.2) , a higher percentage of bilateral tumours (35.7% vs 3.40%) and a smaller tumour size (59.4±31.5 vs 33.1± 18.6mm) in the hereditary group when compared with sporadic group. Other findings included: higher rates of multiple tumours and malignancy in the hereditary group. Meanwhile a wide range of symptoms and catecholamine phenotypes were reported in both groups but hypertension and hypersecretion of noradrenaline respectively were the commonest.

Overall, these results suggest significant differences in age, tumour size and bilateral phaeochromocytoma do exist between both groups and knowledge of this information may be useful in distinguishing between cases. As for the other features, the trends noted provide general information concerning these rare tumours.

Development of a recombinant virus assay for the evaluation of drug resistance mutations in the reverse transcriptase gene of the Human Immunodeficiency Virus type 2

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Knowledge of the clinical relevance of drug resistance mutations is vital for optimal anti-retroviral therapy (ART) selection and can be reliably determined only by phenotypic resistance assays. Recombinant virus assays are quick, cost effective and show low inter-assay variability. Whilst these are widely available for resistance testing for HIV-1, none have previously been developed for HIV-2 which is found predominantly in West Africa. HIV-2 infection poses particular problems for therapy, as the virus is intrinsically resistant to both non-nucleoside reverse transcriptase inhibitors and fusion inhibitors. Potential genotypic resistance mutations to antiretroviral therapy have been identified in the reverse transcriptase (RT) gene of HIV-2, but the clinical relevance of these is currently unknown. We aimed to develop a recombinant virus assay using two components: an HIV-2ROD deletion vector lacking the protease and RT regions of the pol gene and a PCR amplicon coding for the protease and RT region containing the mutations of interest. Electroporation protocols were optimised using the HIV-1 molecular clone pNL4-3. Following electroporation of both components into human T4-lymphoblastoid cells, an RT assay was used to determine the success of recombinant mutant HIV-2ROD generation. Such a recombinant virus assay would allow evaluation of phenotypic drug resistance as well as cross-resistance. This would inform the selection of suitable drugs for salvage therapy, further improving the management of HIV-2-infected patients. The clinical relevance of HIV-2 resistance mutations will be increasingly important as RT inhibitor use becomes more widespread following the increasing availability of ART, especially in West Africa.

Effects of sympathetic nerve stimulation on cardiac electrophysiology in Long QT syndrome 1

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Introduction: Long QT syndrome 1 (LQTS1) is a life threatening cardiac condition arising from reduced activity of the slow activating delayed rectifier potassium channel (IKs), where mortality is associated with surges in sympathetic tone. Symptoms occur due to broad complex tachycardia, which degenerate into ventricular fibrillation (VF) and sudden cardiac death. Mechanisms underlying SCD are not understood but may relate to alterations in ventricular repolarisation. The aim of this study was to examine the effects of sympathetic nerve stimulation (SNS) on effective refractory period (ERP) and inducibility of VF in a pharmacological model of LQTS1.

Methods: The novel innervated heart preparations from adult male guinea pigs (n=6, 450-550g) were used. ERP was measured using a single extrastimulus protocol. Inducibility of VF was investigated using ventricular fibrillation threshold (VFT) with burst pacing. ERP and VFT were measured at baseline (BL), and SNS (3Hz,1V) during periods of control and in the presence of the IKs blocker N-[(3R,4S)-3-hydroxy-2,2-dimethyl-6-(4,4,4-trifluorobutoxy)chroman-4-yl]-N-methylethanesulfonamide (HMR1556). Data are mean+SEM, analysed using Students T-Test. * P<0.05 vs. BL and vs. Control

Results: During control, SNS significantly reduced ERP and VFT (Table). In the presence of HMR1556, the effect of SNS on ERP and VFT was augmented.

	Control			HMR 1556		
	BL	SNS	Change	BL	SNS	Change
ERP (ms)	104+5	93+6**	11+2	130+4	101+3**	29+6*
VFT (mA)	4.2+1.2	2.9+0.9*	1.42+0.5	4.2+1.1	1.3+0.5*	3.2+1.1*

Conclusion: LQTS1 is associated with increased susceptibility to VF during SNS, which is directly related to changes in ventricular repolarisation.

A new tool for assessing the pattern of branching of the cerebral vasculature. Relevance for Alzheimer's disease.

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Accumulation of the protein amyloid-β (Aβ) in the brain is a major feature of Alzheimer's disease. Cerebral amyloid angiopathy in AD reflects an age-related failure of elimination of Aβ from the brain along perivascular drainage pathways. In this study we test the hypothesis that the histological profile of basement membranes in cerebral arteries changes with advancing age and disease process.

Immunocytochemistry with collagen IV was performed on 10 sections of brains with AD and 10 age matched controls. The sections were from the frontal and occipital cortices. Slides with human tissue from the Brain Tissue Resource in Newcastle (http://www.ncl.ac.uk/iah/campus/facilities/nbtr/) were used. We then developed image processing tools to automatically differentiate between normal sections and those from subjects with AD.

The immunostaining for collagen IV is more intense in brains with AD compared to controls. There appear to be more branches of the microvasculature in brains with AD. The functional consequences of these changes most likely will result in alterations of perivascular drainage that lead to failure of elimination of Aβ and alteration of the homeostasis, neuronal dysfunction and dementia. We can now differentiate successfully between the images from normal subjects and those with AD. This is achieved by analysis of the cells present in the image and their structures, especially their branching structure.

These results argue well for future development that uses clinical images from patients at differing stages of AD. As such, we have a new approach to analysing the cerebral vasculature with regard to early diagnosis of AD.

Conclusion: Pioglitazone causes vasodilatation by blocking the influx of extracellular calcium through L-type calcium channels.34% of vasodilatation was inhibited indicating that pioglitazone must also act through other pathways. In addition to reducing the risk of atherosclerosis, "off-target" calcium channel blockade makes pioglitazone beneficial to hypertensive diabetic patients since it lowers blood pressure.

A comparative study of quality of life in irritable bowel syndrome and inflammatory bowel disease

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Background: This study aimed to determine the impact of irritable bowel syndrome (IBS), a functional disorder, and inflammatory bowel disease (IBD), an organic disorder, on health-related quality of life (HRQoL), and the mechanisms by which this occurs.

Methods: 187 gastroenterology outpatients (IBS: 96, IBD: 91) completed the measure yourself medical outcome profile (MYMOP) and various disease-specific HRQoL and symptom instruments. Questionnaires were mapped to determine parallel concepts in IBS and IBD and data re-coded to enable comparative analysis. MYMOP, HRQoL and symptom data were compared via Mann-Whitney U or t-tests and proportions of patients with particular symptoms via chi-squared. Logistic regression analysis was conducted to compare differences in HRQoL once other factors had been controlled for.

Results: Overall HRQoL was worse in IBS (mean: IBS=46, IBD=67, $p<0.001$), as was emotional and social HRQoL. Bowel function was similar, with certain gastro-intestinal symptoms more prevalent in IBD. Chi-squared and logistic regression analysis demonstrated that patients with IBS were significantly more likely to report psychosocial problems, such as embarrassment, depression, lack of sympathy from others and diet affected by bowel problems. Patients with IBD were significantly more likely to report physical symptoms, such as incontinence, urgency, difficulty sleeping and bloating.

Conclusion: HRQoL is significantly worse in IBS, with social and emotional reductions accounting for the difference. Despite this, bowel function is equivalent, or slightly worse in IBD. This study has demonstrated that the mechanisms by which IBS and IBD affect HRQoL differ, with GI symptoms alone not accounting for the impacts of IBS.

Validation of 3 letter and 5 letter per line computerised visual acuity measurements using COMPlog against ETDRS measurements in subjects with AMD

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Introduction: Age-related Macular degeneration (AMD) is the leading cause of visual loss in the industrialized world, and its prevalence has been projected to double by the year 2020. AMD affects the macula, often creating a central scotoma.
Accurate and repeatable visual acuity (VA) measurements are important in monitoring disease progression and treatment efficacy. ETDRS charts are considered the 'gold standard' tests for VA and employ 5 letters per line. The COMPlog computerised VA measuring system, relies on a 3 letter per line assessment. Its advantages include the ease of use, shorter test distances, and an automated scoring system.

Aims: We aimed to determine whether electronic COMPlog measurements agree with those of the 5 letters per line ETDRS charts in patients with AMD.

Method: Timed test and retest VA measurements were taken using 3 and 5 letters per line on COMPlog and the ETDRS charts in random order in 50 patients with wet AMD. Bland and Altman methods were employed.

Results: No significant bias and similar test-retest variability was observed in the computerised 3 and 5 letter per line VA measurements compared to the ETDRS chart. Median test times were 92, 71.5 and 131.5 seconds for ETDRS and COMPlog 3 and 5 letters per line respectively.

Conclusions: The preliminary data is suggestive that COMPlog measurements agree well with and are similarly reliable to the ETDRS chart. In patients with AMD, the use of 3 or 5 letters per line did not appear to affect VA scores although test times are shorter with 3 letters per line.

Presence of autoantibodies in patients with glioma

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Gliomas comprise an aggressive group of heterogeneous neoplasms with dismal survival. Vague initial symptoms and late focal onset predisposes delayed diagnosis with subsequent poor prognosis. Invasive biopsy and current diagnostic challenges emphasise the need to identify novel, specific and non-invasive early-diagnostic techniques. The detection of tumour-associated antigens (TAAs) in patient sera well before symptom onset indicates that autoantibodies may prove a promising diagnostic measure.

High throughput (HTP) antigen production techniques were employed to successfully produce 9 new recombinant TAAs. Sera from adult patients with glioma (n=61) and age, sex and smoking status matched normal controls were collected. Analysis of sera by ELISA tested for the presence of IgG autoantibodies against 22 TAAs (the 9 produced in this study alongside a further 13 antigens produced in-house).

Autoantibody responses towards SOX11, SSX-2, HER-2 ICD and MMP-7 were significantly raised in gliomas compared with matched controls. A six antigen diagnostic panel including the four significant antigens alongside SOX9 and SOX13 elicited 31% sensitivity with 94% specificity (n=61). Additionally, a low-grade (n=17) specific panel comprised of p53 and GFAP, demonstrated 29% sensitivity and 98% specificity.

Autoantibodies to some TAAs are significantly raised in individuals with glioma compared with matched controls. The diagnostic panel described has great promise but further validation is warranted. Its future use may be indicated in screening genetically susceptible patients. Validation of the low-grade specific antigen panel and the identification of a high-grade panel would facilitate a more precise grading and prognostic measure.

Temporal and Spatial Distribution of Matrix Metalloproteinase -2 and its Role in the Pathogenesis of Pre-eclampsia

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Background: Matrix metalloproteinase (MMP)-2 and MMP-9 degrade components of the extracellular matrix and have been implicated in impaired trophoblast invasion in pre-eclampsia (PE). The purpose of this study was to investigate expression of MMP -2 and -9 mRNA in placentae from healthy, PE and IUGR pregnancies, and to elucidate the expression of MMP-2 protein in a gestational series of placentae.

Methods: MMP-2 and MMP-9 mRNA were quantitated using real-time PCR in third trimester placental tissue samples from healthy pregnancies (n=37) and those affected by PE (n=22) and IUGR (n=12). Immunohistochemistry and a weighted histoscore method were used to determine the expression patterns of MMP-2 in placentae from 7-17 weeks' and 34-41 weeks' gestation.

Results: There was no difference in levels of MMP-2 (p=0.75) or MMP-9 (p=0.20) expression between control, PE and IUGR placentae. MMP-2 was greater than MMP-9 mRNA expression in all samples. Median fold expression of MMP-2 relative to MMP-9 was 73.8 (95% CI 58.6–91.8).

A negative correlation between MMP-2 protein expression and gestation in endothelial cells (rs=-0.43, p=0.025) and a trend towards a negative correlation between MMP-2 expression in trophoblasts (rs=-0.33, p=0.093) and gestation were observed.

Conclusions: Placental MMP-2 expression appears to decrease throughout gestation. While we did not find evidence of a difference in MMP-2 or MMP-9 mRNA expression between PE, IUGR or healthy third trimester placentae, this may not reflect in situ MMP activity. Reduced trophoblast invasion in PE may depend on the balance between MMP and TIMP expression, an area which warrants further investigation.

Diagnostic benefit of using 6 lead ECG compared to pulse check alone in high risk population with Silent AF

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Background: Atrial fibrillation (AF) is a major risk factor for ischaemic stroke yet the risk can be dramatically reduced if detected and treated with anticoagulation therapy. Up to one third of AF patients may be asymptomatic. Importantly, this silent variant of AF exhibits a similar stroke risk. AF is commonly detected by an irregular radial pulse rhythm. This method fails to detect silent AF and also causes unnecessary ECG referrals due to ventricular ectopy. However, 6 lead ECG detects silent AF and ventricular ectopy yet is less costly and more accessible than 12 lead ECG.

Method: This retrospective study evaluated 6-lead ECG screening in primary care. 7631 patients were screened across 15 practices in Yorkshire. ECGs were analysed by cardiac physicians and confirmed by consultants. The aim was to detect AF prevalence in the over 65 population, particularly in those previously unaware. Furthermore, to compare the AF incidence with ectopy.

Results: Out of 5,733 patients aged over 65, 237 (4.1%) suffered from AF. Of these only 153 were previously diagnosed with AF, therefore 35.45% were newly identified with screening. Also, ectopy was present in 568 (9.9%) patients.

Conclusion: AF screening identified a high number of previously unknown AF cases. Furthermore, the rate of ectopy was great, almost 10%. Hence, 1 in 10 patients would be referred for an ECG for suspected AF, causing anxiety and unnecessary service cost. AF screening using a simplified ECG system not only detects silent AF but also eliminates false positives from pulse checking and therefore allows better stroke prevention.

Cardiac PMCA 1 and 4 are potential targets for future prevention and treatment strategies for heart failure.

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Heart failure is a common and life threatening condition, with a 5 year survival of only around 50%. Plasma membrane Ca^{2+} ATPase (PMCA) genes have been previously linked to human cardiovascular disease, with PMCA 1 recently being linked to hypertension and both PMCA1 and 4 expression being reduced in heart failure. A novel mouse model, cardiomyocyte specific double knockout of PMCA1:4 ($PMCA^{dcko}$), has been generated in order to study the effect of the concomitant reduction of these genes on the cardiac phenotype. To study the role of PMCA1 and 4 in the development of cardiac hypertrophy and heart failure these mice were subjected to pressure overload by surgically constricting the aorta (transverse aortic constriction, TAC) for two weeks.

Normalised heart weight data reveal that the hypertrophic response induced by TAC is attenuated in $PMCA1:4^{dcko}$ mice compared to controls ($p<0.05$), furthermore no signs of heart failure were detected in this group and Masson's trichrome staining revealed reduced fibrosis ($p<0.05$). Molecular analysis revealed that this may be in part due to decreased induction of the hypertrophic Akt pathway ($p<0.05$). This study provides the novel finding that the cardiomyocyte specific deletion of both PMCA1 and 4 in mice protects the heart against TAC induced hypertrophy and fibrosis. This is preliminary evidence for a novel role for PMCAs in the development of heart failure and a potential mechanism in the form of depressed Akt function. These results highlight PMCA1 and 4 as potential targets for future strategies to prevent and treat heart failure.

General Practitioners' experiences of and views towards using ScriptSwitch®: Qualitative study of GPs who trialled ScriptSwitch®

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Background: Increasing prescribing expenditure in the context of limited overall budgets has resulted in general practitioners (GPs) being under pressure to prescribe cost-effectively. The literature shows that GPs increasingly welcome easily accessible drug cost information, identified as a modifiable factor in altering prescribing behaviour.

ScriptSwitch® is an active, electronic decision support tool which delivers "pop ups" within consultations, integrating national and local information including drug costs, cheaper formulary switches, dosage duration optimisation and relevant safety information. Bradford & Airedale Primary Care Trust, which commissions general practice services, recently trialled ScriptSwitch®. This qualitative study seeks to explore GPs experience of, and views towards, using this software to help understand the barriers and facilitators to employing such software to facilitate more cost-effective prescribing.

Methods: A convenience sample of 8 GPs across 5 practices took part in semi-structured one-to-one interviews, which were audio recorded and transcribed verbatim. Thematic analysis was employed to identify emerging themes in the data. Areas covered in the interviews include exploring: the perceived value and influence on prescribing behaviour of the "pop ups"; why ScriptSwitch® use was terminated by some GPs and/or practices; GPs views on potential improvements to such decision-support software to enhance its influence and acceptability.

Results: Full results will be presented at the conference. Early analysis is revealing themes that can be categorised into: contextual; software-related; and impact-upon-consultation factors.

Conclusion: The full results from this in-depth qualitative study will provide insight into the barriers and facilitators to deploying such decision-support software to aid cost-effective primary care prescribing.

Does physical activity improve concentration? A comparison of performance on tasks of sustained attention after active and non-active periods in the school day

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Background: Physical activity has been associated with improved cognitive function in children. The purpose of this study was to investigate if physical activity at lunch breaks and in physical education (P.E.) lessons influence sustained attention of children in school.

Methods: Participants were 20 typically developing children aged 9-10 years recruited from two local primary schools. Each child performed a computerised neuropsychological test measuring sustained attention twice; once after a P.E. lesson or lunch break, and once after an academic lesson. Teachers completed the hyperactivity and inattentive subscale of the Strengths and Difficulties Questionnaire for each participant.

Results: There was a significant interaction between P.E. lessons/lunch breaks and academic lessons ($p<0.05$), showing that physical activity benefits sustained attention. The interaction of sustained attention between hyperactive children with high Strengths and Difficulties Questionnaire scores and less active children with low Strengths and Difficulties Questionnaire scores was approaching significance ($p=0.082$), with physical activity appearing to have a greater benefit on sustained attention in hyperactive children.

Conclusion:Results indicate that physical activity in P.E. lessons and lunch breaks benefit sustained attention in comparison to an academic lesson. Children experiencing hyperactive and inattentive difficulties may benefit from physical activity in these school periods more so than children without these difficulties.

Comparing The Haemodynamic Effects Of Phenylephrine And Pseudoephedrine In Oral Nasal Decongestants, Using Finometry And Pulse Plethysmography

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Background: Sales of oral nasal decongestants containing pseudoephedrine have been legally restricted due to its high abuse potential, regardless of its proven efficacy. Oral phenylephrine was developed as a replacement product, but concerns have been raised over its low bioavailability and hence its value as a nasal decongestant. Both being systemic sympathomimetic drugs, cardiovascular effects are expected upon their administration.

Objective: To monitor the cardiovascular effects of a single dose of Sudafed® (pseudoephedrine, 60mg) and Sudafed® PE (phenylephrine, 12mg) for a revaluation of both efficacy and safety.

Methods: Ten healthy male volunteers ranging from 18-25 years old took part in two sessions; one for the administration of each drug. Administration of either Sudafed® or Sudafed® PE occurred after twenty minutes of baseline recording. The Finometer®, a continuous, non-invasive haemodynamic monitor and the PulseTrace® PCA2 finger plethysmography device were used to record several cardiovascular variables during the baseline twenty minutes and for two hours after drug administration.

Results: On average, pseudoephedrine was found to decrease stiffness index from 6.7m/s to 6.1m/s ($p<0.05$) and increase peak-to-peak time from 277ms to 296ms ($p<0.05$). Phenylephrine increased peak-to-peak time from 240m/s to 259m/s ($p<0.05$) and total peripheral resistance from 1 monitor unit to 1.2 monitor units ($p<0.01$), but decreased heart rate from 65 beats/min to 60 beats/min ($p<0.01$) and cardiac output from 5.5 litres/min to 4.5 litres/min ($p<0.001$).

Investigation into the interaction between Sirtuin expression and Pancreatic cancer

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Aims: The Sirtuin gene family (SIRT1-7) are thought to play a prominent role in cellular ageing and have been associated with cancer pathology. The aim of this study was to establish if there is a correlation between Sirtuin gene expression and clinicopathological factors and patient outcome in pancreatic ductal adenocarcinoma (PDAC).

Methods: Immunohistochemistry was performed for SIRT1-7 on tissue microarrays of tumour cores from 121 PDACs. Statistical analysis was used to compare sirtuin expression with prognostic indicators, and survival analysis was performed to determine association with patient outcome.

Results: Elevated SIRT3 expression was associated with favourable prognostic markers, such as well differentiated tumours ($p=0.012$). In patients who did not receive chemotherapy, low SIRT3 cytoplasmic expression was associated with reduced overall survival (OS) ($p=0.014$,HR 2.23) and disease free survival (DFS) ($p=0.05$,HR 1.95). SIRT4 cytoplasmic staining was higher in low grade tumours ($p=0.022$). SIRT5 expression was elevated in high risk tumours, such as increased tumour stage ($p=0.045$). SIRT7 expression was higher in tumours with low risk prognostic factors, such as low grade and smaller tumour size ($p=0.018$,$p=0.013$). In patients with survival >12 months, low nuclear SIRT7 expression was associated with reduced OS ($p=0.025$,HR 2.07) and DFS ($p=0.014$,HR 2.22). SIRT3 cytoplasmic and SIRT7 nuclear expression were independent of various prognostic markers in influencing survival and recurrence.

Investigating a potential functional single nucleotide polymorphism in the promoter region of the *transferrin* gene; possible involvement with Alzheimer's disease.

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Background: The Oxford Epistasis Project identified an epistatic interaction between single nucleotide polymorphisms at transferrin -2 and hemochromatosis H63D as a risk factor for Alzheimer's disease; causing iron overload, inducing oxidative stress and resulting in neurodegeneration. Whilst hemochromatosis H63D affects blood iron status and transferrin saturation, the functional effect of transferrin -2 remains unresolved. The core promoter region in liver cells is -125 to +1 base pairs.

Methods: Bioinformatics analysis on the sequence flanking transferrin -2 identified our core promoter region of -144 to +89 base pairs, including the single nucleotide polymorphism. This was amplified in homogenous wild type and mutant samples by optimized polymerase chain reaction, cloned into the Dual Luciferase Reporter Gene Assay System and transfected into human brain cells. Measurement of luciferase expression defined promoter activity.

Results: No significant difference was identified between wild type, mutant and negative control activity, indicating that this region did not function as a promoter of gene expression.

Conclusion:Further research identified a region of -164 to +1 base pairs as the core promoter in brain cells, hence a modified system may prove more conclusive; by using an enhancer for less variable results and methods of defining a functional affect on transcription from a translational effect.

The impact of screening on clinicopathological determinants of outcome in colorectal cancer in the West of Scotland

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Background: There has been limited investigation of the tumour pathological and host-related features indicative of adverse survival in screened colorectal cancer patients. It is therefore reasonable to examine these clinicopathological determinants of outcome to assess the role they will have in the stratification of patient survival in the post-screening era.

Methodology: Patients with a positive faecal occult blood test (FOBT) in NHS Greater Glasgow & Clyde were offered colonoscopy where appropriate. The outcomes of colonoscopy were collected retrospectively from the Scottish Bowel Screening Database and socioeconomic deprivation was calculated using the Scottish Index of Multiple Deprivation. Variables were analysed using χ^2 tests for linear trend on SPSS software.

Results: Of 1266 patients attending for colonoscopy, 8% had a diagnosis colorectal cancer. Risk of cancer at colonoscopy was associated with male sex ($p<0.001$) and increasing age ($p<0.001$), but was non-significant for socioeconomic deprivation ($p=0.642$). Early stage (Dukes A and B) tumours accounted for 66% of colorectal cancers. Dukes stage was associated with vascular invasion ($p<0.001$). Advancing T stage was associated with nodal status ($p<0.001$), peritoneal involvement ($p<0.001$) and vascular invasion ($p<0.05$). Vascular invasion was present in 26% of T1 & 44% of T2 tumours.

Conclusion: The widespread adoption of screening has created a substantial stage migration towards earlier presentation. Vascular invasion appears to be an early feature in the natural history of colorectal cancer and may have important clinical implications. There is no association between socioeconomic deprivation and colorectal cancer at the colonoscopy stage of the screening programme.

The Effects of Maternal Hyperglycaemia on Vascular Endothelial Cadherin (VE Cad) in Fetoplacental Vessels

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Introduction: The prevalence of diabetes mellitus in women and pregnancies complicated by it are increasing. Maternal hyperglycaemia in pregnancy increases risks of complications including macrosomia, congenital malformations, miscarriage and stillbirth. Placental structure leaves fetoplacental vessels vulnerable to the environment of maternal circulation. Maternal hyperglycaemia has adverse effects on fetoplacental vessels, characterised by increased angiogenesis and endothelial disruption. Currently, direct effects of glucose on the endothelium of fetoplacental vessels are unknown. The aims of this study are to investigate the effects maternal hyperglycaemia has on:

1. The presence of VE Cad in fetoplacental vessels.
2. Phosphorylation of VE Cad in fetoplacental vessels.

Methods: Having undergone a 3hour placental perfusion with a euglycaemic media (n=3) and a media containing 15mM glucose (n=3), normal human placentae were subjected to immunocytochemistry and microscopy. Differences in VE Cad immunoreactivity intensity and junctional integrity, via tracer leakage studies, were investigated in small and large fetoplacental vessels. Double labelling of phosphotyrosine (PTYR) and VE Cad was performed. Localisation of PTYR and VE Cad and the number of vessels showing presence of both PTYR and VE Cad staining were recorded.

Results: Small and large fetoplacental vessels perfused with 15mM glucose showed significantly increased tracer leakage (2.7% increase ($p<0.05$), 21.7% increase ($p<0.037$) respectively) and down-regulation of VE Cad ($p<0.05$, $p<0.46$ respectively).From the PTYR results, no conclusions could be drawn as to whether phosphorylation of VE Cad caused the down-regulation observed.
Discussion: Effects seen from the inducement of hyperglycaemia can be compared to fluctuations seen in diabetic patients. The results illustrate that even a single hyperglycaemic episode damages the junctional integrity of fetoplacental vessels by causing a down-regulation of VE Cad.

Tip-apex distance (TAD): a comparison between dynamic hip screw (DHS) and Cephalomedullary nail fixation of extracapsular fractures of the hip.

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Background: Tip-apex distance (TAD) of >25mm is a known predictive marker for screw cut-out in fixation of extracapsular hip fractures. This study was performed to compare TAD achieved using a Dynamic Hip Screw (DHS) to that using a Cephalomedullary nail for stabilisation of extracapsular hip fractures.

Methods: From Oct 2009-Dec 2011, 246 patients with extracapsular hip fractures underwent stabilisation using either a DHS or a Cephalomedullary device [Intra-Medullary Hip Screw (IMHS) or Intertan nail using one proximal screw]. TAD was measured on intra-operative images; mean TAD was calculated and statistical analysis performed using a one-way ANOVA to identify any significant differences between the devices. Median follow-up duration was 12 months (range 2-27 months). Implant-related complications and revision surgery were used as markers of fixation failure.

Results: In the 150 patients in whom a DHS was used, mean TAD was 17.1mm (±6.5mm). Mean TAD in 81 fractures stabilised with an IMHS was 15.3mm (±5.2mm), whilst mean TAD in the Intertan group (15 fractures) was 19.2mm (±6.3mm). TAD was suboptimal (>25mm) in 9.3%, 4.9% and 13.3% in the DHS, IMHS and Intertan groups respectively. These suggest that lag screw position achieved using an IMHS is better than that using a DHS ($p=0.084$) or an Intertan nail ($p=0.067$). Complication rates were similar in all groups.

Conclusion: Cephalomedullary stabilisation of extracapsular hip fractures though technically demanding is safe and reliable. Newer implants should be used with caution due to learning curve as shown by a higher TAD in the group with Intertan nail fixation.

Is Old Blood More Dangerous Than New Blood?

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Background: There is conflicting evidence concerning the association between transfusion of 'old' blood (≥14 days) and increased morbidity and mortality in patients undergoing cardiac surgery.

Aims: In the first UK project of its kind, we accounted for limitations of previous studies to determine effects of storage age of transfused red cells (RBC) on clinical outcomes after cardiac surgery. Outcomes measured were early & late mortality and respiratory & renal morbidity.

Methods: Data from the Sheffield cardiac surgery database was examined between March 2007 and June 2010. A total of 828 patients received 1141 RBC units within two days of surgery. Patients who received more than two units were excluded. Subjects were divided into three groups based on the age of the RBC transfused; 1) <14 days ('new' blood), 2) ≥14 days ('old' blood), 3) a mixture of 'old' and 'new' blood. Data was analysed using chi-squared tests and binary logistic regression to account for confounding factors (such as EuroSCORE and ejection fraction). Survival was estimated using log rank and Kaplan Meier plots.

Results: The effect of RBC storage on operative mortality, renal support and advanced respiratory support using binary logistic regression yielded statistically insignificant differences. The Kaplan Meier 3-year survival plots were also similar across the groups.

Conclusion: Using a novel approach with UK data, our results show there is no association between storage age of RBC units and morbidity or mortality after cardiac surgery. The need for a randomised control trial to finally answer this issue of major clinical importance could not be greater.

How is tuberculosis diagnosed? A retrospective review of laboratory- and clinically-based diagnosis in the UK setting

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Background: Early and accurate diagnosis of tuberculosis (TB) is not only important for the individual affected but for public health and infection control measures. We reviewed the diagnostic method in a cohort of TB patients in an urban UK setting.

Methods: 109 adult patients were notified to the Sheffield CCDC over an 18-month period (January 2010 to June 2011). In each case, laboratory results were reviewed and the method of diagnosis determined. Medical records were reviewed for patients who had no laboratory confirmation of TB.

Results: All cases had at least one sample cultured; 61% (66/109) were culture positive for M. tuberculosis. Of the 43 culture negative cases, 4 patients were smear positive for acid-alcohol fast bacilli; a further 12 had histology suggestive of TB on biopsy specimens. Only 60% (39/65) of pulmonary TB cases had 3 sputum samples sent to the laboratory. 25% of cases (27/109) had no microbiological or histological evidence of TB, of which 8 patients had evidence of a positive IGRA or Tuberculin Skin Test; the remainder were diagnosed purely based on clinical and radiological findings.

Conclusions: Despite advances in rapid TB diagnostic methods, targets are still barely achieved for microbiological diagnosis. In pulmonary disease, 3 sputum samples need to be sent to optimise the chance of a diagnosis. For possible non-pulmonary disease, surgeons need to send samples for both culture and histology. IGRAs have limited value in the diagnosis of active TB; patients clinically deemed to have latent rather than active disease should be denotified.

The positive predictive value of postmenopausal bleeding for uterine malignancy

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Background: A systematic review was undertaken to estimate the positive predictive value (PPV) of postmenopausal bleeding (PMB) for gynaecological malignancy to aid decision making in primary care about whom to investigate.

Methods: Six electronic databases were searched from inception to September 2011. Included studies had to be in English and contain a PPV of PMB for uterine malignancy or allow its calculation. Methodological quality of studies was assessed and data extracted by two reviewers. Meta-analysis was performed where appropriate, obtaining pooled estimates of PPVs.

Results : The initial search identified 3089 potentially relevant studies, 33 met eligibility criteria. The estimated PPV for uterine and endometrial cancer was 0.51% (95% CI 0.27-0.75) and 0.47% (95% CI 0.24-0.70) respectively for a community population aged 45-54. The primary care PPV for endometrial cancer was 1.68% (95% CI 1.43-1.93) in those aged ≥ 35 years. Pooling findings from secondary care studies via a random effects meta-analysis resulted in an estimate of 8.4% (95% CI 6.9-9.9) for the PPV for endometrial cancer and 19.6% (95% CI 13.8-25.5) for uterine cancer. Results from secondary care were unable to be stratified by age.

Identifying Biomarkers of Vascular Cell Senescence

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Background: Evidence is mounting of an important role for cell senescence in the physiological ageing of the human arterial wall that, in turn, is a risk factor in the development of vascular damage. Human vascular function declines with age and is associated with increased numbers of senescent and proinflammatoryendothelial cells that express senescence associated secretory phenotype (SASP).

Aims: Gene expression profiling (transcriptomics) to identify novel genomic biomarkers and potential pathways associated with and specific to both forms of senescence; replicative senescence (REPS) and stress induced premature senescence (SIPS).

Methods: To model REPS, human umbilical vein endothelial cells (HUVECs) were grown and subcultured until they reached passage 31 (P31). A younger population of HUVECs at P5 acted as control. P12 HUVECs were prematurely induced into senescence using tert-butylhydroperoxide. Cells were determined senescent by SAβ-Gal staining. RNA was extracted from samples were checked for purity and integrity with RNA integrity numbers between 9.40-9.90. Gene expression profiles were generated using Illumina Microarray HumanHT 12 beadchips.

Results and Analysis: 12,115 and 6556 differentially expressed genes were observed in REPS and SIPS respectively. 3994 genes were found to be common to both forms of senescence. Cystatin SN was found to be upregulated in both forms of senescence whilst transforming growth factor β-Induced and α-L-Fucosidase was upregulated specifically in REPS and SIPS respectively. Potential pathways involved in REPS were found to specifically involve telomere maintenance whilst more metabolic pathways were found to have changed in SIPS.

Discussion: The beginnings of a panel of proteins can be seen with potential use both in vivo and in vitro. Senescence and the resultant SASP has been implicated in pathology. Novel biomarkers can potentially be used to identify individuals with an increased “arterial age” and at risk of developing cardiovascular disease, who otherwise appear well and healthy.

Expression and function of sweet taste receptors in human uterus

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Objectives: Sweet taste perception is detected by G-protein coupled receptor which functions as heterodimer; T1R2/ T1R3.Evidence suggests an association between pre-term delivery and consumption of artificially sweetened soft drinks. It is possible artificial sweeteners may modulate uterine contractility as recent evidence has shown that saccharin augments bladder contraction. We hypothesized that these receptors are present in human uterus and direct activation of sweet taste receptors by artificial sweeteners alters myometrial contractility contributing to pre-term labour.

Materials and methods: 6 uterine samples were collected with informed consent from pregnant and non-pregnant women during surgical procedures such as caesarean section and hysterectomy. Sections of human uterine wall were cut from paraffin blocks and stained by immunohistochemistry (IHC) to determine presence of the receptor proteins. Uterine homogenates were subjected to sodium dodecyl sylfate-polyacrylamide electrophoresis and immunoblotting to quantify expression and molecular weight of each T1R protein.

Results: Expression of T1R2/T1R3 sweet taste receptors is evident in endometrium and myometrium of non-pregnant and myometrium of pregnant human uterus by Immunostaining. Immunoblotting revealed bands at expected molecular weights in human pregnant and non pregnant uterus. Bands expressing proteins for T1R2 appeared to be denser in pregnant myometrium than in non-pregnant myometrium.

Conclusion: Sweet taste receptors are expressed in the uterus and may provide a target for the action of artificially sweetened soft drinks on myometrial contractility. This action may be enhanced in pregnant myometrium due to increased expression of the T1R2 receptor.

Circulating MicroRNAs in the Assessment of Diabetic Nephropathy

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Diabetic Nephropathy (DN) is a common microvascular complication of long standing Diabetes Mellitus. Currently, the Albumin-to -Creatinine Ratio (ACR) is considered the gold standard in assessment of DN. However, measurement of ACR is associated with several known limitations and as such, more sensitive and specific tests are being sought after. Recently, the discovery of microRNA nucleic acids in the peripheral circulation has shown promising clinical utility as disease biomarkers. The aim of this pilot study was to investigate the circulating levels of 3 kidney specific microRNAs (miR-192, -377 and -215) in relation to DN. A total of 48 subjects were recruited; 9 healthy controls and 39 diabetic patients and 2.5mls of blood withdrawn from each. Total microRNA was then extracted, reverse transcribed and levels then quantified by real time-quantitative PCR. A comparative CT method including RNU6B as endogenous reference microRNA, was then used to determine differences in the levels of target miRNAs within and between groups. Mir-192 and -215, but not miR-377, were detected in the circulation of all subjects. A 26.5-fold and 27.9-fold increase ($p=0.002$) in levels of miR-192 and miR-215, respectively, was observed in diabetic patients when compared to healthy controls. No significant difference in the levels of microRNAs was however found between diabetic subgroups. Levels of these microRNAs were additionally found to be independent of a number of clinical parameters (for example age, gender, duration of diabetes etc). Although further work is warranted, this study highlights the potential role microRNAs have in the detection and diagnosis of DN.

Clinical application of shear wave elastography for assessing carotid plaque

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Background: Atherosclerotic plaque in the carotid artery accounts for 15-20% of ischaemic stroke. Hence, there is increasing interest in identifying and characterising high-risk unstable plaques by assessing their mechanical properties. This information will improve patient selection for surgical treatment. Shear wave elastography (SWE), is a new ultrasound based technique that quantifies tissue elasticity in Young's modulus (YM). The aim was to evaluate SWE in assessing elasticity of carotid plaques and to relate YM to cardiovascular risk factors and ultrasonic features; echogenicity, plaque texture and degree of stenosis.

Methods: Patients with carotid plaques underwent carotid ultrasound scans using greyscale and SWE imaging. A longitudinal section of the carotid artery was imaged. Elasticity of plaque was quantified by measuring YM of the plaque. Echogenicity was classified according to Gray-Weale classification, plaque texture was classified as heterogeneous or homogeneous and degree of stenosis was grouped into mild (<50%), moderate (50-69%) and significant (≥70).

Results: Thirty-eight patients (16 males) of mean age 73 ±12 were recruited into the study. Significant correlation was observed between YM and increasing age and hypertension, $p<0.05$. Gray-Weale plaque classification showed significant difference, $p=0.03$.Echogenic plaques had a higher YM compared to echolucent plaques, 162 ±65kPa and 101 ±25kPa ($p=0.004$).

Conclusion:Shear wave elastography can quantify carotid plaque Young's modulus of different types of plaques. Significant difference in YM for echogenicity of plaques was observed showing potential of SWE characterization of carotid plaque. Further work includes histological classification of plaque stability which is showing promising results in correlating with YM.

The Role of SP-D in Health and Disease

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Background: Pulmonary surfactant protein D (SP-D) is a hydrophilic C-type lectin produced by type II alveolar cells. It is needed to maintain lung sterility. SP-D provides a first line defence by modulating immune function. During airway inflammation, SP-D undergoes nitrosylation in the presence of high levels of nitric oxide, leaving SP-D functionless. This deficiency in SP-D can lead to development of neonatal chronic lung disease. Currently SP-D is not included in surfactant therapy.

Aims: To investigate whether nitrosylated SP-D can be used as a biomarker for inflammation by:
1. Developing the current SP-D detecting ELISA so that it can measure the levels of nitrosylated SP-D.
2. Applying the improved ELISA technique; distinguishing between functional SP-D, and modified (Non- functional) SP-D.

Methods: An SP-D detecting enzyme-linked immunosorbent assay (ELISA) will be used. Human endotracheal aspirates and serum from preterm infants will be tested. The total concentration of SP-D and nitrosylated SP-D in tracheal aspirate samples will be calculated and quantified to determine the ratio of normal and nitrosylated SP-D in the samples.

Results: Preliminary results indicate that SP-D can be nitrosylated using a nitric oxide gel filtration column. I have been optimising the ELISA to calculate the concentration of nitrosylated SP-D (NO-SP-D) from my samples.

Conclusion: Preliminary results indicate that there is a potential to nitrosylated SP-D. A suitable dilution factor has been obtained to test the samples. The ELISA will test the clinical samples to quantify the concentration of nitrosylated SP-D and subsequently provide a prognosis for extent of inflammation.

International Study of Student Career Choice in Psychiatry: Preliminary Findings from the UK Arm

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Background: Psychiatry recruitment in the UK has been problematic for more than 40 years, with approximately only 4% of medical students choosing it as a career. Understanding reasons why this is so is crucial to potentially averting a recruitment crisis. The World Psychiatry Association provided a £60,000 grant for conducting this study, which represents the largest worldwide study into the subject.

Methodology: This was quantitative cross-sectional study. All medical schools in UK approached. Ethical approval was obtained. Final-year students and Deans of medical schools completed a survey that included questions about Psychiatry placements, students' career choices, and attitudes toward psychiatry. Questions were taken from the APT- 18 (Attitudes to Psychiatry Scale, a validated tool for use with medical students).

Results: The first 212 responses received (from 8 medical schools) were analysed. The mean age was 23.7, with 63.6% women (n=124). 2% (n=4) of final-year students made a definite decision to pursue a career in psychiatry, with a further 20.7% (n=42) seriously considering it. Personal or family experience of mental illness was cited as a very important factor for choosing psychiatry. There was little difference for experience of physical illness, a doctor in the family, media, and views of wider friends and family. There was little difference in the overall quality ratings of their clinical placement, lectures and small group teaching between those interested in psychiatry and those not.

Conclusion: The findings have implications in informing, understanding and strategizing future direction for improving recruitment rates into Psychiatry.

Urotensin and Urotensin Related Peptide in Acute Heart Failure

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Urotensin II (UTN) and Urotensin-Related Peptide (URP) are cyclic peptides found in human tissue and plasma. They have been shown to mediate a variety of effects including altering vascular tone depending on the vascular bed, positive inotropy of the heart and fibrosis. UTN levels are elevated in a variety of conditions including chronic heart failure (CHF).

Based on their similar ring structures previous studies have been unable to separate them. We have constructed a valid and reproducible solid phase extraction technique to separate the peptides and in-house competitive chemiluminescence assays to measure plasma UTN and URP in patients with acute HF (AHF, n= 335).

Amino-terminal pro-Brain Natriuretic Peptide (NTproBNP) has been established as a gold standard peptide in HF and so is used to compare to the Urotensin peptides.

Levels of all three peptides was significantly raised during AHF when compared to controls ($p < 0.05$). On logistic regression lower UTN on admission was significantly predictive of death at one year (OR 0.55, $p = 0.044$) whereas lower URP on admission showed a non-significant tendency to being predictive of HF at one year (OR 0.65, $p = 0.180$). Hence, the two peptides may have a complementary role in HF.

Further work into the role of peptides in a larger cohort with longer follow-up could help to clarify the role of the Urotensin system in HF.

An Investigation Into the Activation and Regulation of the Parkinson's Disease Associated Kinase PINK1

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Parkinson's disease (PD) is the second most common neurodegenerative disorder, affecting 1-2% of the ----population older than 65 years of age. PD is characterised by loss of dopaminergic neurones in the pars compacta of the substantia nigra. Mitochondrial dysfunction is thought to play a large role in the aetio-pathogenesis of this condition. Missense mutations in PTEN-induced kinase 1 (*PINK1*) cause autosomal recessive inherited Parkinson's disease. This gene encodes a Ser/Thr kinase that localises predominantly to the mitochondria of cells. To date, little is known about how PINK1 functions and is regulated in cells, since study and biochemical characterisation of the human enzyme is difficult due to its low *in vitro* kinase activity under basal conditions. This research exploits the recent discovery of an active insect orthologue of PINK1 from *T. castaneum* (TcPINK1) to investigate the effect of the mitochondrial uncoupler, CCCP on the stabilisation and catalytic activity of PINK1. Evidence is presented showing that CCCP induces stabilisation of hPINK1 on depolarised mitochondria, and new data exploring the effect of CCCP-induced mitochondrial depolarisation on TcPINK1 activity is presented. These findings will aid with future studies aimed at understanding how the activity of PINK1 is regulated and how PINK1 functions in cells subject to mitochondrial damage. Hopefully such studies could provide valuable clues as to the complex molecular mechanisms underpinning PD and how mutations in PINK1 result in an early-onset familial form of PD.

The Entrainment Test for Tremor Assessment

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Background: Diagnosing psychogenic tremor is challenging, usually relying solely on history and examination. However, clinicians may disregard the outcome of observational tests; basing diagnoses on history alone. The entrainment test is described as the most useful bedside test but literature suggests variability in its performance and interpretation. This study investigated the influence of history on clinicians' assessment of the test and variability in its performance and evaluation.

Method: 31 clinicians, recruited from specialist movement disorder centres and conferences, answered a novel questionnaire assessing performance and evaluation of the entrainment test. Clinicians watched videos of patients with organic and psychogenic tremors performing the test. After each video clinicians decided whether the test was positive or negative. They were read a fictional history and given the opportunity to change their assessment.

Results: 4 out of 62 initial assessments changed, independent of the history that the clinician heard (χ^2=1.974, p=0.542).
The mean questionnaire score was 6.7 out of 12 (standard deviation 2.3). Those reporting confidence in their knowledge of the entrainment test scored significantly higher, indicating greater knowledge, than those reporting limited confidence (mean=7.8, standard deviation 1.9, 95% confidence interval, 7.0-8.7 vs. mean=5.2, standard deviation 2.1, 95% confidence interval, 4.1-6.4. t=3.658, p=0.001). 5 clinicians did not include pure entrainment when asked for signs signifying a positive test.

Conclusion: History does not exert undue influence over assessment of the entrainment test, except in a minority of cases. Training and published guidelines are needed to standardise entrainment test methodology.

The Role of Caspase-1, as Part of the NALP3 Inflammasome in the Processing of IL-1B in Human Cord Blood

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Background: The inflammatory mechanisms that trigger labour include leukocyte influx into the myometrium, cervix and fatal membranes. In term and preterm labour, IL-1b is activated by caspase-1 and the NALP3 inflammasome is a multi-protein complex that triggers caspase-1 activation. The study aimed to determine the presence of the NALP3 inflammasome and to investigate the role of caspase-1, in the processing of IL-1b in human cord blood leukocytes.

Methods: Leukocytes were isolated from the cord blood of placenta from labouring and non-labouring women. Techniques used to investigate the expression of the NALP3 inflammation in placental leukocytes include Western blotting and immunoflurescence. IL-1b levels released following leukocyte stimulation with LPS±BzATP±caspase-1 inhibitor were measured using enzyme linked immunosorbant assay (ELISA). One way analysis of variance was used to compare IL-1b levels released in response to different treatments. To compare laboring and non-labouring samples unpaired t-tests were applied.

Results: In immunoflurescence in fetal leukocytes were stimulated with BzATP and LPS prior to being stained with anti-NALP3 antibody immunoflurescence was observed (n=2). When placental leukocytes were co-stimulated with bacterial endotoxin and BzATP there was a significant increase ($p<0.05$) in the levels of IL-1b released compared to the control in both labouring (n=6) samples (36.83±34.88 pg/ml) and non-labouring (n=5) samples (20.21±18.31 pg/ml). When pre-incubated with caspase-1 inhibitor prior to stimulation with LPS and BzATP levels of IL-1b released decreased in both laboring and non labouring groups.

Conclusion: When placental leukocytes were exposed to danger signals LPS and BzATP, assembly and activation of the NALP3 inflammation occurred. The decrease in IL-1b release when leukocytes were pre-incubated with the caspase-1 inhibitor demonstates that caspase-1, as part of the NALP3 inflammasome, has a role to play in the release of IL-1b, and potentially the inflammatory pathway that triggers labour.

The Effects of Diabetes on the Patency and Complication Rates of Brachiocephalic Fistulae.

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The development of dialysis has improved prognosis in end stage renal disease patients. Diabetes-induced renal failure has increased significantly over recent years. Achieving a satisfactory form of access for haemodialysis in diabetics could be time challenging. The antecubital fistula is often considered for these patients, as maturation of radiocephalic fistulae is often poor leading to inadequate dialysis and increased number of central venous catheters and their numerous complications. Patency and maturation rates as well as complicated outcomes are key when following up fistulae. The aim of this study was to report patency rates and complications of brachiocephalic fistulae created consecutively in our dialysis population and examine whether there was a difference between diabetic and non-diabetic patients. One hundred and sixty seven brachiocephalic fistula creations were retrospectively identified between January 2007 and August 2011 using patient databases. Mean age was 64.7 ± 14.1 years. Incidence of access-related complications and cumulative patency were analysed. Patency was calculated using the Kaplan-Meier method. Forty-nine patients had diabetic nephropathy as the causal factor. Of the 167 fistulae created in total 62 (29 diabetics, 33 non-diabetics) resulted in complications. The most common complication was thrombosis. The cumulative patency was 85%, 78%, 70% in diabetics compared to 86%, 82%, 75% in non-diabetics at 6,12, 24 months respectively. The patency and risk of access related complications are indifferent in diabetics and non-diabetics with regard to brachiocephaic fistulae. Therefore, vascular access at the antecubital fossa in diabetics will reduce morbidity due to better outcomes associated with this fistula

Nitrergic innervation of vasa nervorum

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Vasa nervorum are small diameter vessels that supply blood to main nerve trunks and ganglia. Vasa nervorum are known to be innervated by autonomic nerves, but the expression of neuronal nitric oxide synthase (nNOS) has not been studied previously. nNOS mediates vasodilation via nitric oxide synthesis. The biphasic degeneration of nitrergic nerves is implicated in the pathogenesis of diabetic autonomic neuropathy (DAN) – it is suggested that diabetes-induced deterioration of vasa nervorum causes microvascular deficit and neurodegeneration in the major pelvic ganglia (MPG) and sciatic nerve (SN) of rats. Clinical implications of MPG degeneration include bladder and erectile dysfunction, and motor/sensory deficits are associated with SN neuropathy. Our aim was to investigate the expression of nNOS in the nerve fibres innervating the vasa nervorum of rat MPG and SN.

MPG and SN were obtained from non-diabetic rats, fixed in paraformaldehyde, frozen and processed for immunohistochemistry. The expression of nNOS, nerve fibre markers (PGP9.5) and blood vessel markers (collagen-IV) were investigated using immunofluorescence. .

The results show that small diameter blood vessels (20-100 µm) are innervated by a rich network of nerve fibres in the MPG, most of which are nNOS-positive. In conclusion, these results suggest that nitrergic nerves innervate small diameter vessels which supply blood to nitrergic neuronal cell bodies. To our knowledge this is the first demonstration of nitrergic innervation of vasa nervorum and presents a novel nerve-blood vessel-nerve relationship. Future experiments will compare nitrergic innervation patterns of non-diabetic and diabetic animals to better understand the pathogenesis of DAN.

Inter-rater agreement of Neurological Signs

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Introduction: An assessment of inter-rater agreement of neurologists regarding diagnoses based on the neurological history and on neurological examination findings.

Methods: In the neurological examination aspect, two neurology doctors examined the same patient and recorded their results using a standardised proforma. In typical case histories part the doctors were asked to assess whether they would thrombolyse the described patient, and for their opinion about the diagnosis. The kappa statistic was used to assess the inter-rater agreement.

Results: The mean age of the patients was 55 years (SD 15). For the neurological examination there was very good agreement for inspection (kappa=0.82) and coordination (0.81), good for cerebellar (0.75) and power (0.63), moderate for reflexes (0.57), tone (0.51) and gait (0.42) and fair agreement for sensation assessment (0.35). There was no overall significant difference between grades of health professional.

Observable clinical signs (0.79) are significantly better agreement than elicitable signs (0.49).

For the theoretical patient histories 94% of the respondents correctly thrombolysed, and 79% of respondents correctly diagnosed the patients.

Conclusion: The most important result of this research is that of the significantly better agreement of Observable signs (inspection, coordination and cerebellar signs), in comparison to Elicitable ones (tone, strength, reflexes, sensation), which are more patient and doctor dependent.

The finding of only moderate inter-rater agreement for some neurological signs is of relevance to the telemedicine consultation, where the assessing doctor is reliant on another's findings. The traditional clinical neurological examination may need to be adapted in light of these findings.

Assessment of the Discriminant Validity of a New Infant Malnutrition Screening Tool with Body Composition Analysis

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Prevalence of malnutrition is high in hospitalised patients and often goes unnoticed and untreated. NHS guidelines now state that all patients should be nutritionally screened on admission; however there is no specific validated tool available for infants. A new tool is recently under development at Yorkhill hospital in Glasgow, the infant Paediatric Yorkhill Malnutrition Score (iPYMS). This tool encompasses four steps, each an established predictor of malnutrition. Each step bears a score, and a total score ⍰2 indicates high risk of malnutrition. The ability of iPYMS classification and another validated screening tool for children and infants (STRONGkids - Screening Tool for Risk on Nutritional Status and Growth) to discriminate between children with high and low fat stores was explored in 181 infants. iPYMS, STRONGkids and measurements of skinfolds and mid-upper arm circumference (MUAC) were carried out and converted to z-scores (WHO 2006). 29.3% were at high risk of malnutrition with iPYMS and 9% with STRONGkids. All anthropometric and body composition indices were significantly lower in those infants at high risk of malnutrition with STRONGkids compared to those at low risk ($P<0.05$); for iPYMS that was the case for all measurements but skinfolds. iPYMS malnutrition risk classification had ~60% concordance with nutritional status classification by body composition (skinfolds and MUAC z-scores cut-offs below the -1.33 SD). Respectively, STRONGkids had ~80% concordance. iPYMS has fairly good ability to discriminate between patients with high and low levels of body fat but needs further improvement before its use in clinical practice.

Producing and evaluating a novel Lentiviral vector for β-thalassaemia Gene therapy

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Introduction**:** β-thalassaemia, a single gene disorder affecting the β-globin gene, results in the formation of defective haemoglobin A. Treatment presently incorporates regular blood transfusions and currently the only option for a 'cure' is with hematopoietic stem cell (HSC) transplantation. Fewer than 30% of affected individuals have HLA compatible siblings, and in light of the characteristic dilemmas surrounding HSC transplantation, β-thalassaemia has become a target for gene based therapies. The approach essentially involves the use of recombinant HIV viruses, known as lentiviral vectors (LV) in mediating gene delivery.

Method**:** Antoniou's group have recently devised a number of "GLOBE" constructs with the inclusion of regions physiologically present within the endogenous human β -globin gene, previously deemed insignificant, and therefore, omitted from all known published constructs to date. The inclusion of a full β-globin 2nd intron (850bp) has been added, yielding the latest generation of LV, GLOBE 4. The aim of this project was to conduct a comparative expression analysis between the GLOBE-2 (control) and GLOBE -4 vectors to evaluate whether the inclusion of the full 2nd intron allows (i) efficient LV production (in contrast with previous findings observed with gammaretroviral vectors) and (ii) increases β-globin mRNA levels. Lentiviral vectors were produced via cell transfection, and subsequently used to transduce our HSC model, the murine erythroleukemia cell (MEL). The quantity of vector derived human β-globin expression was quantified via qPCR and RT-qPCR analysis to determine the level of expression per LV copy.

Results**:** Average viral titres obtained for the GLOBE- 2 and GLOBE-4 constructs were $7.2x10^7$ and $5x10^7$ viral particles (vp)/ml respectively, incurring a 31% variance despite a 600bp difference in size. The relative amounts of β-globin expression adjusted to level of expression per vector copy were 0.869 (± 0.21) and 0.061 (±0.07) for GLOBE 4 and 2, thus revealing greater levels of expression for our novel GLOBE 4 construct.

The effects of hypothermia on hypoglycaemic injury to mouse optic nerve, a central white matter tract

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The high metabolic rate of the central nervous system (CNS) and its reliance on the oxidative metabolism of glucose means that deprivation of glucose or oxygen leads to rapid functional deficits. Research on neuroprotective therapeutics for conditions such as hypoglycaemia and ischaemic stroke have been focussed primarily on grey matter, showing little regard for protection of the myelinated portions of the CNS. Therapeutic hypothermia is neuroprotective in both white and grey matter for conditions of ischaemia; here it is investigated in isolated glucose deprivation.

The objective was to measure the effects of temperature on the recovery of compound action potential (CAP) area following 60 minutes of aglycaemia-induced axonal injury in the mouse optic nerve.
Mice were killed via schedule 1 cervical dislocation and optic nerves dissected out. Axonal function was assessed using evoked supramaximal CAPs.

60 minutes of aglycaemia with subsequent glucose reperfusion lead to a 34.7 ± 3.8% mean recovery of CAP area at 37˚C. Hypothermia and hyperthermia imposed throughout aglycaemia and glucose reperfusion lead to mean recoveries of 91.3 ± 8.1% and 10.3 ± 13.8%. Hypothermia and hyperthermia solely during aglycaemia gave mean recoveries of 73.8 ± 5.9% and 15.6 ± 5.3%. Hypothermia during glucose reperfusion alone gave a 71.3 ± 20.5% mean recovery.

The results show hypothermia to be protective and hyperthermia to be damaging in aglycaemia-induced white matter injury. Hypothermia was neuroprotective regardless of when imposed. The findings here highlight the potential use of TH as a clinical neuroprotective strategy for severe hypoglycaemic episodes.

Student Learning Needs in Psychiatry

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Background: To the authors' knowledge, very limited number of studies has been conducted into what materials medical students use to learn for their psychiatry undergraduate placement. This study aims to explore this area in more detail, and identify any gaps not adequately filled currently. It also explores student interest in psychiatry and whether they are considering pursuing it as a future career.

Method: Medical Students completed questionnaires about their psychiatric undergraduate placement at Manchester University (2010-2011).

Results: 126 out of 144 students responded, giving a response rate of 87.5%. Students spent a mean of 10.1 hours a week studying psychiatry (outside formal teaching) using various materials. Handouts from lectures or tutors were most commonly used (by 95.2% of respondents) with journals and podcasts being the least common (18.5% and 17.5% respectively). Psychiatric textbooks were the most useful for learning about psychiatry.

Students identified the need for better quality, more structured and more frequent teaching (n=58). Specifically they stated they wanted more lectures, small group teaching, mock OSCEs, and interviews with simulated or real patients to aid their learning of the subject. They also identified a need for greater clinical experience and increased availability of resources such as textbooks.

Conclusions: It appears that despite the growing popularity of the internet, students at Manchester still prefer textbooks to audio books and podcasts to learn. However much can be done to improve on the learning needs of students which, if addressed, may help with the recruitment crisis currently facing psychiatry.

Teaching Old Drugs New Tricks: Rationale for the Redeployment of Valproate, an Anti-Convulsant, and Niclosamide, an Anti-Helminthic Agent, as a Combination Therapy Against Multiple Myeloma

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Multiple Myeloma (MM) is an incurable plasma B cell neoplasm. Current best treatments are associated with significant comorbidites rendering the majority of older patients ineligible. Following a screen of 100 licensed, well-tolerated drugs from the BNF, we identify potent selective anti-MM activity of valproate and niclosamide (VaN) combination therapy, mediated through targeting the mitochondria.

MM cell lines and primary MM bone marrow samples were treated in vitro and cell viability, mitochondrial function and levels of oxidative stress response genes measured using flow cytometry, immunofluorescence assays and molecular techniques. Niclosamide demonstrated potent anti-MM activity against cell lines and primaries and induced a significant decrease in free light chain secretion. Niclosamide uncoupled oxidative phosphorylation causing mitochondrial membrane depolarisation and production of mitochondrial superoxide. Valproate had very little anti-MM activity alone, however in combination with niclosamide, enhanced mitochondrial superoxide production by regulating mRNA, protein levels and acetylation status of genes involved in the antioxidant response including SIRT3, a mitochondrial deacetylase, and manganese superoxide dismutase (SOD2) a key regulator of mitochondrial superoxide levels. Importantly, no induction of mitochondrial superoxide was observed in normal donor cells. VaN therapy also showed enhanced activity with the widely used anti-MM agent melphalan.

Valproate and niclosamide (VaN) have potent, selective anti-MM activity at clinically achievable concentrations, mediated by the generation of oxidative stress levels that are lethal for MM cells. These data, taken in the context of the known safety profiles of valproate and niclosamide, provide rationale for their use as a combination therapy in the treatment of MM.

The paracrine effect of mesenchymal stem cell conditioned media on TGF-β1 induced fibroblast to myofibroblast differentiation.

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Hypothesis & Aim: Idiopathic pulmonary fibrosis (IPF) is an incurable fibrotic lung disease where myofibroblasts are believed to play a key role in the pathogenesis. A mesenchymal stem cell (MSC)-mediated regenerative therapy has been proposed. MSC-mediated anti-fibrotic effects have been demonstrated in animal lung fibrosis models; however their effect on myofibroblast differentiation is unknown. This study will aim to determine the paracrine effects of MSC on myofibroblast differentiation.

Method: Human normal lung (CCD-8Lu) and IPF (LL29) fibroblasts were differentiated into myofibroblasts by TGF-β1 (5ng/ml) treatment for 24-hours. MSC-mediated inhibition of differentiation was assessed by co-incubation of fibroblasts with MSC-conditioned media (MSC-CM) and TGF-β1 for 24-hours. Reversal of TGF-β1 induced myofibroblasts was conducted by treating the cells with MSC-CM for 24, 48 and 72-hours. Determination of myofibroblast differentiation was assessed by immunocytochemical detection of α-smooth muscle actin (α-SMA) expression.

Results: Myofibroblast differentiation was achieved in (86.27+2.57%) and (86.69+2.51%) of CCD-8Lu and LL29, respectively. A significant reduction of myofibroblast differentiation was noted in both cell types; CCD-8Lu (56.54+3.67%) and LL29 (51.77+3.01%) following co-incubation with MSC-CM and TGF-β1 vs. TGFβ1 alone ($p<0.001$). A significant reversal of myofibroblast differentiation was observed following administration of MSC-CM vs. serum-free culture media ($p<0.001$). The duration of MSC-CM exposure influenced myofibroblast reversal in CCD8-Lu and LL29 cells; (81.7+0.43%) and (73.26+0.70%) at 24 -hours, (72.15+0.81%) and (60.57+4.27%) at 48-hours, (57.63+4.54%) and (60.65+4.9%) at 72-hours.

Conclusion: MSC inhibits and reverses TGF-β1 induced myofibroblast differentiation through a putative paracrine-driven mechanism. This has exploitative potential for anti-IPF therapeutic strategies.

Identifying characteristics of insulin pump use that predict good diabetes control in patients with type 1 Diabetes

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A proportion of type 1 diabetics fail to achieve glycaemic targets despite continuous subcutaneous insulin infusion (CSII). We examined differences in pump set-up and usage characteristics between patients with target and sub-optimal glycaemic control as well as low and high rates of hypoglycaemia.

198 patients treated with CSII at a single hospital clinic were categorised into those with target [HbA1c <7.5%] and sub-optimal [HbA1c ≥7.5%] glycaemic control. Patients were also divided into those with high [>3 episodes/week] and low [<3 episodes/week] rates of hypoglycaemia [capillary glucose < 4mmol/l].

Patients with target glycaemic control used more basal rates [5.57±2.6 vs. 4.84±1.8; p=0.029] and boluses [6.1±2.1 vs. 5.2±2.1; p=0.004] per day but there were no differences in total daily dose. Every 1 unit increase in basal rates and boluses per day was associated with a reduction in HbA1c of -0.231% (p=0.002) and -0.289% (p<0.0001) respectively. Target glycaemic control was associated with increased rates of hypoglycaemia. Patients with high rates of hypoglycaemia tested blood glucose more often [6.4±2.1 vs. 3.94±2.0; p=<0.0001), gave more boluses [5.75±1.8 vs. 5.15±2.1; p=0.018] and used the bolus calculator more [4.89±2.1 vs. 4.1±2.4; p=0.009] but overrode the bolus calculator more frequently [16.7±19.5 vs. 13.7±20.1%; p=0.02].

Target glucose control was associated with higher number of basal rates and boluses per day suggesting greater engagement with the pump, and more pro-active management of glucose control. Increased hypoglycaemia was associated with more frequent capillary testing, suggesting increased vigilance. Studies exploring CSII use that results in optimal glycaemic control without hypoglycaemia are merited.

Expression of the Splice Variants of ST2 in Placentae from Healthy and Complicated Pregnancy

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Pregnancy complications such as pre-eclampsia (PE) and intra-uterine growth restriction (IUGR) cause significant fetal and maternal morbidity and mortality. ST2 is the receptor for the type 2 cytokine IL-33. IL-33 is an IL-1 family, pro-inflammatory cytokine that stimulates the production of type 2 cytokines from Th2 cells. ST2 has three isoforms including a membrane bound form, ST2L; ST2V, expressed in the gut; and a soluble secreted form, sST2, which acts as a decoy preventing IL-33 signalling. Previous research found higher placental total ST2 mRNA expression in PE compared to healthy pregnancy. The current study investigated relative placental expression of the ST2 isoforms in PE and also IUGR where placental pathology is present but maternal systemic response absent. mRNA expression of the splice variants of ST2 in placentae from healthy (n=50), PE (n=22) and IUGR (n=28) pregnancies was quantified using RT-PCR. sST2 has no unique exon sequence and was estimated using total ST2 minus ST2L expression. Placental total ST2 mRNA expression was significantly elevated in PE compared to healthy pregnancy [2.27 (0.54) versus 1.92(0.41), mean(SD) log mRNA expression relative to control, p=0.021]. There was no difference in ST2L mRNA expression between normal and PE placenta. Estimated sST2 mRNA expression was significantly elevated in PE compared to healthy placenta [2.27(0.54) versus 1.92(0.41), p=0.02]. There was no difference in total ST2, ST2L or estimated sST2 expression between healthy and IUGR placenta. The increased placental total ST2 mRNA expression in PE is due to the sST2 isoform of the receptor and is specific to PE.

How the amount of protein in a maternal diet affects neural stem cell development in 14.5 day old mice embryos.

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Early phases of embryogenesis are susceptible to maternal malnutrition; with an increased incidence of disease in later life. To see whether protein restriction in a maternal diet affects neurogenesis, we examined the effect of a normal maternal protein diet (control; 18% casein), a low protein switch diet (LPS; first 3.5 days: 9% and remainder 18% casein) and a low protein diet (LPD; 9% casein) during gestation.

The pregnant mouse was culled and 14.5 day old embryos brains isolated. The ganglionic eminences neural stem cells were cultured & the numbers of neurospheres counted. These were passaged and secondary neurospheres were counted.

Primary neurospheres showed no significant difference between control & LPS and LPD & LPS; however, a significant difference was seen between the control and LPD groups ($p<0.05$). With the secondary neurospheres, there was no significant difference between any groups.

Neurosphere size within each group was investigated. Primary neurospheres sized 100-199µm, showed a significant difference between all groups; the control had the largest number, followed by LPS then LPD ($p<0.05$). This was also seen in the 200-399µm size range, except between the LPD and LPS groups where there was no significant difference. >400µm neurospheres showed no significant difference between the groups. The size distribution in secondary neurospheres was similar in all groups.

In conclusion, protein restriction in maternal mouse diets has an initial effect on neural stem cells in 14.5 day old embryos. However, this initial deficit is compensated in passaged neural stem cells.

An Old Antipsychotic Drug with New Pharmacology? Investigating Haloperidol's Action on Dopamine D2 Receptor Signalling.

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Background: The dopamine-D2 receptor is a major therapeutic target for antipsychotics which signals through a number of different intracellular pathways. Biased agonists differ from classic agonists/antagonists in that they preferentially signal through one of these pathways. Thus, clarifying the key signal transduction pathways activated by individual antipsychotics may be important in delineating their therapeutic action and side effects in a clinical context. Here, we studied whether the antipsychotic haloperidol and structurally related butyrophenones (droperidol, risperidone, melperone, and domperidone) displayed biased signalling at the long isoform of the dopamine-D2L receptor (D2LR).

Method: Chinese hamster ovary (CHO)-K1 cells expressing an N-terminal SNAP-tagged D2LR receptor and SPAP reporter gene (CHO-ssD2L cells) were used. D2LR inhibition of cAMP production and signalling via β-arrestin were measured indirectly by CRE-mediated SPAP reporter gene and receptor internalization assays, respectively.

Key results: Haloperidol acted as an agonist showing significant internalization ($p<0.05$ using one-way ANOVA and Bartlett's test) in the receptor internalization assay and as an antagonist of quinpirole induced CRE-SPAP responses. Droperidol, risperidone, melperone and domperidone solely acted as antagonists throughout these assays. Dissociation constants for each compound for both assays, pA2 (7.5-10.3) and pKb (7.8-10.2) were derived using Gaddum-Schild analysis, respectively. Differences between these values for each compound were not statistically significant.

Conclusion: This study suggests haloperidol exhibits biased signalling at the D2LR. This characteristic is specific to haloperidol as the other butyrophenones under investigation did not display this.

The Changing Epidemiology of Clavicle Fracture in an Adult Population

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Background: A number of studies have described the epidemiological characteristics of clavicle fractures, including two previous reports from our institution. The Robinson classification system was described in 1998, after the analysis of 1,000 clavicle fractures. We aim to provide a contemporary analysis and compare current clavicle fracture patterns of our adult population with historical reports.

Methods: A retrospective analysis of a prospectively collected fracture database from an institution serving 598,000 was conducted. Demographic data were recorded prospectively for each patient with an acute clavicle fractures including age, gender, mode of injury, fracture classification, and the presence of associated skeletal injuries. Fractures were classified according to the Robinson system.

Results: A total of 312 clavicle fractures were identified, occurring with an incidence of 55.9/100,000/yr (CI 49.8-62.5) and following a bimodal male and unimodal older female distribution. Sporting activity and a simple fall from standing caused the majority of injuries. More than half of simple fall fractures affected the lateral clavicle. Overall, type II mid-shaft fractures remain the most common, but comparison of this series with historical data reveals that the epidemiology of clavicle fractures is changing. We have identified an increase in the average patient age and overall incidence of clavicle fractures in our adult population.

Conclusions: The epidemiological characteristics of clavicle fractures in our adult population are presented. The incidence, relative frequency, and average patient age of type III lateral one-fifth fractures have increased. This epidemiological trend has implications for the future management of clavicle fractures in our region.

Crush Cytology of gastro intestinal malignancy. A cytohistological comparison.

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Introduction: Gastrointestinal malignancies are commonly encountered in medical practice and endoscopic examination and biopsy. Crush cytology of gastrointestinal malignancy is a simple, cheap and readily available technique which increases diagnostic yield and expedites diagnostic work-up of such patients. Compared to biopsy, crush preparations require minute amount of tissues and provide rapid diagnosis.

Material and Methods: All cases of gastrointestinal malignancy of esophagus, stomach and colorectum, which underwent endoscopic examination from January 2007 to September 2011, in Kasturba Medical College and Hospital, Mangalore, India, were included in the study. The diagnosis on crush cytology was compared with histopathological diagnosis, along with review of the patients' records. Diagnostic accuracy, sensitivity, specificity, positive predictive values were calculated.

Results: Total 204 cases of gastrointestinal malignancy were evaluated with endoscopy and crush cytology during this period. Respective histolopathological examination was available in 170 (83.3%) cases. There were 119 cases of histologically confirmed carcinomas with male:female ratio of 2.6 : 1.The most common site of carcinoma was stomach (35.9%) followed by colorectal (29%), oesophagus (26.5%), duodenum and gastroeosphageal junction with 4.3% cases each. Crush smears were inadequate in 5 cases. The sensitivity of crush cytology was 81.1%, with a specificity of 83.7%, positive predictive value 93.4% and negative predictive value of 61%. The diagnostic accuracy of crush cytology was 95.2%.

Conclusion: Crush cytology is a cost effective diagnostic tool with high diagnostic accuracy, specificity and sensitivity, and provides early diagnosis, which is helpful in planning the further management of gastrointestinal carcinoma cases.

The Prevalence of Diverticular Disease in Riyadh, Saudi Arabia

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Background: Diverticulosis is an outward protrusion of the mucosa and submucosa of the colon. Only 5% of patients may develop inflammation of the diverticula (diverticulitis). Life style and eating habits significantly impacts the distributional prevalence of the disease. Diverticulosis is on the rise in developing countries and underreported in countries such as Saudi Arabia. Despite the low complication rates of the disease, immediate intervention is critical due to the severity of the complications once occurred. This is a hospital-based study to assess the prevalence of diverticulosis and its clinical implication on patients.

Methodology: This is a cross sectional study where data were extracted from the colonoscopy medical charts (2006-2011) at the National Guard Health Affairs (NGHA) – Riyadh, Saudi Arabia. Assuming a prevalence of 27%, α= 0.05, β=0.20, and a precision of 0.05, the optimal sample size was 302 subjects. Only 269 charts met the study inclusion criteria and were reviewed. Data was analyzed descriptively to identify both demographic and clinical characteristics of patients with diverticulosis. Moreover, logistic Regression was used to identify significant predictors of "diverticulitis disease".

Results: Diverticular Disease accounted for 7%; it was mainly positioned on the left side (57%). The majority of the patients were male (62%), mean age (63 ±12), mean BMI (29.1± 5.9).The majority of patients were symptomatic (72%), where diffused abdominal pain ranked highest (51%). Use of NSAIDS was the only significant predictor of diverticulitis (P-value: 0.03)

Conclusion: This study act as an exploratory study that can set the ground for future investigational research since it sheds the light on the prevalence of the disease, its clinical implications and possible risk factors.

The effect of socioeconomic factors in the treatment of Multiple Sclerosis

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Background: There are many treatments available for MS; however the fairness of allocation of such has been questioned. Research has shown that access to the Disease Modifying Treatments (DMTs) such as Beta Interferons is influenced by our postcode. The study assesses whether deprivation also plays a role in allocation of the newest MS treatments mainly Tysabri.

Methods: Data was collected from 1,263 MS patients whose MS was managed at the Queens Medical Centre, Nottingham. A binary logistic model was constructed to assess any correlation between treatment allocation and deprivation together with sex, age, MSSS score and time in years between onset and diagnosis.

Results: The results showed that deprivation does not influence treatment of Tysabri, Beta Interferons or Copaxone, which contradicted the previous research. They also showed that as age of MS patients increased, the likelihood of receiving DMTs was reduced.

Conclusion: We can assume that the reduced inequalities in treatment are due to the NHS actively trying to reduce health inequalities, and that as MS drugs have become more established, disparities in their allocation have been reduced. Also the lack of Tysabri allocations may be due to the possible adverse effects such as the risk of progressive multifocal leukoencephalopathy and so physicians are wary about such treatments. Further research is however needed in order to generalise such assumptions to the rest of the UK.

Staged management of complex low birth weight tetralogy of Fallot

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Appropriate management of low weight infants with complex tetralogy of Fallot is often fraught. We present a 2.8kg infant with Di George syndrome and spelling tetralogy with non-confluent pulmonary arteries, the left pulmonary artery being supplied by an aberrant ductus arteriosus from the left common carotid artery. This is truly unique anatomy, never documented before. We performed a pioneering management regime, which included stenting of the outflow tract and the ductus to allow this patient to progress towards an elective surgical correction. This surgery was undertaken 11 months after the initial stenting procedure and was successful; the infant is now growing, and thriving.

Management of complex neonatal tetralogy of Fallot is has multiple approaches and there is no overall consensus as to the best strategy. The use of neonatal outflow tract stenting has added a potential temporizing procedure to our armamentarium. This case illustrates the extremes of complex Tetralogy with the left pulmonary artery supplied by an aberrantly arising ductus arteriosus; providing a major management dilemma in a low weight infant. The pioneering management strategy has made a condition previously incompatible with life, compatible with life until the infants weight and size allows a corrective surgical procedure. This management strategy has the potential herald a new and successful regime for low weight infants whilst they grow to a weight compatible with surgery.

A cadaveric study of subpatellar nerves in relation to incisions used for total knee arthroplasty

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A midline incision (MI) for total knee arthroplasty provides good access to the knee but damages the infrapatellar branch of the saphenous nerve and medial cutaneous femoral nerve causing lateral skin dysaesthesia in 55-100% of cases and occasionally painful neuroma and complex regional pain syndrome. The anterolateral incision (ALI) seeks to prevent this by penetrating the skin in an area of sparse neurovasculature.

A skin and subcutaneous fat flaps were reflected in 12 cadavers (mean age 82.8 ±SD10.3 years) in order to reveal the subpatellar nerves. Following this, the position of both ALIs and MIs were marked to determine the quantity of nerve branches crossing each incision, as well as the number of terminal nerves void of supply. Measurements between the most superior and inferior nerves to cross each incision, as well as the distance from the inferior border of the patella to the tibial tubercle were taken for inter-cadaver analysis of desensitisation.

No significant difference was seen between the numbers of nerve branches crossed by each incision; however, the ALI crossed the nerves further from their origin reducing the likelihood of neuroma formation. The ALI blocked the supply to significantly less terminal nerves ($p=0.026$), which would reduce the area of numbness experienced compared to a MI. Furthermore, the ALI permits faster wound healing as less vascular damage occurs, enabling earlier flexion after surgery without strain on the wound.

An ALI could provide a good alternative to a MI in cases where normal skin sensation takes precedence over incision size.

Recurrent intestinal volvulus In midgut malrotation as a cause of acute bowel obstruction

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Background: Intestinal malrotation occurs when there is a disruption in the normal embryological development of the bowel rotation, elongation and fixation. The majority of patients present with clinical features in childhood, though rarely a first presentation can take place in adulthood. Recurrent bowel obstruction in patients with previous abdominal operation for midgut malrotation is mostly due to adhesions but few cases have been due to recurrent volvulus.

Case: We present the case of a 22 year old gentleman who had laparotomy in childhood for small bowel volvulus and then presented with acute bowel obstruction. Preoperative CT scan showed small bowel obstruction and features in keeping with midgut malrotation. Emergency laparotomy findings confirmed midgut malrotation with absent appendix, abnormal location of caecum, ascending colon and small bowel. In addition, there was small bowel volvulus and a segment of terminal ileal stricture. Limited right hemicolectomy was performed with excellent postoperative recovery.

Discussion: Midgut malrotation is a rare cause of intestinal obstruction in adult life and only few of such cases have been reported in the literature. Recurrent intestinal obstruction is even rarer in adults who have been previously operated for gut malrotation and few of such cases have been reported.

Conclusion: Midgut malrotation is a rare but an important cause of bowel obstruction in the adult population. The most dreadful and life threatening complication of intestinal malrotation both in children and adults is gut volvulus with possible ischaemic changes and associated high mortality.

Pseudoaneurysm in a patient with Tuberous Sclerosis complicated by multiple renal angiomyolipoma and pulmonary lymphangioleiomyomatosis: A rare manifestation

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Coexistence of renal angiomyolipoma (AML) and pulmonary lymphangioleiomyomatosis (LAM) associated with Tuberous Sclerosis (TS) is extremely rare, first described only in 1994. Spontaneous haemorrhage of renal AML may lead to pseudoaneurysm formation and can be life-threatening. A literature search reveals just four cases of pseudoaneurysm associated with renal AML and TS. This appears to be the first example of renal pseudoaneurysm in a case of TS with renal AML and concomitant LAM.

This case report describes a presentation of a pseudoaneurysm complicating renal AML in a patient with TS with LAM. Previously undocumented, it is important to describe this interesting condition and the treatment choices made in order to improve understanding of its management.

A 46 year old female was admitted with pyrexia, shortness of breath, right-sided loin pain and frank haematuria. Renal US showed bilateral multiple AML and a large solid mass in the lower pole of the right kidney. MRI confirmed it to be a 85mm haemorrhagic mass. CT angiogram showed a 33mm x 27mm pseudoaneurysm contained within this. Due to coexisting lung disease, she was unsuitable for nephrectomy and consequently underwent embolisation. Following this, she developed persisting pyrexia and worsening renal function which eventually settled with conservative treatment. She was discharged and continues to be followed up in the clinic.

This case report is a unique chance to discuss the management choices made for this young woman suffering from a rare presentation of complications arising from Tuberous Sclerosis.

Investigating the Efficacy of a Current Subcutaneous Insulin Regimen during Nasogastric Feeding using Continuous Glucose Monitoring

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Post-stroke hyperglycaemia is associated with detrimental clinical outcomes. Glycaemic disturbances may be exacerbated by nasogastric (NG) feeding. A feeding-specific protocol has been designed for patients with type 2 diabetes (T2DM): intravenous (I/V) sliding scale insulin on Day 1, followed by subcutaneous (S/C) insulin (soluble and intermediate-acting insulin at start of feed; intermediate-acting insulin halfway through feed) on Days 2 and 3. Our aim is to determine whether this regimen achieves good glycaemic control in stroke patients.

Study 1 was a retrospective audit of 19 patients with T2DM requiring NG feeding following stroke. In Study 2, an iProTM2 Continuous Glucose Monitoring device was fitted to 4 prospectively-recruited participants for 3 days to assess glycaemic control.

In Study 1, 13 patients received S/C insulin during feeding (4 followed protocol, 9 received alternative regimens), Most patients (15.4% on Day 2, 25% on Day 3) did not achieve ≥80% of glucose measurements within target (4-10 mmol/L) while receiving S/C insulin. Glycaemic outcomes with S/C insulin were inferior to I/V insulin, with respect to proportion of measurements within target (p=0.006) and mean glucose (p=0.002). In Study 2, the S/C insulin regimen has maintained good glycaemic control in 2 out of 3 patients with T2DM, without inducing hypoglycaemia (<4mmol/L). The non-diabetic patient remained normoglycaemic.

Current practices are highly variable and failing to attain glycaemic targets. A standardised protocol may establish tighter control during NG feeding. In clinical practice, this requires insulin dose adjustments in response to feeding changes, and optimising transition from I/V to S/C insulin.

Risk Factors for Mortality in Patients with Tuberculosis in a Rural Area of Malawi.

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Background: Tuberculosis (TB) is a major cause of morbidity and mortality in the developing world, despite the widespread availability of effective treatment. The rise in the incidence of HIV infection in sub-Saharan Africa over the past 20 years has led to a rapid increase in the incidence and mortality of TB infection. This indicates a need to identify the risk factors leading to TB deaths and to evaluate the impact of HIV infection on TB patients. This will enable the implementation of TB control measures which aim to reduce the mortality of TB infection.

Methods: Data was collected from existing TB registers containing information on patients who registered with TB at Nkhoma Hospital, Malawi, between January 2008 and August 2011. Several factors including age, gender, TB classification & sub-type, HIV status, ART status and CPT status were evaluated for their effect on TB mortality using Pearson Chi-square analysis and crude and adjusted odds ratio calculations.

Results: Out of 917 patients, 220 (24.1%) of patients died during the course of TB treatment. Using multivariate analysis, independent risk factors for TB mortality were old age; male gender, miliary TB, meningeal TB, abdominal TB, and pericardial TB. HIV positive patients who had not started ART during the course of TB therapy were also significantly at risk of death.

Conclusion: These findings suggest that, improved coordination of TB and HIV services, and more effective diagnosis and treatment of extrapulmonary TB could help reduce TB related morbidity and mortality rates in this area of Malawi.

Continuous Infusion Analgesia In Thoracic Surgery (CIATS) Reduces Morphine Usage In Patients Who have Empyema And Undergo Open Decortication.

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Objectives: Continuous infusion analgesia in thoracic surgery (CIATS) used for post-thoracotomy pain control. CIATS consists of a catheter in the wound topped up with 10 mls of 0.25% chirocaine and connected to continuous infusion of 0.1% chirocaine 5ml/hr. We reviewed the impact of CIATS in thoracic surgery in decortication patients.

Methods: 15 cases that had undergone thoracotomy for decortication were retrospectively analysed. 8 had CIATS with morphine PCA (Group1), 7 patients had only morphine PCA (Group2). Patients had supplementary analgesia consisting of paracetamol, tramadol, di-hydrocodeine, and non steroidal inflammatory drugs. Post-operative pain scores, amount of morphine used and length of hospital stay (LOS) were measured.

Results: Mean morphine infused, mean duration of PCA, mean post-operative pain scores on day 1-2 and mean hospital stay recorded in Table1.

Supplementary analgesia utilised in group 1; 3 patients required 1 extra drug, 4 required 2, and 1 required 3. Supplementary analgesia utilised in group 2; 4 patients required 2 extra drugs, 3 required 3, while 1 required 4 different drugs.
Better pain scores and reduced morphine usage in CIATS but not significant. There was statistical significance between the 2 groups in mean duration of PCA usage (p=0.05).

Conclusions: CIATS is efficacious in the management of post thoracotomy pain.

	Group 1(CIATS + PCA)	Group 2(PCA)	P values
Mean total morphine infused (mg)	92	112	p=0.29
Mean duration of PCA used (hrs)	44	66	p=0.05
Mean post-operative pain score D1	2.2	2.4	p=0.37
Mean post-operative pain score D2	1.8	2.7	p=0.22
Mean hospital stay (days)	7	7	p=0.5

From Behcet's Disease to Dilated Cardiomyopathy: A Patients' Journey

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Behcet's disease or the silk route disease is a rare, multi-systemic, autoimmune disease of unknown aetiology. This vasculitic syndrome initially presents with mouth and genital ulcers and later on affects the eyes, intestines and central nervous system. The current rate of prevalence in the United Kingdom is 0.64 per 100,000.

This case study highlights the journey of a 26 year old Caucasian showroom assistant from Liverpool who started developing mouth ulcers in his early teens. Aged 21, he developed genital ulcers which he described as 'tender, open wounds' lasting a few weeks. All possible sexual diagnoses were excluded and he was referred to rheumatology where a pathergy test confirmed the diagnosis of Behcet's disease.

Soon after the diagnosis, he reported constant palpitations and shortness of breath after little or no exertion. A 24 hour electrocardiogram (ECG) showed that he had supraventricular tachycardia, P wave morphology with ventricular ectopics. A diagnostic transthoracic echocardiogram confirmed left sided heart failure and dilated cardiomyopathy with an ejection fraction (EF) of 33%. There was moderate global hypokinesia of left ventricle along with reduced left ventricular systolic function. He was treated with a beta-blocker, an ACE inhibitor and a loop diuretic which improved his EF to 44%. He requires treatment from time to time for episodes of pyelonephritis, epididymitis and recurrent E.coli infections.

In conclusion, dilated cardiomyopathy in a Behcet's patient is a rare presentation with only a few reported cases and symptoms of heart failure should be promptly assessed by echocardiography.

Vitamin B12 and Vitality: A questionnaire study to determine patient perceptions of B12 effect on vitality

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B12 deficiency is common: prevalence ranges from around 4% in young adults to 12.6-14.5% in older adults. Short-term failure of treatment impacts quality of life. A 3-monthly B12 injection is the most popular treatment method, however guidelines on treatment frequency are not evidence-based, and patients report a return of symptoms before receiving their next injection.

Primary care patients receiving B12 injections were identified by GPs and postally surveyed to determine symptom recurrence. The survey was also available for completion via the NACC website. 465 responses were received by April 4th 2012. In the week before injection, over half of the sample reported tiredness, energy levels, concentration, bodily aches and mood as 'Poor' or 'Terrible'. More than 5 symptoms are affected in 54.8% (95% CI: 50.3-59.4) participants. 31% (95% CI: 26.5-35.5) experience symptom onset more than one week before injection. 58.0% (95% CI: 53.5-62.5) participants want the injection more often. A small proportion (15.8% (95% CI: 12.4-19.1)) would prefer oral B12 to an injection.

In conclusion, a substantial majority of participants experience multiple symptoms, often more than a week before their next injection is due. Further studies are required to establish an evidence base for treatment frequency, to minimise symptom recurrence. Oral B12 may be trialled in a primary care setting for those patients that would prefer it.

Case series: Deep peroneal nerve compression in 2 patients caused by an osteophyte arising from the 2nd tarso-metatarsal joint.

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Background: Compression neuropathies of the foot and ankle are uncommon and may be underdiagnosed and underreported in the literature. Deep peroneal nerve (DPN) compression typically causes pain or dysaesthesias in the first dorsal webspace, discomfort at the site of compression and night pain. Compression of the DPN typically occurs beneath the inferior extensor retinaculum. We report two cases of DPN compression recently encountered in our institution. In both cases, the compression was caused by an osteophyte arising from the 2nd tarso-metatarsal joint. This is an unusal presentation of midfoot arthritis that could easily be misdiagnosed. The authors aim to raise awareness of this pathology as a cause of DPN compression in the foot.

Methods: A literature review was performed using medline and pubmed databases. No case reports of DPN compression secondary to osteophytosis of the 2nd tarso-metatarsal joint were found.

Results: Conservative management with orthotics failed in both cases. Patient 1 has recently undergone surgery and is awaiting review. Patient 2 has not yet undergone surgery.

Discussion/Conclusion: Successful management of foot and ankle compression neuropathies is entirely dependent upon identifying the precise site of nerve compression. Recent advances in electrodiagnostic and imaging modalities have increased our understanding of the pathologies associated with these conditions. Sound clinical examination skills are essential and an awareness of all possible causes of foot pain/dysaesthesia is required in order to request the most appropriate investigation in the first instance. The authors feel that midfoot arthritis deserves recognition as a cause of DPN compression.

Characterstics of gestosis in partureints with heart disease

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Background: Heart disease can complicate pregnancy due to increase stress on heart, one of the most common complication is late gestosis of combined form.So in this complex problem particular importance is the further improvement of tactics in term of preservation of parturients and fetus.

Objective: Study of outcomes and characteristics of gestosis in parturients with heart disease.

Materials and Methods: We analyzed 15 parturients with heart disease, aged 19 - 40 years with primigravida - 7 and multigravida - 8. Acquired heart diseases occurred in 10 (66.7%) and congenital in 5 (33.3%). In acquired heart diseases most common being mitral valve insufficiency - 8 (80%) and mitral stenosis - 2 (20%) . Pregnant with compensated heart diseases were 66.7% and cardiac decompensation occurred in 33.3% of pregnants.

Result: Appearance of gestosis in the second half of pregnancy were observed from 19-22 weeks in 10 parturients, from 28 weeks - in 5 parturients. In 7 cases - 1st stage of gestosis in the form of oedema, in 6 cases - in the form of edema and arterial hypertension and in 2 cases in the form of oedema and proteinuria of up to 0.033% were present.
Other obstetrical problems in these parturients were anaemia - 76%, chronic feto-placental insufficiency - 100%, intrauterine growth restriction - 24%, risk of pregnancy termination - 48%.
Delivery related complications like delayed rupture of membranes - 16.8 % of cases, primary and secondary uterine inertia - 38.5%, hypoxia and birth asphyxia were noted in 27.1%. Episiotomy was performed in 44.4% of cases.

Conclusion: Only correct outpatients observation early detection of sub clinical stages of gestosis and their adequate correction to avoid severity especially in parturient with heart disease can ensure a women to the happiness of motherhood.

Counselling of Women in Preterm Labour: Exploring Current Practice and the Benefits of Additional Written Information

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During antenatal counselling in preterm labour, the possible risks and outcomes of early delivery are explained to parents. Current standard practice offers verbal counselling alone to women who are likely to deliver below 35 weeks of gestation.

This study assessed effectiveness of antenatal counselling in preterm labour, and evaluated benefits of providing additional written information.

25 mothers who delivered between 26+0 and 34+6 weeks gestation were recruited, in two consecutive cohorts, at a single hospital. The first cohort received standard verbal information, and the second, additional written information in the form of a newly designed leaflet. Questionnaires were given within one week of delivery, to assess efficiency of counselling, changes in perceived understanding and preparedness, and opinions on the quality of information provided.

The counselling process improved maternal understanding equally in both cohorts with 75% of mothers understanding "a fair amount" or more after counselling. Preparedness was significantly improved post-counselling (p=0.02) with a higher proportion in the leaflet group showing an improvement (75% vs. 43%). More mothers in the leaflet group also felt well-informed (78% vs. 64%), and fewer in this group wanted further information (56% vs. 80%). 100% of those who received the leaflet found it helpful.

Findings suggest written information, as an adjunct to verbal counselling, is beneficial to parents. Participants felt leaflets were useful, as they added to understanding and could be used as a reminder of information. Doctors at the study site have now adopted the leaflets as part of their standard practice.

Health beliefs about preschool immunisations; an exploration of the views of Somali women resident in Birmingham

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Background: Preschool immunisations significantly reduce child morbidity and mortality. Successful immunisation depends on the attitudes of mothers towards vaccinations. The Somali community in Birmingham forms a significant proportion of the growing Black African ethnic group, which has the lowest levels of preschool immunisation. There is no existing evidence regarding the perceptions towards preschool immunisations dominant in this community.

Aim: To explore the health beliefs of Somali women resident in Birmingham regarding preschool immunisations with the intention of assisting healthcare providers to deliver services in a manner sensitive and complementary to the Somali culture.

Methods: Designs: Semi-structured interviews. Setting: Third-sector organisations providing services to Somali women in Birmingham. Recruitment: Somali women who are mother of at least one child under five years old. Analysis: Thematic analysis concurrent with data collection.

Results: Data were collected from 23 participants. General attitudes towards preschool immunisations were positive. However, beliefs were affected by mothers' perceptions of their child's susceptibility to infection as well as a fear of side effects, including Autism. There was evidence of a fatalistic outlook on health, shaped by religious beliefs. Many mothers also feared, and sometimes refused, immunisations due to the belief that they contain gelatine.

Conclusions: Results suggest increased education is needed to improve knowledge and decrease suspicion of immunisations. Time should be taken by clinicians to ensure understanding of the purpose of vaccination in order to reduce fear and speculation. Religious advisers should be updated on the ingredients of immunisations so that they can accurately advise the Somali community.

Brody's Syndrome with autosomal dominant inheritance: An extraordinarily rare case of muscle cramping.

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Brody's syndrome is a rare inherited myopathy affecting just 1 in 10 000 000 births, characterised by exercise-induced impairment of muscle relaxation. Inheritance is typically autosomal recessive, and a significant number of these cases harbour mutations in ATP2A1 which encode SERCA1, the fast twitch fibre isoform of sarco/endoplasmic reticulum Ca2+-ATPase. Rarer autosomal dominant cases have been reported; however, genetic aetiology remains undetermined.

We present L.W., a 49-year-old, female company director, who presents with exercise-induced muscle cramps which exacerbate in the cold. Symptoms date back to early childhood. She has never been able to run and describes difficulty sustaining muscle activity sufficient to ascend a set of stairs. L.W. reports several episodes of prolonged cramps and myalgia associated with pigmenturia, consistent with rhabdomyolysis. Throughout her adult life several differing rheumatological diagnoses have been postulated. Neurological examination was remarkable for mild proximal weakness. Repetitive exercising induced cramping activity that was electrically silent. Creatinine kinase was elevated at 1100IU/L. There is an interesting and complex family history which is likely to reflect an autosomal dominant inheritance spanning three and possibly four generations.

This case represents only the fifth autosomal dominant case of Brody's syndrome reported in the literature. So far, attempts to define a genetic locus have been unsuccessful. This family may elucidate genetic and molecular processes underlying this heterogeneous condition. Such insight may help guide more targeted therapeutic options. This case also exemplifies the formidable diagnostic challenges of rare inherited muscle disease presenting with non-specific musculoskeletal symptomology.

Churg-Strauss Syndrome in a Patient with Allergic Bronchopulmonary Aspergillosis – A Diagnostic Challenge

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Few instances of Churg-Strauss syndrome co-existing with Allergic Bronchopulmonary Aspergillosis (ABPA) have been reported in the literature.

This is the case of a 62-year-old man presenting with shortness of breath, lethargy and weight loss of two stone in three months. He had a history of ABPA, asthma, bronchiectasis, emphysema and unilateral deafness.

Examination findings were normal save a cachectic appearance and a slight right radial nerve palsy. The initial working diagnosis was an exacerbation of ABPA. A full blood count revealed a Haemoglobin count of 9 g/dl and an eosinophil count of 7.91 x109/l. Serum urea and creatinine were 8.3 mmol/l and 133 µmol/L respectively.

Computed Tomography of the chest showed emphysema, bronchiectasis and a ground-glass appearance. A gastroscopy, colonoscopy and subsequently a bone marrow biopsy revealed no cause for the normochromic, normocytic anaemia. Nerve conduction studies showed no sensory response in the right medial and ulnar nerves. The urine albumin:creatinine ratio was raised and there was some microscopic haematuria. He was found to be pANCA positive, with a raised anti-myeloperoxidase titre. He was subsequently treated with oral steroids which led to an improvement in his breathing and renal function, with the neuropathy showing signs of amelioration over the following weeks.

Complex patients with vague symptoms often present a challenge to medical teams caring for them, particularly when no unifying diagnosis is forthcoming. This case highlights the need to approach such patients holistically in a systematic fashion, involving other specialties early to avoid overlooking aspects of patient care.

An unusual presentation of testicular torsion in a young patient

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Testicular torsion is a surgical emergency commonly occurring in childhood. This case highlights an unusual presentation whereby the diagnosis was made after three admissions and thirty hours from symptom onset.

A fourteen-year-old boy presented with gradual onset severe abdominal pain with a one-week history of feeling unwell, diarrhoea and vomiting. On examination he was uncomfortable, apyrexial and tender over the right renal angle, right iliac fossa and suprapubic region. Initially both testes were fully descended, of normal lie and non-tender. Six hours later his left testis was high-riding and slightly enlarged. After another hour his right testis was high-riding and horizontal, lobulated but non-tender. Physical examination was otherwise normal. An ultrasound scan showed heterogenous enlargement of the right testis with no blood flow. Surgical exploration followed by right orchidectomy and left orchidopexy was performed. Right testicular torsion was confirmed, predisposed by bilateral bell-clapper deformity.

Sudden severe scrotal pain and other characteristic features were absent, except for abnormal lie of both testes. This caused unnecessary delay in diagnosis and subsequent intervention, thus necessitated the removal of an extensively necrotic testis that could have been salvaged otherwise by detorsion. Research and guidelines advocate urgent surgical exploration if an acute scrotum is suspected, as increased waiting time and ensuing tissue damage reduce testicular salvage dramatically.

Management of this patient could have been improved by tackling communication with teenagers, relative inexperience of junior doctors, strict adherence to guidelines, and the essential need to recognize that patients do not always present with archetypal 'textbook' symptoms.

Retrospective Study of a Type B Aortic Dissection Population In The University Hospital of Antwerp (UZA)

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Background: Acute complicated dissections are mostly treated via open surgery or with TEVAR. The golden standard for the acute uncomplicated AD's is conservative treatment with rest and antihypertensiva. Retrospectively we explored if this approach can be extrapolated to the UZA-population.

Methods: We collected data from 2003 until 2011 and a total number of 50 patients were included. Using the hospital's database we gathered all useful information concerning type B AD's.

Results: From the total of 50 patients, 23 were complicated and 27 uncomplicated. The male gender clearly overbalanced counting 40 men and 10 women. Most dissections were seen between the age of 50 and 70. Four Marfan patients were included. Thirty-four patients were initially treated conservatively from whom 26 were uncomplicated and eight complicated. Eight patients had open surgery and all of them showed one or more complications. Eight patients were treated with TEVAR, seven were complicated. From the conservative uncomplicated 23 survived, however 3 of them developed a complication obliging open surgery. In the conservative complicated group 5 patients survived from whom 3 eventually underwent open surgery. Five patients survived in the open complicated group and one was lost to follow up (LTFU). The complicated type B AD's treated with TEVAR held 2 survivors and 2 were LTFU. The one uncomplicated who was treated with TEVAR was LTFU.

Conclusion: UZA also considers conservative treatment in uncomplicated type B dissections as the golden standard. We can also notice that there is no advantage in trying to treat complicated type B AD's on a conservative base. Furthermore our data imply that the prevalence of type B AD's is higher in men. The factors responsible for this probable correlation need to be explored in the future. In case of a complicated type B dissection an open approach seems to have a better outcome.

Auto-antibodies in SLE: Is Antigen Microarray the Future in Autoimmunity Diagnosis?

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The successful diagnosis of Systemic Lupus Erythematosus (SLE) is based on clinical presentation as well as multiple autoantibody serological testing; both of which are expensive and time-consuming. This study aimed to optimise and henceforth illustrate the potential use of antigen microarray to detect various autoantibodies for the purpose of screening as well as disease monitoring. Serum samples were obtained from SLE patients (n=19) and healthy controls (n=7). The serum was analysed by antigen microarray technology to detect 8 known SLE antigens, a Rheumatoid Arthritis (RA) antigen and several positive control antigens. Optimum results were obtained when antigens were printed in trehalose PBS-Tween onto aminosilane slides (Nexterion ®). The lowest background and highest signal-to-noise ratios were obtained when serum was diluted in antibody diluent (Dako). The main finding of this study was that patients had significantly higher autoantibody presence in 3 of the SLE antigens tested: Nucleosome, Ribonucleoprotein and Ribosomal P ($P<0.001$, $P<0.001$, $P<0.005$), in addition to the RA antigen CCP2 ($P<0.001$). Furthermore, antibody levels from patients on treatment correlated with disease improvement. These results suggest that microarray is an efficient technique to monitor and detect a wide variety of antibodies in multiple patients simultaneously, doing so at a relatively lower cost then current methods. This demonstrates the need for further development of this technology due the potential for providing a means of mass screening, early diagnosis and reliable monitoring of autoimmune disease including, but not limited to, SLE.

Vaccination uptake and timeliness on the Bijagos Archipelago

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Uptake and timeliness of childhood vaccination on the Bijagos Archipelago, Guinea-Bissau: a cross-sectional community-based study

Background: Vaccination uptake and timeliness are important for protection against childhood infectious diseases, especially in Guinea-Bissau where childhood mortality is high. This study assesses vaccination uptake and timeliness for a population in Guinea -Bissau and identifies predictors of full and timely immunisation.

Methods: A random 60% household sample identified 872 participants; data were collected by a cross-sectional community-based survey using an abridged validated questionnaire. Uptake for each vaccine was calculated by eligibility. Kaplan-Meier time-to-event analysis was used to show vaccination timeliness. Binary logistic regression was used to identify predictors of fully immunised status. A linear regression model identified predictors of timely vaccination, which was defined using a score.

Results: Vaccination uptake ranged from 50.4% (OPV1, 95% CI 48.2-52.6) to 92.9% (Pentavalent 1, 95% CI 91.8-94). 18.3% (95% CI 16.6-20) participants had received all recommended vaccines by one year of age. Only 10.7% (95% CI 9.3-12.1) of participants received all vaccinations within the recommended time periods; timeliness ranged from 39.5% (Yellow Fever vaccine, 95% CI 37.7-41.6) to 63.5% (BCG, 95% CI 61.4-65.6). Maternal tetanus immunisation and proximity of participants' village to hospital were significant predictors of fully immunised status; the latter was also predictive of timely immunisation, as was access to a private latrine.

Conclusion: Coverage varied between vaccines but in general was reasonable, surpassing latest national estimates. Timeliness was poor; a large number of children were unprotected for several months before vaccination. Efforts are needed to improve timeliness; these should include community outreach nursing and health education, guided by qualitative research.

An Evaluation of the Management of Child and Adolescent Anorexia Nervosa by CAMHS Fife: A qualitative Study of Views of Healthcare Professionals

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Background: Anorexia Nervosa (AN) is a severely debilitating and dangerous disorder that requires a prolonged, multidisciplinary approach to overcome it. In females, it has the highest mortality rate of any other psychiatric disorder. Despite this, the evidence base for the best treatments is weak and there is a patchy distribution of specialist, outpatient services throughout the UK. This research aimed to evaluate Fife's model of service provision for adolescent AN sufferers. Furthermore it aimed to gather healthcare professionals' perspectives on this service and the new models used, and discuss any changes which could benefit the current service.

Methods: A qualitative approach was used. Semi- structured interviews were carried out with nine healthcare professionals involved in the management of child and adolescent AN in Fife. The results were transcribed and Framework Analysis was used to analyse the results.

Results: Fife provides an outpatient service for AN patients. Less ill patients are treated by two specialist Eating Disorder (ED) nurses. The more severely ill patients are treated by a multidisciplinary team. This team supplies intensive, community based therapy to all acutely ill psychiatric patients with the ethos of avoiding, where possible, inpatient care.

Conclusion: Fife has a well structured and effective AN service which fulfilled almost all the NICE guidelines. Although a solely specialist multidisciplinary ED service would be 'gold standard', there is insufficient funding to provide this throughout the UK. Fife's model seems a pragmatic compromise which may be a good template for other regional CAMHS services to adopt.

Pre-operative liver function predicts survival and recurrence after hepatectomy for hepatocellular carcinoma (HCC) arising from non-cirrhotic/non-fibrotic liver: a European perspective

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Background: In western countries, most HCC cases occur against a background of cirrhosis. This study evaluated outcomes and prognostic factors following hepatectomy for HCC arising in non-cirrhotic/non-fibrotic livers.

Methods: Patients undergoing hepatectomy for HCC were identified from a prospectively maintained database. Patient demographics, pre-operative biochemical and haematological factors, intra- and post-operative clinical details, and tumour pathology were analysed against overall survival (OS) and disease progression-free survival (PFS).

Results: 57 patients underwent hepatectomy for non-cirrhotic/non-fibrotic HCC. Median PFS was 33 months and OS was 37 months, with 3- and 5-year OS of 48% and 39% respectively. 42% developed recurrent HCC. In univariate analysis, the ratio of AST or ALT to the upper end of the normal range affected both OS and PFS [$p<0.001$ (survival), $p<0.001$ (recurrent)]; whereas pre-operative bilirubin ($p=0.04$), percentage lymphocyte count ($p<0.03$) and neutrophil/lymphocyte ratio ($p<0.05$) were related to PFS. Excluding non-hepatic recurrence, pre-operative liver enzyme ratio were significantly elevated among patients whose disease recurred ($p<0.01$). There was a non-significant trend towards poorer survival for patients with poorly differentiated tumours ($p=0.07$). Tumour size, number of tumours, resection margin, micro-vascular invasion and capsular involvement were non-significant for both OS and PFS. Using multi-variate analysis, pre-operative liver enzyme ratio was an independent factor related to OS and PFS after hepatectomy.

Conclusions: Pre-operative liver function may be a prognostic factor for OS and PFS after HCC resection in non-cirrhotic/non-fibrotic livers.

The administration of prostin during the induction of labour at a district general hospital

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Induction of labour (IOL) is carried out when further duration of pregnancy could put the mother and/or the baby at risk. IOL is associated with risks including uterine hyperstimulation and therefore, pregnant women undergoing induction should be managed with care.

At St Peter's Hospital, one cycle of prostin is inserted vaginally to induce labour. This is given based on the patient's Bishop score, which is assessed by performing a vaginal examination. According to trust guidelines, after six hours the woman's Bishop score is reassessed and, if less than ten, further prostin is given.

I looked at whether women being induced were given a further dose of prostin if their second Bishop score was below ten. I analysed the labour notes of 61 women undergoing IOL between January and February 2012. I recorded the first Bishop score, the time of first prostin, the time of second Bishop score assessment and whether prostin was given.

Twenty women out of a total 52 (38.5%) with a second Bishop score below ten were not given prostin. Seven of these women were given prostin further into the induction. The average time between first and second prostin in this group of women was 19 hours 54 minutes.

The administration of the second dose of prostin at St Peter's hospital is not consistently carried out according to trust guidelines. This can lead to an unnecessary lengthening of the IOL process. As a result, the trust has applied for a license to induce labour using slow release prostin.

An audit of peripheral intravenous cannulation technique in the Emergency Department: improving infection control practice using the Accuvein AV300

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Background: Peripheral intravenous cannulation is one of the most common procedures performed in the Emergency Department (ED), aiding investigation and treatment1. Clinical audit was used as a tool to examine the technique and performance of this skill in the ED of Leicester Royal Infirmary - highlighting areas for improvement.

Methods: Guidelines facilitated the development of audit criteria and standards2. As a result, a proforma was designed to observe 100 adult patients requiring peripheral intravenous cannulation in the majors area of the ED. All data collected were coded and entered into a spreadsheet for analysis, and an initial recommendation for change was made. A further 100 patients were observed in the re-audit (200 patients in total).

Results: The first audit cycle highlighted deficits in the overall performance of the procedure including: inadequate drying time after skin cleaning (43%); re-palpation at the insertion site (41%).
The use of the hand-held infra-red vein illuminator AccuVein AV3003 was chosen as a novel approach to improve these deficits and was subsequently evaluated in the second audit cycle.There was a significant reduction in the rate of re-palpation (down from 41% to 24%). All other criteria improved, but remained similar.

Conclusion: This audit has raised awareness of peripheral intravenous cannulation technique in the ED. The use of the AccuVein AV300 significantly improved infection control at the cannula insertion site, enhancing patient care and safety. A tailored inter professional education package has recently been established to promote the introduction of the device into daily clinical practice.

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Investigating the role of Fascia Iliaca blocks in the preoperative management of hip fracture patients-a junior doctor service

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About 75,000 hip fractures occur annually in the UK and the incidence is expected to increase. Acute pain control, traditionally managed with systemic analgesia, is crucial to outcome. Often there is a delay in pain-relief administration. Furthermore, there is a risk of systemic side effects. We performed a prospective case-control audit to analyse the role and efficacy of alternative forms of analgesia like fascia-iliac blocks (FIB).

One hundred and four consecutive hip fracture patients were prospectively recruited and equally divided into; cases (patients receiving FIB) and controls (patients receiving systemic analgesia). Adequately trained junior doctors performed all blocks. The outcome measures included the time of initial analgesia, total pre-operative dose of analgesia, regularly measured pain scores from admission to 24 hours pre-operatively and any complications.

The pain scores were significantly lower ($p=<0.05$) in patients receiving FIB at 2, 8 and 16 hours pre-operatively. The timing of initial analgesia was also quicker in patients with FIB (25 compared to 40mins). FIB patients required fewer doses of systemic analgesia. The block was successful in 83% patients. There were no complications.

The implementation of European Working Time Directive, Hospital at Night, shift-system and the reduction in the number of medical staff has increased the burden on Emergency Departments. Junior doctors are often at the forefront of service delivery and can actively contribute to adequate pain management of hip fracture patients. FIB, performed by junior doctors, is not only safe and effective analgesia but also provides an opportunity for junior doctors to improve current clinical practice.

Assessing the timeliness and completeness of the discharge summary within a community hospital: A clinical audit of 158 patient cases

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The discharge summary allows for effective dissemination of patient information between the hospital and GP, ensuring for the continuity of care that a patient receives subsequent to discharge. However, given the increasing concerns that hospitals are failing to deliver discharge summaries in a timely and complete manner, the present audit examined the quality of current discharge summary practice within a Merseyside community hospital. Assessment was done by systematically selecting 158 discharge summaries from 8 medical consultant teams over three months. The extent to which discharge summaries were generated in a timely and complete manner were analysed according to current local and national guidelines respectively. Only 42% of discharge summaries overall were typed up within the current local guideline period with only one of the eight consultant teams being able to do so consistently. There was also considerable variation amongst consultant teams regarding the completion rates of discharge summaries with regards to medications on discharge, follow-up instructions and past medical history in particular. In conclusion, to consistently ensure for a timely and complete dissemination of patient information a more standardised format is required. Given the potentially disruptive nature of introducing an electronic discharge summary platform, at least in the short term, this audit recommends a standardised dictation template to slowly phase in the benefits of a standardised discharge summary process. The author has developed a template which is currently being implemented across the hospital which may ultimately pave the way towards a fully integrated electronic discharge summary process long-term.

An Audit of Medication Review in Palliative Care

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Background: Medication review is an integral part of good medical practice. It is of particular importance when treating the elderly and end of life patients to avoid polypharmacy and thereby reduce side effects, reduce medication burden and improve concordance in these vulnerable patients.

Method: The medical notes of all patients admitted during a one week period were retrospectively reviewed to identify how frequently medication reviews at admission were carried out. Following liaison with the Medication Safety Department a ward-specific proforma was devised to assist in carrying out medication reviews at admission. The proforma was then introduced and trialled in the department to be used on admission of every patient. A second assessment of medication review on admission was completed after four weeks of trialling the proforma.

Summary of results: The initial audit identified that only 37% of patients had a documented medication review on admission. Following introduction of the proforma, 100% of patients had a medication review.

Conclusion: Junior doctors frequently omitted patient medication reviews at admission to hospital. The introduction of a proforma to assist with medication review on admission resulted in complete compliance. It is also proposed that a clearer medication review (and therefore clearer documentation) will assist with communicating changes in medication to primary care on patient discharge.

Investigating the effectiveness of an indoor residual spraying programme in reducing the public health burden of malaria in a Malawian community

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Introduction: The global health burden of malaria is vast and Malawi is particularly badly affected; thus an effective method of malaria control is badly needed. In 2009, an indoor residual spraying programme (IRS) was commenced in the Nkhoma, Malawi. A population of 60,490 were targeted by the programme which aimed to reduce malaria incidence in the region by 25%.
This project was designed in order to evaluate the effectiveness of the programme.

Methods: Two different study designs were used. A retrospective cohort study compared outpatient malaria cases in in sprayed and non-sprayed areas (the catchment areas of Chimbalanga and Matapila health centres respectively) during selected monthly periods between December 2008 and March 2012.
In addition, a case control study analysed data from a parasitaemia survey of 148 randomly selected children <5 years to observe the relationship between living in a sprayed home and contracting malaria. Both used secondary data held by Nkhoma Hospital Public Health Department.

Results: The cohort study showed that the introduction of IRS to Chimbalanga had coincided with a reduction in malaria incidence in children <5 years and adults. Insufficient data were available to produce any findings regarding malaria incidence in pregnant women. The parasitaemia survey revealed that children who lived in a sprayed home were 24.26% less likely to contract malaria.

Conclusion: The introduction of IRS appears to have contributed to a reduction in malaria incidence in the Chimbalanga region. Living in a sprayed home offers protection from malaria for children <5 years.

Steroid Reduction Adherence in Post Renal Transplant Patients

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The aim was to assess compliance with the steroid reduction regime in renal transplant patients. Renal transplantation offers patients improved mortality, morbidity and quality of life compared to renal replacement therapy. It is beneficial to slowly dose reduce steroids in transplant patients accepting that altering immunosuppression therapy carries a risk of acute rejection.

Standards:

1. Patients received triple combination immunosuppressant therapy. Standard Expected 100%
2. Post-renal transplant patients are on prednisolone. Standard Expected 100%
3. Corticosteroids were dose reduced in 5mg increments over the 6 post-operative weeks. Standard Expected 100%
4. Patients with acute rejection were given high dose methylprednisolone. Standard Expected 100%

Method: Retrospective case note audit of 45 consecutive patients transplanted between April and October 2011. Data was recorded on a spreadsheet.

Results: Combination immunosuppression therapy: mycophenolate mofetil, tacrolimus and prednisolone was used for all patients.

Appropriate steroid reduction to 5mg was only achieved in 56% (n=25), compared to an expected performance of 100%.

Performance level for treatment of acute rejection was 100% (n=6).

Conclusion: Overall performance levels were desirable; all patients received correct immunosuppression therapy with acute rejection episodes treated appropriately. Many patients received higher doses of prednisolone for longer than expected. Steroid reduction has not achieved a desirable performance level with factors contributing to the poor performance being easily modifiable.

Paediatric Day Case Tonsillectomy a Safe, Feasible and an Economical way to treat patients –Yorkhill Experience

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Introduction: Day case surgery is widely encouraged as it has many benefits. In this study we evaluate the feasibility of paediatric tonsillectomies as day cases surgery procedures in a tertiary paediatric centre.

Methods: The outcome of paediatric tonsillectomy performed as day case procedures were studied for four months. We recorded complication rates in comparison to the standard in-patient practise

Results: 23 paediatric patients were included in this study. The age of the patients ranged from four to 11 years, with mean age of 6.5. No patients suffered postoperative complications within the first 24 hours. Two patients were re-admitted due to a post-operative complication (8.6%) and one patient for a non-operative cause (4.3%) beyond the initial 24 hours.

Conclusion: Paediatric Day Case Paediatric Tonsillectomy is a safe, feasible and an economical way to manage patients.

Ophthalmic uses of Botulinum Neurotoxin

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Background: Botulinum neurotoxin (BoNT), a neuromuscular inhibitor used in the management of facial dystonia and strabismus, provides symptomatic relief from the unwanted effects of abnormal muscle contracture. Research or audit into its use is poor, related to the lack of benchmarks from published data and the low clinical importance often given to the conditions treated.
Greater awareness of clinical governance, and the need to standardise patient care has raised the importance of these conditions and their treatment. Evaluation of current practice is now considered a priority in order to establish new guidance, set standards, monitor clinical practice, and patient satisfaction with their care.

Aims: To identify
- Ocular conditions requiring BoNT treatment
- Factors influencing treatment outcome
- Patient perceptions of efficacy
- Need for change in practice

And additionally, publish and dissemination findings to improve quality of patient care.

Methodology: Without a diagnostic code-index or clinical database, patients were identified from a strabismus clinic logbook and prospectively for dystonia clinic attendees. Retrospective data collection was then carried out from patient records.

Results: One hundered and sixty eight patient records were identified. Diagnostic categories of Dystonia patients clearly formed two main groups: blepharospasm and hemifacial spasm. 90% of dystonia patients showed identifiable and treatable exacerbating factors, however few triggers were adequately treated. Most strabismus clinic patients received BoNT to plan surgery. 24 patients (40%; 95% confidence interval, 29% to 53%) were corrected to the level expected post-operatively.

Conclusion: Exacerbating factors including psychosocial issues influence diagnosis and treatment outcomes in dystonia. Similar conditions are reported in strabismus patients. High volume treatment clinics do not allow the time to identify or manage these. This particularly in dystonia patients may influence success and need for treatment. In strabismus patients this oversight affects quality of care.

An audit of the implementation of NICE and Health Protection Agency guidelines for the investigation, management and notification of TB and study into relationship between vitamin D levels and MTB for UK and non UK resident patients.

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Introduction: Literature of functions of vitamin D has demonstrated a potential immunomodulatory role for response to Mycobacterium tuberculosis (MTB) infection. There is potential use for vitamin D for prevention and treatment of MTB. There may be a link to vitamin D levels and country of origin as a large proportion of MTB patients are of non-UK origin.

Aims: To study MTB epidemiology and measure time between arrival in UK to diagnosis of infection for non-UK residents. To measure levels of vitamin D and its biochemical markers in infected patients. To assess the implementation of NICE guidelines in MTB management.

Method: A retrospective study analysing records of 75 MTB infected patients, who were treated in the Infectious Disease department (UK) between 2007- 2011. The audit tool was devised from NICE guidelines (2006).

Results: Fifty one patients were non-UK origin; 47 % developed disease within 2 years of arrival in UK and 25% within first 5 years. Extra-Pulmonary MTB is more common in immigrants from Asia and the Middle East. All patients, 63% had some biochemical evidence of vitamin D deficiency. Those tested for vitamin D deficiency all had significantly low levels. Audited standards for diagnosis by sputum analysis and x-ray were met by 54% and 26% respectively. 82% had correct duration of treatment. 42% had notified the Health Protection Agency (HPA).

Conclusion: The results show a potential significant relationship between vitamin D and MTB. Comparison of results with vitamin D levels in uninfected UK and non-UK origin patients would prove valuable.

How reliable is the wells criteria as a screening tool for pulmonary embolism in a district general hospital?

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Background: The Wells Criteria is a 7-criterion screening tool developed in Canada to help screen patients with a high probability of having a Pulmonary Embolism (PE). This helps the clinician decide if the patient merits further investigations such as a Ventilation-Perfusion Scan or a Computed Tomography Pulmonary Angiogram (CTPA) which whilst being the gold standard for PE diagnosis, can be extremely costly and also exposes patients to significant radiation. Our retrospective analysis aimed to determine the sensitivity & specificity of Wells Criteria for diagnosis of a PE.

Methodology: The notes of all patients who had a CTPA in 2011 were identified and the relevant data extracted. Data was then analyses using the SPSS Statistical Software.

Results: There were 44 patients who had a CTPA in 2011. A Wells Score of more than 4 indicated a high likelihood of PE whilst a Wells Score of 4 or less indicated a low likelihood of PE. Results are summarised in the table below.

		CTPA		
		Positive (PE present)	Negative (no absent)	
WELLS SCORE	>4	13 patients	4 patients	Positive Predictive Value = 76.48%
	≤4	2 patients	25 patients	Negative Predictive Value = 92.59%
		Sensitivity = 86.67%	Specificity = 86.21%	

Conclusion: The Wells Criteria had a sensitivity of 86.67% & specificity of 86.21%. This suggests that if used in combination with clinical judgement, the Wells Criteria can be a reliable screening tool for exclusion of PEs. This certainly will be helpful in smaller hospitals where financial resources and radiological expertise may not always be available.

Severity Scoring and Chest Radiograph Interpretation - Improving the Quality of Care for Hospitalised Community Acquired Pneumonia

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Introduction: Worldwide population-based studies of community acquired pneumonia (CAP) requiring hospitalisation have reported overall incidence between 1.1 and 4 per 1000 population per annum.[1] CAP is associated with high and variable mortality rates; in the UK this has been reported between 5.7 and 14%.[1] The management of CAP is therefore an important issue.

Method: A 70 day prospective casenote review between March and May 2011. The audit included all patients admitted to the respiratory wards via the Acute Medical Unit (AMU) with CAP. Hospital and national guidelines were reviewed and audit standards set.

Results: Data was collected on 47 patients, 24 male, mean age 74.9 years.100% had chest radiographs, 74.5% interpreted by AMU doctor, respiratory specialist and radiologist. There was common agreement in radiograph interpretation in 68.6% of patients. 100% had FBC, 97.9% U&Es, 63.8% LFTs and 57.4% CRP. Severity according to CURB65 was scored in 39 patients (82.9%), correctly scored in 27 patients (69.2%). According to assigned CURB65 scores, 47.5% had blood cultures, 40% had sputum cultures, 33.3% had atypical serology sent appropriately. Mortality rate was 21.3%. 62.5% of patients that died had incorrectly scored severity.

An audit of temperature on arrival to recovery and availability of intra-operative warming in operating theatres

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Inadvertent perioperative hypothermia is well-known and preventable consequence of anaesthesia, which is associated with negative patient outcome. These include greater intraoperative blood loss, increased rate of infection, possible cardiac events, pressure sores and longer stay in hospital. Hence, maintaining normothermia perioperatively can modify these adverse outcomes.

This was a prospective audit of peri-operative temperature and availability of intra-operative warming. The data was collected by a FY1 doctor based in the main recovery of ARI theatres for five days. All patients who came into the main recovery post-operatively were included. A total of 196 patients' temperature was taken on arrival to recovery and availability of warming in theatre was obtained from the anaesthetics chart.

The results showed only 7% of patients had temperature less than 36 degree. Theatre 6 (ENT) and theatre 11 (trauma) had the highest percentage of hypothermia with 23% respectively. The procedure was shorter than two hours in 92% of the hypothermic patient. Fluid warmer and forced air warming were available almost 50% of the time while temperature probe are only available 34% of the time. 61.5% of patients with core temperature <36 did not have fluid warmer and 77% did not have forced air warming.

This audit shows that some patients were becoming hypothermic in theatre, even those having short procedures and this may be detrimental to their recovery. The authors recommend that temperature should be taken routinely prior to induction, monitored in the theatre, and patients actively warmed if their temperature falls even during short procedures.

Hygiene Behaviours and Trachoma on the Bijagos Archipelago, Guinea Bissau.

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A Cross-sectional Study Investigating Hygiene Behaviours in Communities Hyperendemic for Trachoma on the Bijagos Archipelago, Guinea Bissau, West Africa.

Trachoma, a neglected tropical ocular infection, is a major public health problem on the Bijagos Archipelago, Guinea Bissau. The World Health Organization endorsed the 'SAFE' (Surgery, Antibiotics, Facial cleanliness, Environmental improvements) strategy to eliminate blinding trachoma; this has yet to be implemented effectively in this region.

Methodology/results: A cross-sectional household survey examined associations between hygiene behaviours and the presence of trachoma. Data were gathered from 186 households using observations, a hygiene behaviour questionnaire and examining children less than 10 years of age. Presence of trachoma in a household was revealed by collaboration with an on-going prevalence survey.

Multiple logistic regression found households are more likely to have trachoma if they contain children with ocular discharge (OR 1.88; 95%CI 1.21-2.93) or if they report removing ocular discharge from a child's face using a towel (OR 6.93; 95%CI 2.35-20.42) Households are less likely to have trachoma if parents (OR 0.20; 95%CI 0.050-0.77) or the mother and child together (OR 0.19; 95%CI 0.045-0.80) are responsible for a child's face washing. The greater the volume of water stored in a household for hygiene purposes, the less likely that household was to have trachoma.

Conclusion: Associations between hygiene behaviours and trachoma in a household contribute to understanding the disease in this environment. A household hygiene promotion campaign is recommended to aid implementation of the 'F' and 'E' components of the SAFE strategy and improve hygiene practises. Qualitative research and an in-depth risk factor study are recommended to further understand trachoma in this under-researched environment.

Evaluate the effect of intravitreal Bevacizumab (AVASTIN) injection for diabetic macular oedema

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Introduction: Bevacizumab is an anti-VEGF (vascular endothelial growth factor) agent and it has originally been licensed for the treatment of metastatic colorectal cancer. However, it has also been used as an off-label drug for the treatment of diabetic macular oedema (DMO). This audit is to evaluate the effect of intravitreal Bevacizumab injection for DMO in Raigmore Hospital.

Method: This audit was done retrospectively. It involves all patients (total of 6) with DMO who have had intravitreal Bevacizumab injection over a state of 15 month period (from 15/04/2010-15/07/2011). All those patients had failed laser photocoagulation treatment before. The main outcomes was measured in terms of the changes in the best corrected visual acuity(BCVA) and central retinal thickness(CRT) by optical coherence tomography(OCT). The changes in BCVA were measured by comparing the mean baseline BCVA with the mean final BCVA during the 15 month period. Similarly, the changes in CRT were measured by comparing mean baseline CRT with the mean CRT in final OCT during the 15 month period.

Results: This audit involved 6 eyes (6 males; average age 68). All patients received average of 3 treatments during the 15 month period. BCVA has worsened from mean baseline BCVA of 0.625(logMAR) to final BCVA of 0.763(logMAR). Meanwhile, CRT has worsened from baseline CRT of 546μm to final CRT of 578μm.

Conclusion: Intravitreal Bevacizumab injection was not effective in treating DMO in Raigmore Hospital.

The Real Spectrum of Migraine

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Background: Perhaps surprisingly to those who have escaped the wrath of migraine, the WHO regards this condition as the most disabling illness, comparable even to the likes of highly stigmatized conditions such as quadriplegia and dementia. Diagnosis and management not only require clinical aptitude, but also the ability to apply basic concepts in neuroscience; such skills remain suboptimal for a number of physicians, with almost 50% of patients remaining undertreated or undiagnosed. Here, we present two case reports, one to demonstrate the atypical way by which this disorder may present and the second to provide evidence for the re-emerging continuum model of migraine. The latter rather boldly refutes the existence of tension-type headache (TTH) as a clinical entity, regarding it instead as a milder form of migraine.

Case Summaries: A 16-year-old male patient suddenly collapsed whilst playing football. He had been experiencing severe dizziness for the preceding few months with nausea and a mild headache. A cardiology review did not elicit a cardiac cause and he was eventually commenced on migraine-specific therapy. A 15-year-old male patient complained of recurrent headaches, which began with severe neck pain followed shortly by a headache, localized to his right temporal area. There were no other symptoms of significance and he did not respond to TTH-specific therapy.

Conclusion: With almost a third of neurology outpatient referrals comprising of headache complaints, it is clear that migraine is greatly misunderstood by the medical profession. Embracing the continuum model of migraine may lessen the impact of this disabling condition.

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