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1. Cognitive Impairment after stroke.

Helen Martin, Gillian Mead

Primary Aims:

(1) An audit to assess whether a formal cognitive screen carried out in those who have suffered a stroke? When was this undertaken and which tool was used?

(2) How many received a new diagnosis of dementia?

Methods: The 80 most recent consecutive discharges were identified using Trak from three stroke units in South Edinburgh. Data was extracted from paper case notes and anonymously entered onto a database where basic statistical tests were performed.

Results: 69% of patients received a cognitive assessment as an inpatient. The most commonly used assessment tool was the ACE-R (52%) which was carried out a mean time of 3.9 days after admission. Two patients received a new diagnosis of dementia and one patient a new diagnosis of cognitive impairment.

Conclusions: National guidelines all advocate screening for cognitive impairment after stroke. However, currently there is a lack of consensus on screening and follow up procedure.

Within this audit, the percentage of patients receiving a cognitive assessment in hospital after stroke (69%) is falling below these guidelines.

A national, clear and standardised pathway of care would reduce the heterogeneity of post-stroke care and increase the efficacy of identifying and managing cognitive impairment after stroke.

2. "Assessment of the pathogenic traits of *Campylobacter concisus* isolated from paediatric inflammatory bowel disease."

Gary Thomson, Susan Berry, Georgina Hold

Introduction: *Campylobacter* is a genus of gram negative bacteria containing species, such as *C. jejuni*, which are well known pathogens. However, the pathogenic potential of less well characterised *Campylobacter*is currently being examined, specifically regarding the development of inflammatory bowel disease (IBD) due to the increasing isolation of these species from IBD patient biopsies. This study assessed the pathogenic traits and impact on host response of *Campylobacter concisus* isolated from paediatric IBD.

Methods: Colonic epithelial (HT-29 and Caco-2) cells co-cultured with *Campylobacter concisus* isolates from paediatric IBD biopsies were assessed for bacterial adherence and invasion using scanning electron microscopy and gentamicin protection assays. Pre-treatment with TNF-alpha was used to simulate an inflamed colonic environment in order to assess if this affected outcomes of co-culture. Additionally, host cell responses to *C. concisus* infection were assessed using real time quantitative PCR to quantify inflammatory gene expression and quantification of (pro-inflammatory) cytokines.

Results: *C. concisus* was shown to adhere to HT-29 and Caco-2 cell lines although only selected isolates demonstrated marginal evidence of invasion but only when co-cultured with inflamed HT-29 cells. Presence of *C. concisus* increased or sustained IL-8 gene expression of inflamed cells and increased IL-1β expression but suppressed PTGS2 gene expression. Additionally, *C. concisus* co-culture increased production of IL-8 by inflamed HT-29 cells whilst reducing the production of IFN-γ.

Discussion: This study suggests *C. concisus* possesses the pathogenic traits of adherence and invasion to epithelial cells when already inflamed. Additionally, the cytokine response of HT-29 cells stimulated by *C. concisus* suggests the species does have pathogenic potential, but this may not be definitively pro-inflammatory and should be further investigated as a potential pathogen in inflammatory bowel disease.

3. The Role of Wt-1 in Angiogenesis

Lucie Ferguson, Richard McGregor, Patrick Hadoke, Nick Hastie

Angiogenesis is an essential process for organ development, growth and tissue repair and is also implicated in tumour pathogenesis. The Wilms' tumour gene, *Wt1*, initially was thought to be a tumour suppressor gene. However, it has now been implicated in a number of processes, including blood vessel formation. The aim of this study was to investigate the function of *Wt1* in the sponge model of angiogenesis as well as determining whether *WT1* is expressed in human breast cancer. Using synthetic sponges implanted in C57Bl6 mice, and removed in a time-course experiment at days 3, 7 and 21, we noted an increase in *Wt1* positive blood vessels between days 7 and 21. Next, utilising a lineage tracing transgenic mouse line (mTmG construct), we attempted to verify the cell type from which the angiogenic vessels derived. Finally, we analysed 30 human breast cancer samples (alongside matched controls) and found that *WT1* was expressed in the endothelial cells of human breast cancer tissue but not in controls. These results suggest a role for *Wt1* in angiogenesis (shown in the mouse model) and for *WT1* in breast tumourogenesis, indicating a possible future therapeutic target.

4. Epidemiology of Pneumocystis Pneumonia Cases Lothian 2000-2013

Francesca Heard

Introduction: Pneumocystis pneumonia (PCP) is caused by the fungus *Pneumocystis jirovecii*, an opportunistic pathogen that is a significant cause of morbidity and mortality in HIV positive patients and those on immunosuppressive drugs. This study aims to determine the epidemiology of PCP in Lothian 2000-2013 and investigate the impact of immunosuppressive drugs and co-morbidity on infection and mortality.

Methods: A retrospective epidemiological analysis was carried out on data on patients that tested positive for PCP in 4 hospitals in Lothian (Royal Infirmary Edinburgh, Western General Edinburgh, St John's Hospital Livingston and Royal Hospital for Sick Children, Edinburgh), supplemented with data collected from TRAK and patient notes.

Results: PCP cases have significantly increased since 2010 ($p<0.001$), which coincides with a change in diagnostic test for PCP. Co-morbidity was significantly associated with PCP infection ($p< 0.001$) and renal transplant patients were identified as group that rates have increased in. Type of immunosuppressive drug had a significant impact on 30-day mortality due to PCP ($p=0.034$).

Conclusion: Increasing rates of PCP in Lothian in recent years may be due increase in diagnostic accuracy. However, immunosuppressive drugs and co-morbidities are significantly associated with PCP infection indicating certain immunosuppressants and co-morbidities may increase risk of PCP. Renal transplant patients are particularly susceptible to PCP infection, emphasising the lack of national guidelines on prophylaxis for non-HIV immunocompromised patients. Patients on certain immunosuppressive drugs may have a greater need for this owing to the significant relationship between immunosuppressive drugs and mortality.

5. Difference in Left Ventricular Remodelling and Hypertrophy between Genders in Patients with Aortic Stenosis

Chris McKelvey, Calvin Chin

Introduction: Studies have shown different prognoses between genders in patients with aortic stenosis. In response to aortic stenosis, the left ventricle initiates a hypertrophic response leading to increased LV wall thickness. Although this is initially beneficial, it ultimately proves maladaptive leading to decompensation and heart failure. It is known that males present at an earlier age with systolic heart failure, whereas women present at a later age with diastolic heart failure (preserved ejection fraction). Left ventricular hypertrophy and remodelling may play an important role in accounting for these differences.

Aim: To determine any differences in LV remodelling and hypertrophy between genders, in patients with aortic stenosis, using cardiac magnetic resonance (CMR) to categorise patients into the six pre-determined LV remodelling groups.

Methods: 114 patients with previously categorised mild to severe aortic stenosis were scanned with CMR (age68±12 years old; males 64%). The average of three measurements of maximal wall thickness at each segment of the 17-segment model of the LV was calculated. Asymmetrical forms of remodelling and hypertrophy were defined by a regional wall thickening ≥13mm and >1.5 fold the thickness of the opposing myocardial segment. This along with LV mass index and the LV mass/volume ratio were used to categorise patients into one of six groups of LV remodelling– normal, concentric hypertrophy, concentric remodelling, asymmetrical hypertrophy, asymmetrical remodelling and eccentric.

Results: 36% of males were found to have concentric hypertrophy compared to only 12% of females ($p=0.007$), while 54% of females had a normal LV structure compared to only 29% of males ($p=0.001$).

Conclusion: There is a significant difference in LV remodelling between males and females, $p=0.03$. Oestrogen may play a protective role in LV remodelling, and further studies could investigate the possible benefit of oestrogen therapy in preventing the progression to heart failure.

6. A case control study to compare the phenotype of children in Lothian with Autism Spectrum Disorder with either a sub-microscopic deletion or a duplication

Rachel Nelson, Sarah Clegg

Introduction: Genetic syndromes are aetiological in 10% of autism spectrum disorder (ASD). There is much interest in susceptibility genes that may contribute to the remaining 90% of "idiopathic" autism. In the last 5 years chromosome array genomic hybridisation has made it feasible to identify sub-microscopic chromosomal abnormalities. These are either inherited or de novo and have been reported in 10-35% of ASD cases. The aim of this study was to identify children with ASD and a sub-microscopic deletion or duplication and draw conclusions about the correlations between the genetic abnormality, whether inherited or de novo, and the child's phenotype.

Methods: The supports need system database of children was systematically reviewed and 34 patients met the inclusion criteria of being under 18 years old, having a diagnosis of ASD and a sub-microscopic deletion or duplication. The genetic diagnosis, whether inherited or de novo, family history, peri-natal and neonatal history and phenotype were recorded.

Results: Those with a sub-microscopic deletionwere six times more likely to experience birth complications (odds ratio 6.00, 95% CI 0.64-55.95) and three times more likely to have dysmorphic features odds ratio (3.25, 95% CI 0.73-14.40). The odds of maternal bleeding, low birth weight (<2.5kg), learning disability and structural anomalies were also increased in those with a sub-microscopic deletion. Those with a sub-microscopic duplication were twice as likely to have a family history of ASD compared to those with sub-microscopic deletions.

Conclusion: Sub-microscopic deletions were more likely to be de novo and associated with a more "severe" phenotype of ASD with an increased prevalence of learning disability, structural anomalies and dysmorphism. Sub-microscopic duplications were more likely to be inherited, associated with a family history of ASD and a present with a milder phenotype. Identification of these genetic abnormalities in children may allow early targeted intervention.

7. A Comparison Between the Effects of Heat-Stress Dehydration and Dietary Restriction Dehydration on Cognitive Function

Leo R Brown, Hugh Richards

The negative effects of dehydration on physical performance have been extensively researched, but comparatively few studies have assessed how dehydration can influence cognitive function. Important variations between different methods of dehydration and their effects on cognitive function have been identified, yet more research is also required within this area. This study sought to further examine the effects of dehydration on cognitive function by comparing heat-stress induced dehydration to dietary restriction dehydration and their effect on a number of measures of cognitive function. Eight participants were dehydrated using an environmental chamber while another eight did not eat or drink for 18 hours; at which point both groups had lost approximately 2.5% of their initial body weight. Although declines in mean scores were mostly seen for the visual search, Stroop and digit span tests, it cannot be concluded from these results that either hydration status or method of hydration have a significant effect on cognitive function. The combined effect of hydration status and method was found to be significant for the numeric and alpha numeric trail marking tests, with values of $F_{1,14} = 6.845$, $p = 0.020$ and $F_{1,14} = 5.735$, $p = 0.031$ respectively. There was, however, no known reason for this significant interaction. Future research should aim to further investigate this area in order to accurately determine the effects of these two methods of dehydration on cognitive function.

8. A Review of the Levels of Evidence and Study Design of Recent Preclinical Papers

Sky Koh Wei Chee, Hamish Simpson

Background: Poor quality research has little or no value; hence it is vital that we ensure any research carried out is to a high standard. Many clinical researches adhere to the CONSORT guidelines for the reporting of their trials, but these seem lacking when it comes to preclinical trials. This article aims to investigate which of the CONSORT guidelines, where appropriate, are applicable and highlight those requiring more improvement, and the reasons for its lack of usage.

Methods: Using a structured search strategy, articles published in the *Journal of Orthopaedic Research* and *Arthritis & Rheumatism* in 2012 were reviewed using Wiley Online Library. All clinically related and patient based studies were excluded. The remaining full text articles were assessed manually if they adhere to individual clauses stated in the CONSORT guidelines.

Results: 854 articles were assessed and 381 were preclinical studies. Studies did well in writing a concise extract, introduction, methods, discussion and statistics. 62% of studies that could have been randomised were not, and 77% that could have been blinded did not have this done.

Conclusion: Current preclinical studies are not optimally designed and more should be done so that they follow the relevant clauses in the CONSORT statement.

9. Sources of bias in transgenic studies of stroke pathophysiology: systematic review and meta-analysis

Zhaobo (Paul) Liu

The search for a "magic bullet" drug for stroke treatment has been futile. Many drug candidates showed efficacy in animal studies but failed to deliver in clinical trials. This caused many to question the viability of the animal model itself. Does this failure indicate that animals are not suitable for experimenting drugs meant for human use? Or does the problem lie with poor study quality and experimental design? Transgenic animal models are used to identify gene targets for drug development. This study aims to identify sources of bias in transgenic studies of stroke. Using methods of systematic review, we identified 343 unique publications. We assessed them for impacts of study quality and design on infarct volume and neurobehavioural score. We found significant impact for randomisation of animals to ischaemia induction, blinded assessment of outcome, type of ischaemia induced, type of anaesthetic used, the method of occlusion and the time at assessment. Publication bias analysis found that there is an overstatement of efficacy of 51.4% for infarct volume, our primary outcome, with a non-publication rate of 7.9%. This suggests that poor study quality and design, in addition to publication bias, might have contributed to translational failure in stroke therapy research.

10. Conducting SIGN audit in hip fracture management

Hannah Tan, Fail M, Kearns R, Kinsella J

Introduction: Hip fractures are prevalent in the elderly population of the UK affecting 70-80,000 of the population annually. There is a consistent and persistent mortality rate of around 7-10% at one month and 30% at one year. Moreover, a significant burden of morbidity and mortality exists if surgery is delayed for more than 48 hours. We audited standards of care as described in SIGN Guideline 111 for the management of hip fracture in older people in a Scottish hospital to assess current management and identify potential areas for improvement.

Methodology: We retrospectively examined the case-notes of 13 randomly selected, elderly patients admitted with hip fracture. A SIGN audit tool designed to be used alongside SIGN guideline 111 was used to evaluate standards. This consisted of the following questions in 3 specific fields:

1. Operational
    - Whether the patient was assessed within an hour of arrival
    - If there were any delays in surgery
2. Risk Assessment
    - General nursing aspect of patient care e.g. pressure sore risk, pain, hydration & nutrition, mobility and functional ability etc.
3. Multidisciplinary Input
    - The holistic management of the patient

Results:

	Cycle 1
Number of patients audited	13
Median total operation score (max 5)	4
Median total risk assessment score (max 11)	11
Median multidisciplinary score (max 4)	4
Median overall compliance score (max 20)	19

Conclusion: The management of hip fracture in elderly patients at GRI is mainly consistent with the standards set in SIGN guideline 111. Despite these positive findings, not every patient with a suspected hip fracture was assessed within an hour of arrival as recommended by SIGN, reducing the Total Operational Score. Outcomes relating to risk assessment and multidisciplinary Input met SIGN standards and staff should endeavour to maintain these at current standards.

11. Are pre-operative urodynamic studies (UDS) useful for patients awaiting pelvic organ prolapse (POP) surgery?

Shahira Hussain, Woods K, Oliver L, Agur W

Introduction: The coexistence of POP and stress urinary incontinence (SUI) has been well documented in numerous studies. The concurrence rate of these two conditions is over 60% and over a third of patients who need surgery for either condition require concomitant surgery. A urodynamic study (UDS) is performed in patients with POP to ascertain the underlying pathophysiology of urinary incontinence to allow for an appropriate management plan to be devised. The aim of this audit was to identify how pre-operative UDS influences the decision for concomitant continence procedure for women who have POP surgery.

Methodology: This was a retrospective study of patients who had POP surgery and underwent preoperative urodynamics. Patients with symptomatic POP (requiring surgery) who also had stress urinary incontinence (SUI) were referred for UDS to determine whether a concomitant continence procedure would be appropriate at the time of the POP surgery.

Results: 33 of the 48 patients (69%) had only a POP repair done despite the fact that 9 of these patients were found to have USI on UDS (Fig. 1). Of the 48 patients who underwent pre-operative UDS, only 6 (12%) went on to have a concomitant procedure (Fig. 2).

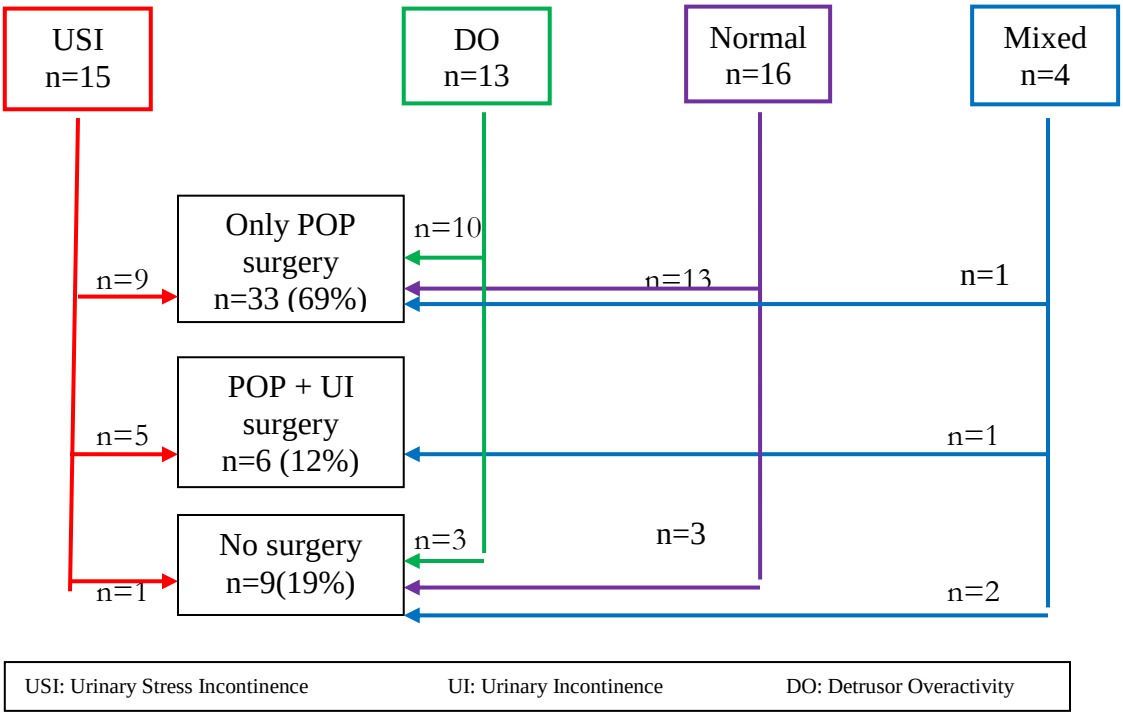

Figure 1: UDS diagnosis & resulting procedure performed in patients awaiting POP surgery with SUI

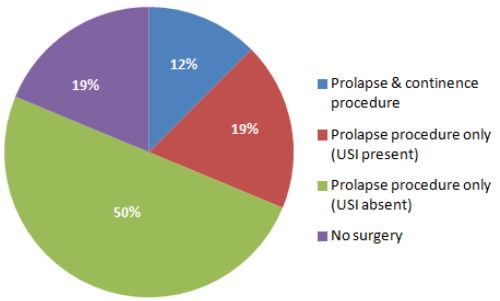

Figure 2: Outcomes of UDS in patients awaiting POP surgery with SUI

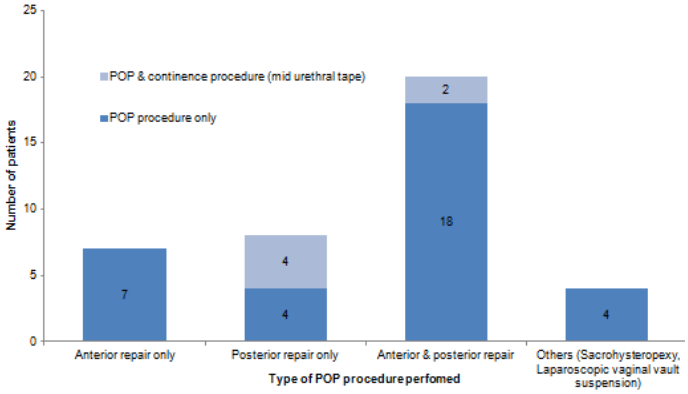

Figure 3: Procedures performed following UDS

Conclusion: Only 12% of women with combined prolapse symptom requiring surgery and stress urinary incontinence had concomitant procedures. Women awaiting prolapse surgery who are symptomatic of stress urinary incontinence should be fully counselled regarding the potential of a concomitant continence procedure prior to referral for urodynamics.

12. Adaptive Iterative Dose Reduction (AIDR) reconstruction algorithm on raw data for 640MDCT coronary CTA allows significant reduction in radiation dose while maintaining image quality with low noise.

Nicholas Png, John Hoe

Background/Aim: The study was performed to assess the difference in radiation dose while maintaining high image quality and low noise coronary CTA images performed on a 640MDCT scanner using an iterative reconstruction algorithm (AIDR) to reconstruct Cardiac data, which works in raw data and image space, compared to using filtered back projection and a de-noising software (FBP+DS).

Methods: 200 consecutive patients were scanned using 100/120kVp and 150-580mA on a 640MDCT scanner. 100 (group1) had CTA images reconstructed using AIDR while 100 (group2) used FBP+DS. Radiation dose was measured as extended dose length product (DLPe) and the estimated effective dose, measured in mSv, was calculated using the algorithm: mSV=DLPe x 0.014. The data was obtained from the CT machine after each scan. The quantitative assessment of image noise and qualitative assessment of image quality for noise and mottle was conducted by 2 independent observers.

Results: Average effective radiation dose was 1.76±1.33mSv for group1 and 3.88±2.51 for group2, demonstrating a mean radiation dose reduction of 55% in group1 compared to group2. Average image noise and mean signal to noise ratio were 28.7±3.74 and 17.2±4.5 respectively for group1; and 26.3±5.32 and18.7±4.65 for group2.

Qualitative assessment of image quality score was 3.77±0.48 (3=good,4=excellent) for group1 and 3.76±0.36 for group2; image noise mottle score for group1 was 2.17±0.78 (2=medium mottle,3=low mottle) and 2.71±0.75 for Group2.

The average Body Mass Index was 26.0±4.27 for group 1 and 26.7±4.49 for group 2. 14% of group 1 and 34% of group 2 were scanned using 100kVp.

26 % of patients in Group1 received effective radiation dose of <1mSv with none in group2.

Conclusion: It is possible to achieve significant radiation dose reduction of up to 55%, with some receiving <1mSv, while simultaneously maintaining images with excellent image quality and low noise using AIDR instead of FBP+DS.

13. Assessing the deformity in Peyronie's Disease: What is best?

Gregory Tan

Introduction: An accurate assessment of the deformity is essential in assessing and counselling patients with Peyronie's Disease. Our aim was to introduce a new device, the Vacuum Globe into our service for the assessment of the deformity, and assess/validate various tools for the ideal assessment modality.

Methods: Five tools were prospectively assessed in consecutive new patients presenting to our service; patient's perception of deviation, photos taken by the patient, and 3 different artificial erection tests (the Vacuum Globe, constriction rings applied after vacuum erection and intracavernosal alprostadil - Caverject®). Dorsal and lateral views of the penis were photographed for each test and the angle of curvature measured. A good correlation was taken to be a difference of $<10^{\circ}$.

Results: 27 patients have been assessed to date. Only 46.7% of patients accurately estimated their deformity. 9/27 patients (33.3%) brought photos, of which 6 (66.7%) were suitable. Only 5/10 patients (50%) who were asked to bring photos, complied.

The Vacuum Globe provided the best assessment in 11/27 patients (40.7%), while Caverject® was best for 4/27 patients (14.8%), and both were equal in 12/27 patients (44.4%). The Vacuum Globe was as good, or better than Caverject®, at assessing the deformity in 23/27 patients (85.2%). Constriction rings were not supreme in any patient.

Conclusion: Patients' perception and photographs are unreliable forms of assessment. The Vacuum Globe is a suitable first line modality in assessing and counseling patients with Peyronie's Disease. This has safety and cost implications.

14. Can We Make Bones Heal Better and Quicker by Feeding Them The Right Stuff?

Alexandra Haddon, Julie Crockett, James D Hutchison

Introduction: Fractures are a major health concern. The UK incidence is estimated at 3.6 fractures per hundred people per year and is rising due to increasing risk factors such as osteoporosis and the growing elderly population. In 2000, the health and social care costs of hip fractures alone was estimated at £726 Million. Due to this, fracture repair is an important area of research. Treatment has recently focussed on optimising the pathways within osteoblasts to increase their proliferation and mineralisation, and through this bone repair. Another area that potentially limits osteoblast function is the quantity of conditionally essential amino acids available. These amino acids are rate limiting to anabolic processes such as fracture repair.

Aims: This study aimed to investigate whether supplementing osteoblasts with the conditionally essential amino acids increased their proliferation and mineralisation abilities.

Methods: Primary murine calvarial osteoblasts were cultured in test medium containing 0μM to 2,500μM of arginine, cysteine, glutamine, histidine, lysine, proline, taurine and tyrosine. Osteoblasts were treated for 72 hours to assess cell viability, via an MTT assay, and 21 days to assess mineralisation, via an Alizarin Red Stain (ARS), and osteocalcin expression, via PCR.

Results: Osteoblasts supplemented with glutamine showed a significant concentration-dependent increase in the cells viability and mineralisation. This increase in osteoblast viability was further enhanced in the presence of arginine and lysine. High concentrations of cysteine, histidine and tyrosine had a negative concentration dependent effect on both osteoblast viability and mineralisation.

Discussion: Glutamine appears to have the greatest effect on osteoblast proliferation and mineralisation. More research is required to identify exactly how these amino acids act within osteoblasts and further investigate the potentially synergistic effects of glutamine with arginine and lysine.

15. Hyaluronic acid/platelet count ratio as screening tool for the exclusion of clinically significant oesophageal varices in patients with cirrhosis.

Samantha Kestenbaum

Introduction: Universal endoscopic screening for clinically significant oesophageal varices (OV) is associated with poor utilization of medical resources and low patient satisfaction. Due to the rising prevalence of chronic liver disease, a novel screening tool is required.

Aims: To evaluate the diagnostic accuracy of serum hyaluronic acid (HA) concentration, platelet count and HA/platelet count ratio in predicting the presence of clinically significant OV. The reproducibility of the screening parameters and the false negative rate will also be determined.

Methods: The diagnostic accuracy of the non-invasive biomarkers was evaluated in the estimation cohort (122 patients) with receiver operator characteristic curves. The reproducibility and false negative rate of the optimal cut off value for the HA/platelet count ratio was assessed in the validity cohort (145 patients) and liver transplant cohort (48 patients), respectively.

Results: HA/platelet count ≥ 2.645 was the most accurate non-invasive biomarker for detecting clinically significant OV. This novel ratio has a high negative predictive value at 92.1%.

Conclusion: The clinical significance of the HA/platelet count ratio ≤ 2.645 is in reducing the number of unnecessary endoscopy investigations by predicting the absence of clinically significant varices.

16. Salt Handling in Hypertensive and Congenic Rats

Colin Rooney

Human essential hypertension is a complex, multifactorial trait under polygenic control. It is believed that there are a number of causal genes, which together contribute to between 30% and 50% of variation in blood pressure among individuals. Before my project the group identified several blood pressure quantitative trait loci (QTLs) using a genome wide scan in an F2 cross between the stroke prone spontaneously hypertensive (SHRSP) rat strain and the normotensive Wistar Kyoto (WKY) rat strain. In order to confirm this, a number of congenic strains were produced by introgressing WKY chromosome 3 congenic intervals into the SHRSP background. This project used two of the seven congenic strains produced: SP.WKYGla3d (3d) and SP.WKYGla3f (3f). 3d and 3f were chosen because haemodynamic measurements showed that 3d had captured the QTL for pulse pressure regulation while 3f had not. The diurnal variation of pulse pressure was also measured. The results suggested that 3f followed the SHRSP pattern of minimal control while 3d and WKY were more able to regulate their diurnal variation in pulse pressure. This pattern became more pronounced under salt loading. As the kidney is the main organ responsible for maintaining salt balance in the body, real-time PCR was used to determine how the expression level of certain important ion channels, present in the kidney, differed between the four strains. This was done with the aim of ascertaining how the level of gene expression of these channels differed between the strains and how a salt-loaded diet affected this. The channels chosen were ENaC (due to its importance in the regulation of salt balance) and NKCC2 (due to its location on chromosome 3 within both 3d and 3f congenic intervals). The results indicated that NKCC2 plays a role in the regulation of pulse pressure diurnal variation through differential salt handling.

17. Time from presentation to diagnosis of malignant mesothelioma in the western region of Glasgow from January 2010 to December 2012

Emma Leighton

Malignant mesothelioma (MM) is a destructive pleural tumour, which is related to previous asbestos exposure and has a poor prognosis. Delay in time from presentation to diagnosis could negatively impact a patient's life expectancy and their opportunity to claim compensation. The standard set in this audit was: "MM should be diagnosed within 3 months." Aims were: to quantify the average time taken from presentation of symptoms to diagnosis of MM in patients in west Glasgow between January 2010 and December 2012, and to compare this to the set standard. Smoking status was also looked into to examine whether this factor affected speed of diagnosis.46 of 47 patients met the inclusion criteria.NHS Clinical portal was used to collate data.71.7% of cases met the standard of the audit, with a mean time-frame of 3 months 13 days. Symptoms patients presented with did not make a substantial difference to the time of diagnosis. Respective percentages of patients meeting the standard were: 69.3%with chest pain; 71.3% with dyspnoea; 71.7% with both chest pain and dyspnoea; and 79.8%with "atypical symptoms". Of ex-smokers, 48.5% met the standard of the audit and 46.2% did not. Interestingly, a greater number of patients were life-long non-smokers in the group meeting the audit standard(30.3%) compared with those not meeting this standard (23.1%), perhaps suggesting a lower threshold for investigation in non-smokers. 28.3% of patients did not meet the standard of the audit, which is an indication for intervention to improve patient management. For example education programmes for individuals with previous asbestos-exposure could be initiated. Following this it would be necessary to re-audit to measure if there has been an improvement in the number of patients meeting the standard. The implementation of a positive change will hopefully facilitate more efficient diagnosis of MM.

18. Is reduced white matter integrity in the inferior fronto-occipital fasciculus (IFOF) associated with sub-clinical psychotic-like experiences?: A Diffusion Weighted Imaging and Clinical Interview Study

Daniel Creegan, Erik O'Hanlon, Helen Coughlan, Niamh Higgins, Francisco Amico, Mary Clarke, Lucy Power, Emmet Power, Mark Heneghan, Jessica Ryan, Mary Cannon

This study aimed to examine the changes in white matter integrity in the inferior fronto-occipital fasciculus (IFOF) in young people categorised as At-Risk for schizophrenia compared to matched controls.

23 At-Risk adolescents and 23 controls matched for age, gender and handedness were selected from the Adolescent Brain Development Study. Risk for Schizophrenia had been determined using the K-SADS screening instrument (1) during a clinical interview conducted by trained psychologists. All subjects underwent a diffusion-weighted MRI scan. ExploreDTI was used to report measures of Fractional Anisotropy across the IFOF using Constrained Spherical Deconvolution (CSD) based methods.

No significant difference was found between the two groups on statistical analysis of FA measures.

The study was limited by the small sample size but suggests that at this stage in development a pre-clinical population of adolescents categorised as At-Risk for Schizophrenia does not exhibit reduced white matter integrity in the IFOF.

Ethical approval was granted by The Medical Research Ethics Committee of Beaumount Hospital.

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19. Intra-operative frozen section for suspected early-stage ovarian cancer: 12 months of Plymouth Experience

Elizabeth McFadyen

Aims/Objectives: This audit aimed to validate our last 12-month experience with the use of intra-operative frozen section service in suspected early-stage ovarian cancer in Plymouth Hospitals. The diagnostic concordance between the results of frozen section and those of paraffin block were evaluated.

Background: Ovarian cancer is the leading cause of death from gynaecological cancer in the UK, and its incidence is rising. A diagnosis can be made on cytology, but tissue biopsy is generally required for a definitive diagnosis. Discrimination of benign and malignant tumours during surgery in gynaecological patients with adnexal masses is important for the management of the patient.

Materials and methods: We retrospectively evaluated the definitive histo-pathological results of 36 patients who underwent surgery between September 2012 and September 2013 at Plymouth Hospitals Trust, for ovarian masses and on whom frozen section was performed. Sensitivity, specificity, positive predictive values, and negative predictive values, of each group (benign, borderline and malignant) were assessed.

Results, Summary/Conclusions: Among the frozen-section results, 23 (63.9%) were benign, four (11.1%) were borderline, and 9 (16.7%) were malignant. Of the definitive paraffin block results, 21 (58.3%) were benign, three (8.3%) were borderline, and 12 (33.3%) were malignant. In 29 of the 36 (80.6%) frozen sections, frozen-section results gave the same diagnosis as did results of the paraffin blocks, In 7 (19.4%%) cases, the results were discordant. In our opinion, the data presented make a strong case for this type of service to be better adopted and used more widely in the diagnosis of ovarian tumours in gynaecological oncology surgery.

20. An audit of the use of colposcopic directed biopsies for the diagnosis of CIN

Rebecca Horgan, Paul Byrne

A recent meta-analysis on the accuracy of colposcopic directed cervical biopsies to diagnose CIN 2 and CIN3 found a pooled sensitivity of 91.3% and a specificity of 24.6%.

The objective of this audit was to determine the accuracy of colposcopic directed biopsies in the diagnosis of cervical intra-epithelial neoplasia (CIN) at the Rotunda Hospital. The study period was 1st January 2011-31st December 2012.

A retrospective review of the Mediscan database was performed to determine the number of patients who underwent a colposcopic directed biopsy showing CIN1,2 or 3and who underwent a Large Loop Excision of the Transformation Zone (LLETZ)showing CIN on histology. The data was analysed using Microsoft Office Excel 2010 and SPSS. The correlation between biopsy histology results and subsequent LLETZ histology was examined.

A total of 526 women fulfilled our inclusion criteria. The biopsy histology and LLETZ histology for these patients are displayed in the table below. The strength of association (Cramer's V) between the biopsy histology and LLETZ histology was found to be 0.31. Our study found that78 women who had CIN2on biopsy had CIN1 on LLETZ and 81 women who had CIN3onbiopsy had CIN1(34) or CIN2(47) on LLETZ histology.

	CIN1 (LLETZ)	CIN2 (LLETZ)	CIN3 (LLETZ)	Total
CIN1 (biopsy)	33 (56%)	14 (24%)	12 (20%)	59 (100%)
CIN2 (biopsy)	78 (33%)	94 (40%)	61 (26%)	233 (100%)
CIN3 (biopsy)	34 (15%)	47 (20%)	153 (65%)	234 (100%)
Total	145	155	226	526

Based on LLETZ histology, our study found that colposcopic directed biopsies detected high grade disease in 355/381 cases, giving a sensitivity of 93.2% (95% Confidence Interval 0.9103 to 0.9533).The apparent decreasein severity of CIN grade between biopsy and LLETZ histology could be attributed to the removal of small lesions of higher grade disease by the cervical biopsy.

21. Association between Pre-operative Pain and Joint Wear Patterns in Total Knee Replacements

Lachlan Dick, Daniel Porter, Tony Sim

Introduction: Osteoarthritis is a chronic condition characterised by cartilage loss in synovial joints causing pain and reduced joint function. Whilst conservative management is possible, a total knee replacement (TKR) provides symptomatic relief and improved function for most patients. However, there is little understanding of the association between damage seen in osteoarthritis, pre-operative pain and whether particular compartment wear affects this.

Method: Bone offcuts from 25 patients undergoing a TKR were analysed to assess the cartilage damage within each knee compartment (anterior, medial, lateral and posterior). The Outerbridge Classification system was used to assess damage and ImageJ software used to calculate the exact area of damage. SF-12 scores for each patient were collected and processed with the damaged area using SPSS to determine any correlation.

Results: None of the compartments showed any strong correlation with the SF-12 scores. The posterior compartment had the strongest correlation and statistical significance ($r = -0.350$, $p = 0.086$) although none of the other compartments showed similar correlation.

Conclusions: The results suggest that there is no association between pre-operative pain and compartmental joint wear. However, a larger sample size is needed to reproduce these results with statistical significance.

22. Interim Analysis of IRNMAN incorporating validation of analysis software (IRNMAN – Iron Nanoparticle enhanced MRI in the Assessment of myocardial infarctioN)

Isla Cameron, Colin Stirrat

Introduction: Inflammation after myocardial infarction is detrimental to myocardial recovery. Magnetic Resonance Imaging with ultra small super paramagnetic particles of iron oxide (USPIO) can detect inflammatory cells in the myocardium. When inflammation peaks and how long USPIO stays in the myocardium after administration was explored and also in-house software was validated against Siemens software used in image analysis.

Methods and Results: Voxels from each programme's maps were sampled and compared using Bland-Altman methods following software updates leading to increasingly close results with standard deviation of 4.295. Sixteen participants' results were analysed, using regions of interest on R2* maps, for percentage difference in R2* value with time following USPIO administration (at various time points) in infarct vs non-infarct myocardium. This indicated inflammation was higher in infarct areas but this difference decreased with time. Percentage R2* increase in infarct areas following a dose of USPIO with time until a second dose was administered was found to be 16 days ($p=0.0001$).

Conclusion: Software programmes correlate closely with a small number of points outlying. Cardiac MRI and R2* maps can be used to track inflammation post-MI, however more data is needed to identify precise time points.

23. The study of *in vitro* activity of plasma-derived and recombinant factor IX.

Cheryl Lau

Background: Current methods of measuring factor IX (FIX) activity rely on functional FIX assays based on the activated partial thromboplastin time (APTT), which is not a physiological test. Recombinant FIX (rFIX) is known to have a reduced *in vivo* recovery as compared to plasma-derived FIX (pdFIX), but this could possibly be due to limitations of the APTT-based assays used to measure both recovery and potency of FIX concentrates. Measurement of tissue factor (TF)-initiated thrombin generation may provide a more comprehensive assessment of FIX activity.

Objectives: To compare thrombin generation of pd- and rFIX by TF-initiated thrombin generation assay and compare these findings to APTT-measured FIX activity.

Methods: A range of concentrations of pd- and rFIX were prepared based on product-labelled potency. Activity and thrombin generation at each concentration was measured by 1-stage APTT-based FIX assay and calibrated automated thrombography respectively.

Results: FIX activity of pd- and rFIX measured by one-stage FIX assay were comparable at equivalent labelled concentrations. Thrombin generation assay showed that pd- and rFIX had comparable endogenous thrombin potential, lagtime and time to peak, but at higher FIX concentrations (≥0.5IU/mL) peak thrombin measured for rFIX was substantially higher than that for pdFIX. Approximately three times higher levels of activated FIX (FIXa) were found in rFIX compared to pdFIX.

Conclusion: There is potential for the use of low TF-initiated thrombin generation assay in assessment of FIX activity.Reduced *in vivo* recovery of rFIX compared to pdFIX might be due to higher levels of FIXa present in recombinant concentrates, causing overvaluation of concentrate potency measured by APTT-based FIX assay.

24. 3D Printing in Medicine

Nauman Hafiz, Tom Beddis, Laurence Guillot, Vivek Majumder, Chris Marshall, Ruaridh McCusker, Abbey Wrathall

Three-Dimensional (3D) Printing is a novel technology in medicine with many applications. In our project we looked at its current and prospective uses. We analysed prosthetics made using 3D technology and compared them to like prosthetics made by conventional means. We also reviewed 3D printed hearing aids; 3D printed hydroxyapatite jaw prosthetics; and3D printing's use in the fabrication of a tracheal splint to treat infant tracheobronchomalacia. Finally, we looked at the use of 3D printing to make replicas of patient's organs in order to train surgeons and medical students, and also inform patients about their condition. We drew our research from research papers, review articles, technology websites and by contacting a researcher forefront in this field. We looked at the positives and negatives of 3D printing and came to the conclusion that 3D printing would be an important innovation in modern medicine, if the issues of cost and availability are addressed. Prosthetics can be formed to meet the patient's needs and fit their bodies perfectly. In surgery, the 3D printed hydroxyapatite bone analogues have a much shorter biodegradability time than conventional materials, are perfectly matched to the patient deformities and have no chances of rejection. 3D printing can help combat the shortage of cadavers for surgical and medical training. Patient specific models can be printed and used for pre-operative surgical planning and for improving the patient's knowledge of their disease. The possibility of 3D printed organs from stem cells was also investigated; however this technique is still in its infancy, with very few current examples. It is, nevertheless, still a very real possibility, and a promising field of study.

25. Otological conditions requiring emergency admissions to a tertiary referral centre

Marianne Gallanagh, Muhammad Shakeel

Background: Limited published data exists on the otological conditions requiring in-hospital treatment. Cost effective utilization of resources mean minimal hospital stay and focus should ideally be on treating the patients on outpatient basis.

Aim: We investigate the pattern of emergency otological admissions to our department. We aim to establish the common admission diagnoses; the equipment required in the ward treatment room and to identify the training demands of the nursing and medical staff involved in their management.

Methodology: Retrospective chart review of a prospectively maintained departmental database. All eligible patients were audited over 3 years (2010-2013). Information collected includes demographics, source of referral, clinical presentation, admission diagnosis, investigations, management and outcome.

Results: A total of 128 patients (113 adults and 15 children) were identified. There was equal number of female and male patients. Common conditions requiring in-hospital management included Perichondritis of pinna = 32, severe Otitis externa = 25, Mastoiditis = 18, Otitis media = 12, Vertigo = 10, Malignant otitis externa = 8, Brain abscess = 5 and Pinna haematoma = 5. Four patients had facial nerve weakness secondary to Ramsay hunt syndrome and 5 patients developed facial palsy secondary to acute otitis media. Most of the patients were referred by their general practitioner but some patients presented to the accident and emergency department. The patients with neurological complications underwent CT scan before surgical intervention was instituted according to the diagnosis. Others were treated conservatively and Ciprofloxacillin and Co-amoxiclav were the two most commonly used antibiotics.

Conclusions: The commonest ear emergencies requiring admission to our unit are perichondritis of pinna, otitis externa and mastoiditis. Early diagnosis and prompt treatment is essential to prevent any long term morbidity and mortality. Perhaps attention is required to identify preventative measures for these otological emergencies.

26. Nanoparticles: Revolutionising Brain Cancer Diagnosis and Therapy

Sadaf Sohrabi

Due to the delicate and complex nature of the brain, serious limitations exist for current brain cancer treatment options explaining the condition's strikingly low survival rate. Therefore, there is a need for the development of novel solutions to revolutionise the diagnosis and treatment of brain tumours. In this work, a thorough critical review of results available in scientific literature regarding the ground-breaking applications of nanoparticles for the diagnosis and treatment of brain tumours has been undertaken.

Various properties of nanoparticles render them suitable for drug delivery to the brain, including the ability to cross the blood-brain barrier– one of the biggest obstacles facing clinicians in the delivery of therapeutics. As a result, therapeutics that could treat brain tumours cannot reach the brain due to the restrictive effects of this barrier. Using appropriately designed nanoparticles, scientists have been able to carry such drugs (e.g. Paclitaxel) successfully through the blood brain barrier, increasing uptake of the drug by tumour cells and enhancing cytotoxicity compared to free administration of the drug.

The advent of nanoparticles has also resulted in major advances in brain cancer imaging, both pre- and intra-operatively. Conventionally, gadolinium MRI contrast agents are used, however iron-oxide nanoparticles have been identified to have numerous advantages in comparison, including overcoming the risk of nephrogenic systemic fibrosis, a higher circulating half-life, greater uptake by tumour cells, and crucially, creating far superior images.

Additionally, nanoparticles can also enable the utilisation of methods that have previously been very limited in their success e.g. thermotherapy and gene therapy.

We conclude that nanoparticles have the capacity to overcome the barriers posed in some critical aspects of brain cancer diagnosis, management, and treatment. As our knowledge in the area of nanotechnology improves, nanoparticles are likely to play a central role in the future clinical management of brain cancer patients.

27. Evaluation of Clinical Decision Tools in Detecting Early Symptoms in Pancreatic Cancer

Cindy Lai, Stephen Pereira, Geri Keane

Introduction: Pancreatic cancer is the 5th most common cause of death in the UK. It has one of the worst 5 year survival rates (<4%) out of the all common cancers. The symptoms are often non-specific, most of which arise later in the disease process when curative surgery is no longer viable. 50% of patients are diagnosed following emergency presentation resulting in lower survival rates compared with other routes of diagnosis. The clinical decision tools QCancer ® and Risk Assessment Tool (RAT) have been developed and used in primary care to identify patients at risk of pancreatic cancer in order to aid early diagnosis.

Aims: The aims of this study were to devise and pilot a symptom questionnaire to determine the efficacy of existing decision tools in identifying symptoms of pancreatic cancer and to determine the prevalence and timing of associated symptoms.

Methods: This was a hospital based case control study which involved the piloting of a novel symptom questionnaire. The questionnaire included symptoms from both current clinical decision tools for pancreatic cancer: the QCancer® tool and the RAT. The frequency of symptoms, the timing of onset as well as the management of condition were retrospectively reviewed via face to face interviews with patients diagnosed with pancreatic cancer (n=6),cholangiocarcinoma (n=6) and benign pancreatobiliary disease patients (n=13).

Results: The median QCancer ® 2013 score is higher in pancreatic cancer patients (2.47%) compared with cholangiocarcinoma patients (0.74%) and benign pancreatobiliary patients (0.44%). Out of all the symptoms in the questionnaire, unintentional weight loss, abdominal pain, heartburn, back pain, steatorrhoea, diarrhoea, fatigue, depression, changes in taste and insomnia were reported by a majority of pancreatic cancer patients.

Conclusion: Patients with pancreatic cancer presenting with key symptoms have the potential to be identified earlier by clinical diagnostic algorithms in primary care.

28. Telaprevir: treatment option for Hepatitis C Type 1 infection in a West of Scotland population.

Darren Raffo

Introduction: Treatment options for Hepatitis C have been evolving rapidly over the past decade aiming to achieve a Sustained Viral Response (SVR) 6 months post treatment. Ribavirin and PEGylated α-IFN therapy (RBV-INF) has been the mainstay of treatment for many years. SVR has been observed in up to 41% of patients treated with this double therapy. More recently Telaprevir (TVR), in conjunction with RBV-INF, has shown promise in phase III clinical trials, 88% of patients displaying SVR.

Aim: Assessment of the effectiveness of hepatitis C treatment, with RBV-INF-TVR, comparing cirrhotic and pre-cirrhotic patients in the general population.

Method: A retrospective sample of 17 (9 cirrhotic, 8 pre-cirrhotic) patients was identified, each completed their course of 4 weeks of Rib-INF as well as12 weeks of RBV-INF-TVR and had their viral load checked at 0,4, 8 and 12 weeks.

Results: 4 weeks of RBV-INF significantly reduced viral load in cirrhotic patients ($p<0.01$, one-way ANOVA) but not in pre-cirrhotic patients ($p>0.05$).No patients attained an undetectable viral load on double therapy. Introduction of Telaprevir further reduced the viral load in both cirrhotic (111,462.0±64,485.0 to 29.8±26.4, mean±SEM) and pre-cirrhotic patients(9,3513.0±58,979.0 to 129.8±124.8,mean±SEM) and maintained significantly lowered levels than week 0 in both groups at 8 ($p<0.001$,one-way ANOVA) and 16 weeks ($p<0.001$). An undetectable viral load was attained in 62.5% of pre-cirrhotic and 66% of cirrhotic patients at week 8. At 16 weeks, 2 patients, 1 from each group maintained a measurable viral load with 15 of 17 patients reaching SVR at 6 months.

Conclusion: RBV-INF-TVR attained SVR in 15 of 17 patients with relapse occurring in two cirrhotic patients at 6 months. The individual effect of Telaprevir is difficult to interpret and we propose further study with larger patient numbers and observe the effect of Telaprivir on different genotypes of Hepatitis C virus.

29. Sensory Dysfunction and Pain in Total Hip Replacement Scars

James Ho, David E Porter

Objectives: To assess and objectively quantify the prevalence of sensory dysfunction in the form of innervation density, and the subjective experience of pain, around total hip replacement scars(THR). The study also aims to establish any factors which may predispose to greater sensory dysfunction.

Methods: In a cross-sectional study, sensory nerve function was assessed by means of light touch (LT) and 2-point discrimination (2PD) on 40 male subjects. Subjects were verbally questioned on the frequency and severity of pain around the scar if present. Additional patient information was obtained through TRAK. Statistical analysis was conducted with significance level of $p \leq 0.05$.

Results: LT/2PD was significantly poorer ($p<0.001$) on the operated side compared to the contralateral limb. LT function *improved* after 5 years ($p<0.01$), and frequency of scar pain, which was invariably of low severity, after 3 years ($p=0.037$). Sensory deficit was also found to be increased in diabetics and possibly following posterior approach surgery.

Conclusions: Sensory dysfunction and pain around the scar is common following THR, but can be expected to improve with time. These findings may support informed patient care, and result in more realistic patient expectations and understanding, and therefore improved satisfaction. Further work on the effect of surgical approach, comorbidities and type of anaesthesia is required.