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WJMER

World Journal of Medical Education and Research

An Official Publication of the Education and Research Division of Doctors Academy

In this edition, these topics and more....

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Introduction

The World Journal of Medical Education and Research (WJMER) is the online publication of the Doctors Academy Group of Educational Establishments. Published on a quarterly basis, it's aim is to promote academia and research amongst all members of the multi-disciplinary healthcare team including doctors, dentists, scientists, and students of these specialties from all parts of the world. The principal objective of this journal is to encourage the aforementioned from developing countries in particular to publish their work. The journal intends to promote the healthy transfer of knowledge, opinions and expertise between those who have the benefit of cutting edge technology and those who need to innovate within their resource constraints. It is our hope that this will help to develop medical knowledge and to provide optimal clinical care in different settings all over the world. We envisage an incessant stream of information will flow along the channels that WJMER will create and that a surfeit of ideas will be gleaned from this process. We look forward to sharing these experiences with our readers in our subsequent editions. We are honoured to welcome you to WJMER.

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WELCOME

'*The medical and the scientific problems of this world cannot be solved by skeptics whose horizons are narrowed by practical realities, we need women and men who dream of things that cannot be and ask, 'Why not?*'
- Professor Egon Diczfalusy, Karolinski Institute.

Dear Colleague,

We are delighted to welcome you to the inaugural edition of World Journal of Medical Education and Research (WJMER). At WJMER, we are aware that medicine is a vast and dynamic area in human scholarship with rapid advances and an ever burgeoning demand placed on it by society to ensure good quality healthcare. It is therefore essential to have a global perspective on different aspects of research, recognition of symptoms, management of diseases, interesting cases (both common and rare), clinical audit and topical issues. WJMER aims to reconcile seemingly disparate Western practices and medical implementations in other cultures as well as encouraging publications and research from pioneers in the profession.

This edition proudly brings an array of selected articles from the developments at the forefronts of antithrombotic stroke prophylaxis in AF patients to a manuscript that outlines the contentious discussions about the ethics underpinning research involving ethics committees and informed consent. The editors also had the fantastic opportunity to interview the illustrious Professor Byrne, oncoplastic surgeon and professor of medical education at Manchester medical school. On the opinion piece section of our journal we have a highly perceptive personal insight from the silver medalist of the World University Anatomy Challenge 2012. Other articles include how film can be utilized as a learning tool, and for those who are considering elective opportunities we provide an insider's guide to clinical placements in Lebanon.

This special issue of WJMER includes selected book chapters which provide insight into specialties such as cardiology, cardiothoracic surgery, and review articles on wound healing and wound management. We also collated abstracts that were showcased in the *Future Excellence* International Academic and Research Conference (IARC) held in Manchester, United Kingdom in August 2011. The conference, under the auspices of Doctors Academy and the Royal College of Surgeons of Edinburgh, provided a unique platform for junior doctors and medical students to share interesting clinical observations and innovative ideas with fellow colleagues, and encouraged exchange of information and the transfer of knowledge from all corners of the globe. Over 280 abstracts were submitted, which underwent several rounds of rigorous judging before a handful was invited to present at the conference. The abstracts cover a broad array of topics ranging from laboratory analysis of *Clostridium difficile* and *E. coli,* post-natal depression in Kenya and complications of transphenoidal pituitary surgery. Delegates had a choice of submitting their work for poster presentation or for oral presentations which were further subdivided into research, clinical work and audit categories. First, second and third prizes were awarded to the top presentations in each category by an esteemed panel of judges and, in addition, the best oral presentation across the categories was awarded the prestigious 'The Doctors Academy – University of Dundee Award in Academia and Research' Prize. WJMER plans to invite the winners of these prizes to submit their full articles, which will be eagerly awaited in subsequent editions.

We hope that you find this edition of WJMER as enjoyable and indeed stimulating to read as it was for us to compile it.

With very best wishes,

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Table of Contents

WJMER
World Journal of Medical Education and Research:
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Stroke Prevention in Patients with Atrial Fibrillation

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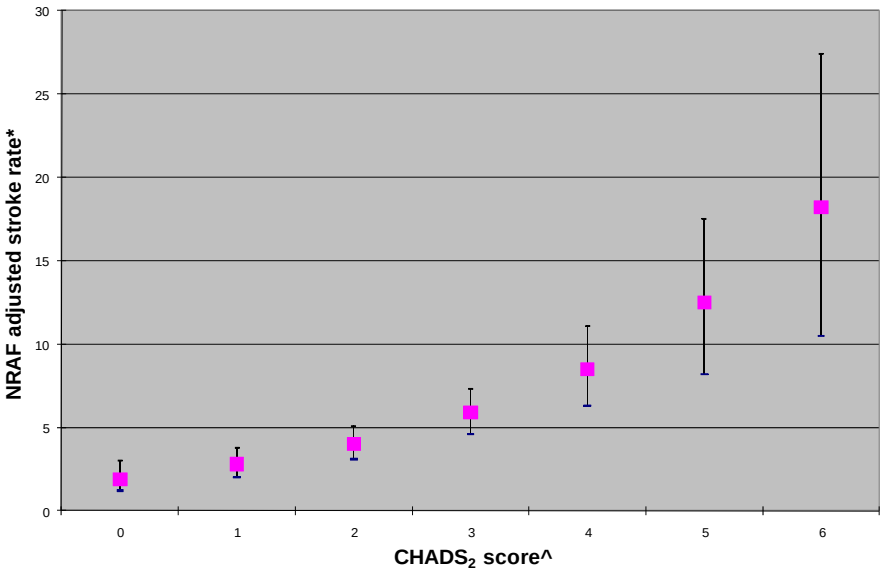
Introduction

Atrial fibrillation (AF) significantly increases a patient's risk of developing vascular events, such as stroke (one in six strokes occurs in patients with a background of AF), systemic embolism and vascular death. The risk of cerebral embolism in patients with AF and recent transient ischaemic events or previous strokes is around 12% per year with an annual mortality rate of 5%. The current evidence recommends that the best therapy in terms of risk prevention is anticoagulation; the ACTIVE W trial, which compared anticoagulation with a combination of aspirin and clopidogrel, was stopped early due to anticoagulation clearly being the superior option. However, in practice, anticoagulation is not always a suitable option. Medical contraindications such as intracranial bleeding, severe active bleeding, recent brain, eye, or spinal cord surgery, malignant hypertension, severe thrombocytopenia and other factors, e.g. compliance issues, reluctance to have regular INR checks, etc may preclude anticoagulant therapy. In such situations antiplatelet therapy and other treatment modalities appear to be more desirable options. In this short review we discuss the various treatment options under the umbrella term antithrombotic therapy and we also explore a surgical treatment, based on currently available evidence, for prevention of cardio-embolic strokes in patients with non-rheumatic AF.

Risk Stratification

Patients with AF can be stratified into high and low risk groups for developing strokes depending on their co-morbidities and risk factors, which may also influence how aggressive we are in our management. AF patients who are at high risk of developing strokes include patients over 65 years of age, those with previous strokes or transient ischaemic attacks (TIA), hypertensive, diabetics, or those with poor left ventricular function. The low risk group includes those less than 65 years of age with no other risk factors. The $CHADS_2$ scoring system has been developed to further classify patients where a patient scores 2 points if they have had a previous stroke or TIA and scores 1 point for each of the following risk factors: recent congestive heart failure, hypertension, age > 75 years or diabetes mellitus. As shown in figure 1, the risk of developing a stroke rises exponentially with every additional point. Hence prophylactic treatment should be started promptly especially for those in high risk categories.



^CHADS2 score is calculated by adding 2 points for having a prior stroke or TIA, and 1 point for the following – recent congestive heart failure, hypertension, age > 75 years, diabetes mellitus.
* The adjusted stroke rate is the expected stroke rate per 100 patient-years from the exponential survival model assuming that aspirin was not taken. – Pink squares indicate the adjusted stroke rate and the lines above and below indicate the 95% confidence interval.

Figure 1: Risk of Stroke in National Registry of Atrial Fibrillation (NRAF) Participants, Stratified by $CHADS_2$^ Score
Adapted from: Gage BF, Waterman AD, Shannon W, et al, 2001. Validation of clinical classification schemes for predicting stroke: results from the national registry of atrial fibrillation. *JAMA* 285(22):2864-2870.

Anticoagulation

Since 1989, there have been several randomized clinical trials investigating the use of anticoagulants for primary and secondary stroke prevention in patients with non-rheumatic atrial fibrillation. Five large primary prevention trials have shown a reduction in the incidence of ischaemic strokes by 65% with warfarin therapy. The recent Birmingham Atrial Fibrillation Treatment of the Aged study (BAFTA) compared the use of warfarin therapy adjusted to INR 2.5 with low dose aspirin (75mg) in patients over 75 years of age. In 973 patients who were prospectively followed up for 2.7 years, there were 24 significant events (21 strokes, 2 other intracranial haemorrhages and one systemic embolus) with warfarin therapy; 48 significant events (44 strokes, one other intracranial haemorrhage and three systemic emboli) occurred in the cohort assigned to aspirin therapy. The European Atrial Fibrillation Trial (EAFT), a large secondary prevention trial, randomized 1007 AF patients with recent TIA or minor stroke into anticoagulant, 300mg aspirin or placebo groups. After a mean follow-up of 2.3 years, 8% of patients on anticoagulant therapy developed a vascular event compared to 17% in the placebo group of patients. Haemorrhagic events in anticoagulated patients were 2.8% yearly with no intracranial bleeds identified.

Another antiplatelet drug, indobufen was compared with warfarin in the Studio Italinano Fibrillazione Atriale (SIFA). The incidence of any strokes for patients on indobufen was 5% compared with 4% for those on warfarin therapy. Patients on indobufen had a greater percentage of ischaemic strokes (3.9%) compared to 2.2% for those on warfarin, but this was partially offset by the slightly increased haemorrhagic strokes for patients on warfarin (0.88% compared to 0.2%).

Another approach which has been investigated in the Stroke Prevention in Atrial Fibrillation III (SPAFIII) and Second Copenhagen Atrial Fibrillation, Aspirin and Anticoagulation study (AFASKII) is whether low-dose warfarin which would require much less monitoring in addition to aspirin therapy would be efficacious in reducing thrombotic events. SPAFIII compared a regime of low-dose warfarin combined with 325mg aspirin against adjusted dose warfarin and was terminated after 1.1 years as patients on combination therapy developed a much higher rate of ischaemic strokes and systemic embolic events (7.9% per year as compared to 1.9% for those on adjusted dose warfarin). AFASKII randomized subjects into fixed low dose warfarin (1.25mg per day) alone, low dose warfarin and 300mg aspirin in combination, 300mg aspirin alone and compared the results against adjusted dose warfarin (INR 2.0-3.0). Findings from this trial indicated that in the first year patients on adjusted-dose warfarin had a lower rate of developing ischaemic strokes or systemic embolic events but after 3 years, there were no significant differences between the groups. Haemorrhagic events in both trials in all cohorts were insignificant.

Important clinical issues when starting warfarin therapy include the optimal intensity and when to initiate treatment. A case-control study found that risks of stroke rose steeply when INRs fell below 2.0 and that the risk of bleeding increased significantly when INR was above 4.0 with a steep increase of intracranial haemorrhages when INR reached 5.0 or above. The current guidelines recommend lifelong anticoagulation, maintaining INR levels between 2.0 and 3.0 which is in agreement with the published evidence. The International Stroke Trial randomized patients to 14 days of either aspirin or heparin therapy within the first 48 hours of developing an acute ischaemic stroke. Of the patients who were in AF, the heparin group had lower rates of recurrent ischaemic strokes but this was offset by increased rate of haemorrhagic strokes compared to the non-heparin cohort. Although not specifically investigated, patients with large strokes seem to be particularly prone to haemorrhagic transformation. Hence early anticoagulation in patients with AF particularly those with acute large strokes is not advised, especially not within the first 14 days.

Dual Antiplatelet Therapy

Another option in antiplatelet therapy to consider is if combined antiplatelet treatment is more effective than a single agent. As different agents have different modes of action, it would seem that using multiple treatments would be synergistic and give better protection against thrombotic events such as myocardial infarction and ischaemic stroke. The ACTIVE A trial enrolled 7554 patients with AF in whom anticoagulation was contraindicated, randomising them to receive aspirin (75-100mg OD) plus either clopidogrel (75mg OD) or a placebo. The patients taking clopidogrel were shown to have a significant reduction in vascular events (particularly disabling stroke) after 3.6 years compared to those taking the placebo. However, these patients were also shown to be at a much higher risk of bleeding complications, with a 57% higher incidence of major bleeding events (mainly GI bleeds). This suggests that, although dual antiplatelet therapy does reduce the risk of vascular events, the risk of bleeding does limit the use of these medications.

Other antithrombotic agents

Other emerging medical treatments include anti-Xa agents such as Rivaroxaban (Xarelto®) and Apixaban (Eliquis®) and oral direct thrombin inhibitor such as Dabigatran (Pradaxa®). Connolly et al ran a noninferiority trial involving 18,113 patients with AF and an increased risk of stroke, who received either a fixed dose of dabigatran (either 110mg or 150mg) or adjusted dose warfarin. They were followed up on average for 2 years (median duration), with the primary outcome being stroke or systemic embolism. It was found that those patients receiving 110mg dabigatran had a similar incidence of stroke/embolism compared to those on warfarin but lower rates of haemorrhage (3.36% in warfarin group compared to 2.71%, with p = 0.003). Those patients receiving 150mg dabigatran had a reduced incidence of stroke/embolism compared to those on warfarin (1.69% per year on warfarin compared to 1.11% with p < 0.001). However, the risk of major haemorrhage was similar in both groups. Results have been newly revised (fig. 2) but have not influenced the conclusions of the trial. As a result of this trial, the higher dose (150mg) but not the lower dose (110mg) of Dabigatran has recently been approved by the Food and Drug Administration (FDA) for risk reduction of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. In addition, Dabigatran would be easier to administer (since it is an oral preparation) and monitor, therefore, it may be suitable for some patients who cannot take warfarin for lifestyle reasons. Both Rivaroxaban and Apixaban′ also show promising results with comparable results to warfarin in terms of stroke prevention in patients with non-valvular AF and indeed may even have less risk of severe intracranial and major bleeds compared with warfarin.

Therapy	Trials	Participants	Relative Risk Reduction (95% CI)
Adjusted-dose warfarin compared to placebo	6	2900	62 (48 to 72)
Aspirin compared with placebo	6	3199	22 (2 to 38)
Adjusted-dose warfarin compared with aspirin	5	2837	36 (14 to 52)
Adjusted-dose warfarin compared with low-dose warfarin	3	893	38 (-20 to 68)
Aspirin compared with low-dose warfarin	2	934	15 (-42 to 49)
			Relative Risk (95% CI)
Adjusted dose warfarin compared with a)110mg Dabigatrin b) 150mg Dabigatran	1	18,113	a) 0.91 (0.74 to 1.11) [published] 0.90 (0.74-1.10) [revised] b) 0.66 (0.53 to 0.86) [published] 0.65(0.52-0.81) [revised]

Figure. 2: Summary of medical antithrombotic therapies
Adapted from Hart et al Ann Intern Med 1999

Surgical treatment

A novel method of managing patients with chronic AF is the percutaneous closure of the left atrial appendage as most cardio-embolic thrombi are formed in the left atrial appendage. The recently published multicentre randomized non-inferiority trial where AF patients scoring a $CHADS_2$ score of 1 or above were enlisted to undergo this procedure or to continue on warfarin therapy. The probability of non-inferiority was greater than 99.9% and the higher rates of adverse events (major bleeding, pericardial effusion and device embolism) were mostly due to periprocedural complications.

Other preventative measures

There are a number of issues to consider in optimizing the management of patients with AF who are at a high risk of a vascular event. Primary prevention, lifestyle changes and control of risk factors such as diabetes and hypertension are important, as for every extra point on the $CHADS_2$ score, the expected stroke rate in AF patients per 100 patient years increase exponentially with AF as illustrated above (fig. 1).

Management of AF itself is another factor, so efforts should be made to adequately control ventricular rate. Rhythm control strategies offer no survival advantage, hence rate control and anticoagulation is the best option for high risk patients.

Conclusion

Anticoagulation with adjusted-dose warfarin is currently the most effective stroke prevention therapy for patients in AF. For those with contraindications, antiplatelet therapy can be used to reduce recurrent ischaemic events, although to a lesser degree. Results of clinical trials with newer antithrombotic agents are promising. As these drugs have a number of advantages over warfarin, they may eventually replace it as the drugs of first choice.

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Follow-up Chest X-ray Following Regression of Community Acquired Pneumonia

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Community acquired pneumonia (CAP) is a common condition, affecting 5 per 1000 adult population in the U.K, and is a major cause of morbidity and mortality. Although it has a predilection for the elderly in the population, it affects people of all ages, and as evidenced in the recent Paul Hurst case, it can strike a healthy young man and kill within 24 hours of contracting the illness. The severity of CAP is stratified by the CURB-65 classification framework which gives guidance on requirement of admission, and which intravenous antibiotics need to be instigated.

After discharge from hospital, those with persisting symptoms or signs, smokers or those above the age of 50 are advised to have a follow-up chest X-ray to exclude an underlying malignancy[1,2,] as complete resolution of radiological CAP changes occur within 6 weeks in 73% of people. Holmberg and Kragsbierg found that an underlying malignancy is an important cause of slow resolution of signs and symptoms of pneumonia and two prospective studies reported that people diagnosed with pneumonia who are above a certain age and who smoke are at a high risk of developing lung cancer – 17% of smokers over age of 60[1] and 11% of smokers over age of 50. Hence an analysis of patient follow up after discharge would be of interest not only academically, but may also highlight any shortcomings on a clinical level.

As part of the management, CAP patients discharged should be reviewed by the GP and those at higher risk should have a follow-up chest X-ray to exclude an underlying malignancy. A retrospective audit was conducted on the 100 CAP patients from Princess of Wales Hospital, Bridgend identified between September 2008 and February 2009, using the RADIS system to identify if they have had an outpatient repeat chest X-ray in 6 weeks following their admission to A&E. The results are illustrated in figure 6.

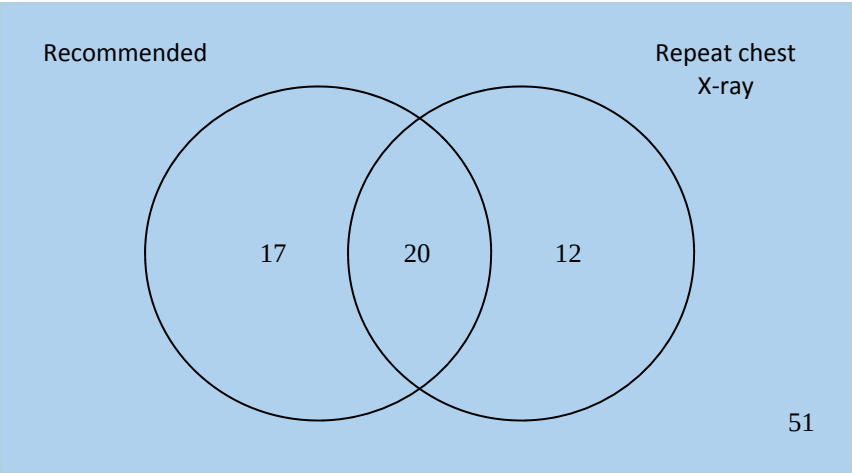

Figure 1: Repeat chest X-ray at 6 weeks following discharge from hospital. 37 patients were recommended by radiologists to have a repeat chest X-ray, 32 patients had a repeat chest X-ray in outpatients following their recovery. The remaining 51 were not recommended nor had a repeat chest X-ray after discharge.

Of the 100 patients analyzed in this audit, 93 of them had risk factors (either aged >50 or is a smoker) which would warrant a follow up chest X-ray in 6 weeks following discharge. However, only 37 patients were recommended a follow-up by the radiologists and of these, only 20 patients attended. Two patients were given an appointment but did not attend. Twelve other patients, of which 11 were over 50 years of age, had a repeat chest X-ray following the resolution of CAP. The remaining patient was under the age of 50 and a non-smoker, so a repeat chest X-ray was unnecessary in this case according to the guidelines. Of the 32 patients who had a repeat chest X-ray, 14 had completely resolved, 4 partially resolved, 3 had persistent shadowing, 2 had developed a pleural effusion, 1 had minor increased lung markings, 1 had a retrocardiac shadow, 5 were unreported and 2 went on to have a CT which showed suspicious looking lesions.

In summary this audit shows that after discharge 93% of patients should have had a follow-up chest X-ray in 6-8 weeks following recovery, but only 49% of them attended. Given that previous studies reveal that of patients diagnosed with CAP, 17% of smokers over age of 60[1] and 11% of smokers over age of 50[1] had an underlying malignancy, it would reflect best practice if GPs played a more active role in reviewing patients at 6 weeks after the diagnosis of CAP has been made and requesting a repeat chest X-ray for those at higher risks.

Upon publication of this article, we intend to distribute our findings to the radiology department in the Princes of Wales hospital with a view to positively influencing clinical practice by reminding practitioners of the current guidelines on this matter and then conducting a repeat audit to ascertain if appropriate action has been taken.

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Interview with Professor Ged Byrne:
Consultant Oncoplastic Surgeon and Professor of Medical Education in Manchester Medical School

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'It was my weaknesses, not my strengths, which best helped me to serve humanity …'
Professor Ged Byrne

Professor Ged Byrne MD, FRCS, NTF, FHEA

Imagine waking up one morning to discover that your hometown has been bombed and the country where your family and friends live in has been engulfed by war overnight. Alarming reports start trickling in of a burgeoning civilian mortality rate and carnage that is seemingly ubiquitous. What thoughts and feelings enter your mind? This was the case with me and may very well be the harrowing reality for those whose loved ones presently reside in Syria (our thoughts and prayers go out to our breathren in Syria). I vividly recall this period in my life; indeed memories of those dark days have not faded and return to haunt me from time to time. However things could have turned out far worse for me had it not been for the presence of a truly incredible individual in my life, Professor Ged Byrne. Professor Byrne was Hospital Dean for clinical studies in 2006 during the siege of Lebanon and was my first point of contact. I deem his being in my life at that time an act of Divine Providence for had it not been for his intervention I would not be composing these lines right now as Dr. Ahmed Hankir. My case is testament to Professor Byrne's pioneering method of personalized mentoring and how effective this technique of tutoring, for both professional growth and personal development, really is. So I met up with Professor Byrne in the Marriott Hotel after all of these years in order to reveal the person behind the

professor and discover how he became the compassionate man he is, the worldly healer who had the capacity, of both 'heart and mind', to rescue me from the depths of my own despair. And so the interview begins and an extraordinary trajectory is uncovered…

AH: Thank you Professor Byrne for accepting my request to be interviewed for World Journal of Medical Education and Research. My first question is this, where do we begin?
GB: [smiling] you tell me Ak.

GB: I was born in Liverpool in 1965 to a traditional working class family. My father was a freelance joiner and my mother was unemployed at the time of my birth. I attended the local Catholic primary school and then received a scholarship to enrol in the Christian Brother School in Birkenhead. When I turned 18, I took 12 months off following A Levels and founded a charity that dealt with drug abusers and homeless people. Growing up in Liverpool at that time was a remarkable experience. Football was regarded, and still is, as sacrosanct so it followed that if you were no good at the beautiful game you were invariably ostracized and even labelled an outcast. This social exclusion had a profound effect on my values and mindset.

I then matriculated into Manchester Medical School in 1984 and obtained my MBChB in 1989. I did my house jobs in the Northwest. A position in Glasgow University as an Anatomy Demonstrator followed. It was during this time that I sat the MRCOG part 1 and the MRCS part 1. I relocated to the West Midlands and was entered into the basic surgical scheme in Birmingham City Hospital. This was followed by a gap year in Madras, India. Whilst in India, I developed a pronounced and previously absent cultural sensitivity which sparked my interest in global health. I then returned to the UK and worked in Kidderminster where I forged a firm friendship with Sir John Temple who was post-graduate dean in the West Midlands at the time. Sir John Temple was tasked by Sir Kenneth Calman to launch the Calman training scheme. Consequently I was selected to become the first surgical SpR in UK history.

In 1993-1997 I developed an interest in postgraduate medical education (training of surgeons). I was secretary of the association of surgeons in training in 1998-1999 and president in 1999-2000. I was awarded a one year fellowship in breast cancer research in 1997 with Professor Bundred as my supervisor. I obtained my MD in 1999, was a lecturer in surgery in 1999-2000 and senior lecturer in 2000. I was hospital dean of undergraduate clinical studies in South Manchester University Hospital Trust from 2004 to 2008. I launched the Academy, a novel vehicle for delivering medical education, in 2010 and have been its director ever since. I was awarded a National Teaching Fellowship (NTF) in 2009 which is the highest award for tertiary education in the United Kingdom. I am the only practicing surgeon to have received this award.

AH: What is a good doctor?

GB: A good doctor is a human being who has sufficient insight in the core business of improving patient health which comes hand in hand with developing creativity, leadership and team work. The problem with modern day medicine is re-defining what we mean by doctor. In the advent of progressive management care pathways there is a decrease in the intelligent intervention by erudite physicians. This may be an opportune moment to quote Lord Cohen who pronounced that the three important things in medicine are 'diagnosis, diagnosis, diagnosis'. A good doctor is someone who people empower on their behalf to align their understanding of medical knowledge to mitigate patient exposure to risk of harm. It is crucial to realize that a good doctor must have the manner and acumen to inspire a person to empower him with that responsibility and privilege. For example, a nurse may follow and implement an algorithm but it is the doctor's role to weigh up and reduce the risks as far as is possible by utilizing scholarship. Above all else, a doctor has to have sufficient self awareness, 'embellished' with humanity, listening, understanding and empathy. In my experience humor at the right time is the most effective therapeutic tool and indeed laughter therapy has been used by patient groups.

AH: You once quoted Don Corleone in a lecture event. Do you have a quote that you can share with us?

GB: I have an educational quote which is as follows: "don't submit your student to your learning because they were born at a different time to you. It is our imperative to recognize that society is rapidly changing. Designing, developing and delivering new methods in medical education is part and parcel of the work we are doing in the Academy".

AH: Who is your role model?

GB: Ian Maclennan who is a consultant surgeon in MRI and who was dean of clinical studies. Sir John Temple and Sir Neil Douglas (president of the academy of Royal Colleges) are also personages I derive immense inspiration from. I consider having a role model important and my advice to medical students would be to have one.

AH: What are your views on the reform in Medical Education in Manchester Medical School?

GB: I am not as interested in curriculum reform as I am in changes in the learning environment. I am particularly interested in the seminal works of my colleague fellow medical educationalist Professor Dornan and we have been developing experience based learning and the healthcare system that surrounds patients and how to make this conducive for learning. This is what the Academy is all about in fact. Moreover, I am also interested in the teacher who is the purveyor of medical education. I am a firm believer that life experiences are what shape and motivate people and these are the elements that make for an exceptional medical educationalist in my contention.

AH: Thank you for sharing with us your thoughts and life experiences.

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Review Article
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World University Anatomy Challenge 2012
A Doctors Academy Event

An article from the silver medallist of the World University Anatomy Challenge 2012, a competition consisting of 219 participants from 116 Universities representing 36 countries

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The understanding of form and function of the human body is the basis of the entire edifice of medicine. Thorough understanding of the intricate details allows one to fathom pathology and consequently administer the correct antidote. A sound knowledge of anatomy is crucial in understanding the relationship between form and function. My concern is that the importance of anatomical knowledge in the making of a doctor is becoming increasingly under-appreciated with possible regressive changes being made in the undergraduate medical curricula.

The invigorating World University Anatomy Challenge serves the very good purpose of reviving the students' thought of anatomy as an important component in our medical education. It inspires medical students such as me to delve into the depths of anatomical minutiae. The challenge is particularly unique in that it draws together a large number of medical students from all over the globe who enjoy participating actively in an international event. As a participant of the first 'World University Anatomy Challenge' in August 2012 that was held at the *Future Excellence* International Medical Summer School in Manchester, UK, it has been a pleasure to behold the presence and interaction of so many student peers who despite the demographic differences share the same basic knowledge, a similar enthusiasm, and an identical urge to learn and challenge themselves further. The challenge also plays the role of a formative assessment to help participants assess their current grasp of anatomy knowledge, and a very good asset for the curriculum vitae. The World University Anatomy Challenge is a golden opportunity for all those seeking recognition for their good anatomy knowledge.

I believe that my medical education hitherto at the University of Malta has been comprehensive and has included sufficient opportunities and experiences that allowed me to gather an adequate knowledge of anatomy. My own experience in the challenge gave me a strong sense of pride as I represented my University and my home country, Malta to the extent that I was affectionately referred to as, 'The Man from Malta'.

Please follow this link for further information and to participate in the World University Anatomy Challenge 2013:
http://www.doctorsacademy.org/AcademyCMS/default.asp?contentID=980

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Fundamentals of Acute Wound Healing

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Abstract

Acute wound healing is a complex process activated by damage to body tissue. The process occurs in a series of well-coordinated bur overlapping stages occurring in a temporal manner. Firstly, haemostasis occurs immediately after wounding to prevent excessive blood loss. Shortly after, inflammatory processes including the complement system are activated to protect the wound from foreign particles and bacteria, and also to accelerate the wound healing process. During proliferation, fibroblasts contribute to the formation of the new extracellular matrix and new epithelial tissue. Finally, long-term collagen remodeling occurs in an attempt to normalize skin integrity. The article reviews the normal wound healing process and the underlying key molecular and cellular mechanisms.

Introduction

In order to understand pathological conditions that are due to abnormal wound healing processes (i.e., fibrosis and chronic ulceration), one must first comprehend the physiological process of wound healing. Any injury resulting in tissue damage in the human body activates an acute healing response. The acute wound healing process comprises a series of coordinated cellular processes carried out in a controlled manner.[1]

Acute wound healing occurs in four well-characterised and overlapping stages (Figure 1):

1. Haemostasis
2. Inflammation
3. Proliferation
4. Remodeling & Scar Maturation

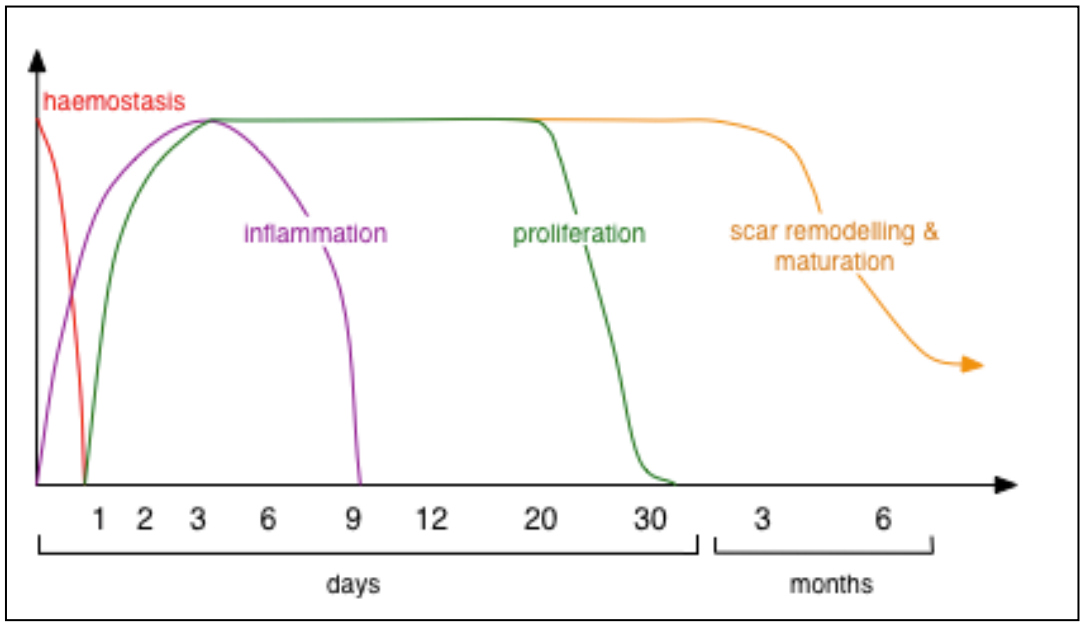

Figure 1: The Stages of Wound Healing. Haemostasis starts immediately after a wound has been created. Inflammation occurs from about 15 mins to 9 days, and proliferation is active from day 3 onwards and can last for up to a month. Scar remodeling and maturation continues for months after the wound has been created.[2]

Haemostasis (Immediate)

Clinical signs: blanching, formation of clot.

Damage to the microvasculature of a tissue results in extravasation of blood into the site of injury. Meanwhile, the following processes are triggered to achieve haemostasis:[2]

- local vasculature constricts to reduce further blood loss
- a coagulation cascade is triggered that leads to the formation of thrombin.

Thrombin catalyses the conversion of fibrinogen to fibrin. Activated fibrin monomers are polymerized by covalent cross-linkage by Factor XIII. Fibrin polymers bind to platelets to form the haemostatic plug, which appears as a clot.[3]

Inflammation (15 min – day 6)

Clinical signs: erythema, pain, swelling and heat (the well characterized rubor, dolor, tumor and calor stigmata as identified by the ancient Greek physician Galen)

Inflammation occurs in two phases – the early phase and the late phase.

Early phase (days 1-2)

Vasodilation and increase in the permeability of capillaries promote the movement of inflammatory proteins and cells into the wound from the intravascular compartment. Mast cells produce histamine and leukotrienes which cause vasodilation. Clotting products such as kinins and thrombin also enhance capillary permeability.[1,4]

The complement system is also activated in the early inflammatory phase. Complement factors C3a and C5a are chemoattractants which attract inflammatory cells (e.g. macrophages) into the wound. Growth factors (e.g. PDGF), cytokines (e.g. IL-8) and chemokines (e.g. GRO-α/CXCL1) attract polymorphonuclear cells (PMNs), which move to the site of injury by adhering to the vascular endothelium (margination) and traversing the vessel wall (diapedesis). PMNs are able to phagocytose foreign particles and bacteria, and are also capable of secreting other cytokines, including tumour necrosis factor alpha (TNF-α).[5,6]

Late phase (days 2-3)

Monocytes transform into macrophages upon arrival at the site by a number of chemoattractants including fibronectin, elastin, complement factors andgrowth factors (PDGF, VEGF, TGF-β). Macrophages are in turn capable of phagocytosis and the production, storage and release of pro-inflammatory factors. Macrophages produce cytokines such as certain interleukins and TNF-α that drive the inflammatory process. They also stimulate angiogenesis and collagen production by fibroblasts.[5]
T lymphocytes regulate the wound healing process, albeit not in a straightforward fashion. Depletion of CD4 and CD8 cells alter wound strength, whilst dendritic γδ epidermal T cells (DETCs) release factors which stimulate the growth of keratinocytes and fibroblasts.[7]

Proliferation (day 3 to week 2)

Clinical signs: pink, soft and granular appearance (granular tissue)

During the proliferation phase, fibroblasts migrate to the wound, the temporary haemostatic plug is replaced by new extracellular matrix and granulation tissue is deposited.

Fibroblast migration

A number of factors (TGF-β, PDGF, fibronectin, etc.) attract fibroblasts to the site of injury. Fibroblasts are present nearby and can also be derived from mesenchymal cells. Fibroblasts produce proteins and attract other factors which are required for the formation of the extracellular matrix, such as fibrin, fibronectin, and hyaluronic acid. Fibronectin provides a scaffold to which other fibroblasts can bind. Later, fibroblasts also release proteoglycans and collagen which are crucial for ECM formation.

Formation of the extracellular matrix

The extracellular matrix (ECM) comprises fibrous structural proteins (collagens, elastin) and adhesive glycoproteins.[8]
Function of ECM:

Collagens

Over 20 types of collagens exist, but Type I collagen is the predominant collagen (70%) in wound healing, followed by Type III collagen (30%), and they are produced by fibroblasts.[2]
Collagens give strength to the wound and also allow the activity of other cells vital to wound healing.
The hydroxylation of proline and lysine residues at the endoplasmic reticulum during the intracellular production of collagen is an important step, as it allows collagen polypeptides which are alpha-chains to assume a triple helical structure capable of fibril aggregation. These collagen bundles form the bulk of connective tissue in a healing wound.[5,9]

Other collagens, such as type IV collagen, do not form fibril bundles and instead form part of the basement membrane.

The Role of other proteins in the wound healing process:

Fibronectin and integrins are adhesive glycoproteins that bind to various components of the ECM which are capable of mediating cell signal pathways, cell migration and cell growth in the wound.[8]

Proteoglycans are polypeptides to which various glycosaminoglycans (GAGs) such as hyaluronic acid and heparan sulphate attach. They regulate molecular and cellular activities within the ECM. Hyaluronic acid has the ability to modify adhesions between collagen and cells, thereby permitting the migration of other cells in the ECM. Chondroitin and dermatan sulphates facilitate the process of collagen fibril aggregation.[1]

Granulation (3-5 days) and Angiogenesis

Granulation tissue appears pink, soft and granular (beneath a scab)

The histological appearance of granulation tissue is that of fibroblasts, collagen and formation of new blood vessels.[1,2]

Angiogenesis

•endothelial cells migrate towards the site of injury to replace damaged vasculature, driven by pro-angiogenic factors.

•Pro-angiogenic factors: low pH, increase in lactate, hypoxia, growth factors and cytokines such as VEGF, PDGF, FGF, angiopoietin and TGF-beta.

Endothelial cells express integrins and MMPs to help them move around the ECM.

Re-epithelialization

Keratinocytes from the wound margin migrate to form a new layer of epidermis covering the wound. Migrating and proliferating keratinocytes first forms a new basement membrane and then differentiates giving rise to the stratified epithelium.

Keratinocyte migration and proliferation is stimulated by a number of growth factors and cytokines such as epidermal growth factor (EGF) and nerve growth factor (NGF). The environment in the wound also plays a role in facilitating keratinocyte movement and growth. Re-epithelialization can be completed within two days in shallow wounds.[8,10]

Remodelling & Maturation

Clinical appearance: wound contraction, normalization of skin thickness, and reduced redness.

Remodeling and maturation of the wound starts during the proliferative phase but continues for a long time after injury (up to many months). Key components of wound healing mentioned before such as fibroblasts, collagen and blood vessels also contribute to this phase of wound healing.

Another family of enzymes, matrix metalloproteinases (MMPs), is responsible for breaking down collagen during remodeling of the ECM. Collagen degradation by MMPs is regulated by factors such as TGF-β and PDGF. A balance of collagen synthesis and degradation is achieved after 3 weeks, where type I collagen in the ECM increases in proportion to the other collagen types and proteogylcans.[1]

Eventually, new vasculature stops growing, inflammatory cells reduce in numbers, and the wound contracts about 5 days after the initiation of the wound healing process for a couple of weeks. The granulation tissue becomes a scar made up of fibrous tissue, collagen, elastic tissue, and components of the ECM.[2]

Excessive wound healing

Excess scar tissue is laid down due to overproduction of many components of the wound healing process, two types of which are discussed here.

Hypertrophic scars

Clinical appearance: wounds are itchy, red and raised, and at a later stage pale and flat.

In hypertrophic scars, excess collagen leads to the formation of a scar which is raised. The risk factors for the formation of hypertrophic scars are:[2]

Scars lying across lines of skin tension
Areas of excessive skin movement
Deep skin burns
Wounds left to granulate

Keloid scars

Clinical appearance: scar that has grown beyond original wound, raised, red initially but pale as time goes on. May persist and grow for many months.

Keloid scars are more aggressive than hypertrophic scars in that the scar extends beyond the original wound into normal tissue. Collagen synthesis as compared to hypertrophic scars is increased 3-fold, and 20-fold compared to normal skin. The composition of cross-linked, mature collagen is also lower in keloids.[2,11]

They are more common in people of Afro-American ethnicity, and familial predisposition seems to play a significant role.

Scarless wound healing

Scarless wound healing occurs in the human foetus, and also in areas of the body such as the oral mucosa. Essentially, scarless wound healing progresses through similar stages of cutaneous wound healing, except for the absence of scarring. There have been several hypotheses of how the processes differ; the lack of scar formation in the oral mucosa can be due to altered or dampened inflammation, differential modulation by fibroblasts, or the presence of stem cells that allow replacement of new cells.[12]

The understanding of scarless wound healing would have clinical implications such as in tissue engineered skin substitutes that is currently being explored.

Conclusion

The wound healing process is a complex and sophisticated phenomenon. A sound understanding of this dynamic process is essential in order to understand pathological conditions attributable to abnormal wound healing. Future novel therapeutics aim to harness the natural scarless wound healing process that is observed in certain scenarios. Further research in this fascinating area is currently ongoing with pioneers in the field making promising advances.

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Abstracts from The International Academic and Research Conference

20th August 2011, University Place, University of Manchester

ORAL PRESENTATIONS

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

The Effects of Ischaemic Reperfusion on Platelet Monocyte Binding in Man

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

KATP Channels- Blood Marker for Endothelial Function?

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Epigenetic Regulation of Epithelial-Mesenchymal Transition in Idiopathic Pulmonary Fibrosis

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

The role for Gli3 in cortical neuronal differentiation

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

Development of a Bilayered Dermal Scaffold Using New Generation Nanocomposite Materials

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

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

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

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

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

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

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

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

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

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

Validation of a biomarker for therapy with histone deacetylase inhibitors

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

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

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

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

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

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

Atypical pneumonia – a confusing case?

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

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

Facial emotional recognition in Parkinson's disease with apathy

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

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

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

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

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

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

Pituitary Tumour Apoplexy in a patient with sinusitis

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

Endoscopic Transnasal Transphenoidal Resection Of Pituitary Adenomas: Initial Results

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

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

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

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

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

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

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

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

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

Childhood Obesity In The West Bank

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Intracytoplasmic Sperm Injection - A Case of Dandy Walker Syndrome

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Investigation of Veins Hypothesis in Multiple Sclerosis

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Evaluation of repeated enzyme immunoassay testing in Clostridium difficile infection

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

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

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

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

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

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

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

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

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

An Unusual Case of Intracaval Leiomyomatosis

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

The Assessment of Psychotic-Like Experiences in Childhood and Adolescence

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

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

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

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

Immature Teratoma of the Omentum

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

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

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

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

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

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

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

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

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

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

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

Reference: NICE clinical guideline 43, issue December 2006

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Audit of adherence to MRSA screening protocol

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

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

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

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

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

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

Laparoscopic cholecystectomy without intra-operative cholangiography

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

Quality of Life After Total or Subtotal Gastrectomy for Gastric Carcinoma

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Summary of Results:

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

Mean Hb pre-op 14.0 & post op 9.9.

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

Overall, average transfusion rate was 2.22 units per patient.

11 patients had 2 units or less transfused

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Clinical Audit of Paediatric Diabetic Retinal Screening

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

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

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

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

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

Are we facing a new epidemic of coronary heart disease?

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

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

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

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

Sexual Health Safeguarding in Teenagers presenting to the Emergency Department

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

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

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

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

The Mights of Mitomycin (An Audit)

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

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

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

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

Results

Table 1: When patients received their MMC

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

Table 2: Break down of time lapse

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

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

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Scoliosis surgery at RMCH and SRFT

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Line sepsis – don't blame your tools!

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

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

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

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

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

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

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

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

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

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

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

POSTER PRESENTATIONS

The Junior Doctor Safety Board

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Background: At Northampton General Hospital a Junior Doctor Safety Board was established with the aim of engaging junior doctors in improving care and safety of patients within the Trust. Based around the theme of improving care and safety of the 'sick' patient, each member carried out an audit. These included audits based on patient handover, anti-microbial therapy, treatment of sepsis and improving interprofessional communication and communication with primary care.

Results: The results of the audits included:
Medication Audit: 863 drug charts were reviewed. Twenty-one percent of these had a reconciliation discrepancy. In 18% of charts, prescriptions were inadequately documented or contained an error.
Allergy Audit: 126 drug charts were audited. Fifty-seven percent of charts with a recorded drug allergy failed to record correctly the specific reaction. Four percent of charts contained no allergy information together.
Discharge Summary Audit: 52% of discharge prescriptions contained an error. These errors ranged from basic prescription errors to failures in highlighting or explaining changes in patient medication.

Conclusion: This project is a junior doctor-led initiative, and highlights how junior doctors can be 'agents of change'. The board has implemented many changes, which include tools to improve interprofessional communication and redesigning the drug chart, electronic discharge notification and electronic handover.

Learning Points

- A self-managed junior doctor team promotes junior doctor engagement and leads to improved patient safety.
- Multiple projects with a common theme can accomplish more than a single large project.
- Well managed audits have a greater chance of achieving completion.

Double Trouble : Bilateral Maxillary Mucocoeles and Cystic Fibrosis

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Cystic fibrosis is one of the UK's commonest inherited life-threatening diseases, it is an autosomal recessive genetic disorder resulting in exocrine gland dysfunction with various clinical manifestations. Whilst targeted newborn screening is effective in identifying those with the condition children are often also diagnosed following the development of respiratory or digestive tract symptoms. Sinonasal symptoms are almost universal resulting in chronic sinusitis or polyposis, these symptoms themselves are rarely the primary disorder resulting in diagnosis. Presented here is the case of a five month old child diagnosed with cystic fibrosis following presentation with bilateral maxillary mucocoeles.

A 5 month old child presented with symptoms of nasal congestion. Initial examination and investigation with CT scan identified the cause to be bilateral maxillary mucocoeles. Following a clinical suspicion the child was investigated for cystic fibrosis and found to be positive. Initially surgical treatment was undertaken for the maxillary mucocoeles by endoscopic bilateral uncapping of the maxillary mucocoele, uncinectomy and middle meatal antrostomy. The child was then followed up with appropriate treatment for cystic fibrosis. At follow up there was no recurrence of symptoms.

Although maxillary mucocoeles are extremely rare they do present in patients with chronic sinusitis or a known diagnosis of cystic fibrosis. To our knowledge there are no reports of this condition being the primary indicator of underlying disease. Following this it is our recommendation that all young children presenting with sinus mucocoeles be investigated for cystic fibrosis to avoid delayed diagnosis and initiation of treatment.

The Impact of Information about Cervical Spine Surgery on Patient Anxiety Levels and the Development of a Multimedia Information Resource to Reduce Anxiety and Enhance the Patient Experience

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Amongst a population of patients due to undergo cervical spine surgery, the levels of information that patients felt they had about their upcoming surgical procedure was evaluated. The correlation between patient knowledge and anxiety levels was explored. Furthermore, patients were asked to evaluate the usefulness of different methods that can be used to deliver information.

The Beck Anxiety Inventory was used to measure anxiety levels. A further questionnaire was used to investigate how informed patients felt and how useful they would find various methods of information delivery.

All patients expressed anxiety related to the upcoming operation. There was a variation in the levels of knowledge that patients felt they had, with 50% stating they had researched this themselves. There was a unanimous resolution that a multimedia resource would be useful to patients in aiding their understanding of the surgical procedure and their stay in hospital. This would also increase the efficiency of the pre-operative clinic by decreasing the repetition of questions asked.

In response to the feedback from patients, a multimedia resource was developed, containing an animation of an Anterior Cervical Discectomy and Fusion (ACDF) procedure. It also contains an introduction to the trust and staff in the department, the role of pre-operative clinic, what to expect post-operatively, a hospital map, anaesthetic information and points of contact. The use of this resource will be audited to evaluate its effectiveness.

Morganella Morganii Infection Following Primary Total Hip Arthroplasty: A Case Report

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Morganella morganii is a gram negative rod from the *Proteeae* tribe of *Enterobacteria*[1]. There are only four case reports of *Morganella morganii* septic arthritis[2-5], but none in association with primary total hip arthroplasty. In a recent analysis of 55 total hip arthroplasties requiring re-operation for infection *Morganella morganii* was not reported.[6]

Our case describes *Morganella morganii* infection in a patient with type 2 diabetes, hypertension and end-stage renal failure requiring dialysis, who underwent primary total hip arthroplasty for severe osteoarthritis. Post-operatively the patient made slow progression. Forty-six days following arthroplasty there was purulent discharge from the wound but absence of pain or systemic signs of infection. This suspected deep wound infection was managed with excision arthroplasty and extended debridement. Cultured soft tissue and pus confirmed *Morganella morganii*. The patient received targeted antibiotics, but their mobility failed to improve and there was no clinical or laboratory evidence of response to treatment. The patient requested withdrawal from haemodialysis and passed away seventy-three days following the index procedure.

In summary we highlight the risk of *Morganella morganii* infection following arthroplasty, which has not previously been reported. Current literature suggests *Morganella morganii* infection is often resistant to beta-lactam antibiotics[3,7] and has an indolent clinical picture which may delay diagnosis[2-5]. In our case both of these factors contributed to a poor outcome. To improve clinical practice we therefore suggest early diagnosis of *Morganella morganii* infection followed by aggressive management including targeted antibiotic therapy.

Standardisation of Clinical Equipment

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We are all familiar with the scenario: turning up to an unfamiliar ward on-call to perform a simple procedure such as venepuncture and being delayed, usually for several minutes, finding all the various pieces of equipment. Our aim was to develop a standardized system across the Trust to minimize the time taken to find clinical equipment on the wards.

To quantify the problem, the time taken to collect certain equipment was recorded on several wards. Eighty data sets were collected and showed the average time taken to find equipment for cannulation, venepuncture, ABG and blood culture was between two and three minutes.

Our proposed solution was to standardise basic clinical equipment in a trolley. The equipment was dictated by a survey of equipment preferences distributed to doctors at North Bristol Trust.

The project was divided into two PDSA cycles (plan-do-study-act). A prototype trolley was developed and data collected over several weeks. This data was analysed and the organisation/equipment revised. A second cycle was performed and further improvements made.

By standardising basic clinical equipment considerable time can be saved. The average time taken to collect equipment necessary for venepuncture was reduced to 32 seconds, for cannulation 53 seconds, arterial blood gas 16 seconds and blood cultures 27 seconds. The main challenge to the success of the project is ensuring that equipment is adequately and correctly stocked. Measures to achieve this include clear and obvious instructions. The team is currently reviewing the success of adding stock levels to the weekend handover list.

Complications of Transcutaneous Metal Devices: Time for Plastic Surgeons to act

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Background: The use of transcutaneous metal devices is common practice on a short or long term basis to stabilise fractures, or to correct deformity. A high incidence of associated infection has been widely reported and there are numerous protocols for prevention and management in Orthopaedic literature.

The aims of this study were: 1) To record the incidence of pin site infection in a Plastic Surgery department. 2) To compare the infection rate in our department with published literature 3) To identify factors that contribute to infection.

Methods: A prospective cohort study was performed auditing all patients presenting to the plastic surgery unit, with any type of transcutaneous metal in situ over a 3 month period. Patients and staff were questioned on wound hygiene, and whether they had been provided with specific protocols. An extensive literature review was undertaken
Findings: Our study revealed an infection rate of 24%. Patients and staff were not aware of preventive protocols. Current literature reports a pin-site infection rate of between 4.5 % and 71%.

Conclusions: 1) Pin site infection is a major problem and no consensus has been reached on the best way to manage pin sites 2) There is variable knowledge of pin-site care amongst the nursing staff 3) There is need for a clearer definition of pin-site infection and a standardised system of assessment, classification and treatment. 4) There is need for more innovative technology in pin-site manufacture as study reveal that the type of material used in the pins does affect infection rates.

Time-lapse Imaging Analysis of Anticancer Pharmacodynamics

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The Structure-Activity Relationship (SAR) is a means by which effect of a drug or toxic agent on cells in culture can be related to its molecular structure. This type of relationship may be assessed by considering a series of molecules and making gradual changes to them, noting the effect upon their biological activity of each change.

We have paired compounds of novel anthraquinones: KP71 and its analogue KP75; KP166 and its inactive form KP167; alchemix and its analogue ZP275. We added these compounds to osteosarcoma cell line U-2OS and carried out some timelapse and flow cytometry experiments.

Cells were placed in a 6 well plate (density~15-20%). Paired drug treatment at varying doses was added and the plate was placed in a sealed environment. Images were taken every 15 minutes over 3 days and were then analyzed.

The same cell lines were treated with the compounds, incubated and analyzed using flow cytometry.

Over 72 hours, the addition of 10nM of KP71 and KP75 showed moderate linear increase in cell number (increase by 180 – 300%) whilst the 100nM of the same substance showed no increase in cell number. The addition of KP167 in both high and low dose concentrations showed minimal difference in cell number compared to the control. Flow cytometry showed the pattern of treated cells at varying stages of growth/division in the cell cycle.

We found that KP71 and KP75 have a dose-dependent effect, KP167 is indeed an inactive drug and Alchemix and ZP275 worked by different mechanisms of action.

The role of Wnt4 signalling pathways in vascular smooth muscle cell (VSMC) proliferation

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VSMC proliferation is a major factor in arthrosclerosis and restenosis. It has recently been shown that proliferation stimulation by platelet-derived growth factor (PDGF) induces Wnt4, which promotes VSMC proliferation via b-catenin signalling.

Within this project, Wnt4s role in VSMC proliferation was investigated.

A dose response experiment revealed that a dose of 500ng/ml recombinant Wnt4 protein induced the highest VSMC proliferation rate (46.33±2.98%).

Wnt4 mRNA was successfully silenced by 63±10.42%, resulting in a decrease of basal proliferation rates and also PDGF stimulated proliferation. It also decreased Wnt4 protein within the cell.

Wnt signaling is mediated by three pathways. The role of these pathways in Wnt4-induced VSMC proliferation was determined.

The Wnt/Ca^{++} pathway was successfully inhibited using CamKII, NFAT and PKC inhibitors. These significantly decreased proliferation in response to 500ng/ml Wnt4, but only the PKC inhibitor significantly reduced proliferation when these inhibitors were used without recombinant Wnt4 protein. The planar cell polarity pathway was inhibited using a JNK inhibitor. This decreased proliferation rates significantly with and without Wnt4.

Canonical pathway signaling was reduced by silencing LRP5 mRNA by 97.3±0.20% and LRP6 mRNA by 91.9±3.79%. This resulted in a decrease of LRP5 protein by 47% and LRP6 by 30%. This translated into a significant decrease in proliferation rates of VSMC in serum free medium, and after addition of PDGF and Wnt4.

This project clearly demonstrates that Wnt4 promotes VSMC proliferation via the involvement of three signaling pathways: the canonical, the Wnt/Ca^{++} and the planar cell polarity pathways. This research has implications for a future novel treatment of atherosclerosis and restenosis

TRAPS: Exploring the effects of mutant TNFR-1 expression on cytokine/chemokine induction by THP-1 cells

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Tumour necrosis factor receptor-associated periodic syndrome (TRAPS) is the second most common autoinflammatory disease and is associated with a range of complications. Monocytes are related to the myalgia and dermal rashes and produce IL-6. The aims of this project is to transfect the THP-1 human monocytic leukaemia cell line, with both the wild type (WT) and mutant C33Y tumour necrosis factor receptor-1 (TNFR1) and compare the range of cytokines/chemokines produced.

Transient plasmid DNA lipofectamine transfections were carried out for both WT and C33Y TNFR1. Human flow cytomix multi-plex kits were used to detect IL-1α, IL-1β, TNF-α, granulocyte-colony stimulating factor (G-CSF), IL-6, IL-8, CCL5 and CCL2. The cytokine/chemokine data was acquired using the FC500 flow cytometer and quantified using the Bender MedSystems FlowCytomix™ Pro software. Following WT and C33Y TNFR1 expression, an increase was seen in IL-6, IL-8 and CCL5 production. With IL-6 levels being statistically significant followed by a border line statistical significance and biological significance for IL-8 and CCL5 respectively. Elevated IL-6 levels demonstrate the importance of monocytes in TRAPS. Furthermore novel chemokine antagonists could be considered the next milestone for treating TRAPS patients. However, a lot more replicates using transfected THP-1 cells are required to refine these results.

Transmission of Alzheimer's Disease via a Prion-Like Mechanism

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Alzheimer's disease, the most common neurodegenerative disease in the elderly, results from aggregation of the Aβ peptide into toxic forms that block long-term potentiation and cause neuronal dysfunction. Injection of brain extracts from Alzheimer's patients into brains of mice expressing the amyloid precursor protein accelerates formation of Aβ aggregates, indicating that Aβ may be transmitted via a prion-like mechanism. We carried out a set of experiments in *Drosophila* models, using motor control and survival assays to represent Alzheimer's disease progression. Our results showed that feeding *Drosophila* expressing Aβ42 with brain extracts from flies of the same strain resulted in a significant decrease in motor control and survival. Experimental trends showed that feeding extracts from younger flies had greater detrimental effects. This supports literature research suggesting that Aβ oligomers formed in early stages of aggregation, rather than mature Aβ fibrils found in older brains, are more effective at seeding the formation of toxic aggregates. Most conclusively, confocal microscopy work on dissected fly brains showed that feeding flies with Aβ42 brain extracts increased the number of toxic aggregates compared to flies fed control extracts, supporting the prion propagation hypothesis. Confirmation of this hypothesis has important implications for medical treatment; for instance in shifting the focus from current therapies which aim to prevent cellular death, or promote neuronal survival, to treatments targeted at immuno-neutralisation of Aβ oligomers. As more is understood about cell-cell transmission of pathology through brains, it is hoped that new pharmacological targets can be identified to combat Alzheimer's disease progression.

Genetic Polymorphisms associated with side effects of antibiotics in children

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Background: Aminoglycoside (AG) antibiotics are widely used in cystic fibrosis (CF) patients to combat *Pseudomonas aeruginosa* infections. However, they can result in significant nephrotoxic and ototoxic effects. Approximately 17% of CF patients suffer from hearing impairment. Several maternally inherited mitochondrial mutations may predispose patients to AG- induced hearing loss. The 1555A>G mutation is the most well-known mutation, with a prevalence of approximately 0.2% in the European population. Previous studies have not sequenced the entire MT-RNR1 gene in CF patients.

Methods: Sequencing of saliva samples in a cohort of 15 CF patients with the MT-RNR1 gene was done. The resultant sequence data were compared against the revised Cambridge Reference Sequence (rCRS) to check for mutations. Results were correlated with AG exposure and hearing impairment.

Results: Two polymorphisms in three patients were found in this study. 709G>A, with a prevalence of 7.14% (0.18, 33.9) was found in one patient with normal hearing. 1189T>C, with a prevalence of 14.3% (1.78, 42.8) was found in two patients with mild to moderate hearing impairment. These three patients were all previously exposed to AGs treatment. The literatures suggested that these were not significantly associated with hearing impairment. However, in the present study, 1189T>C was found in two hearing impaired patients.

Conclusions: This study suggests that the methods used here to screen for mutations are feasible and can be used for a large scale research in the future. Further studies are needed to clarify the role of 1189T>C given that both the patients in this study have hearing impairment.

Effects of Natural Honey on Blood Glucose and Lipid Profile in Young Healthy Pakistani Males

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Background: The objective of this study was to investigate the effects of natural honey on blood glucose and lipid profile in healthy Pakistani individuals with same age, sex, place of living, daily routine and same diet (except honey).

Methods: This study was randomized controlled trials (RCT) conducted in the Army Medical College, Rawalpindi, Pakistan. Duration of study was 4 weeks (from 15th Feb 2009 to 15th March 2009). 70 health subjects were included in the study and randomly divided into two groups of 35 each using random number table. 70g of honey was given to each individual in the experimental group every day for a period of 4 weeks while control group was kept on the same diet as that of experimental group except honey. The fasting glucose, total cholesterol, Low density lipoprotein (LDL), High density lipoprotein (HDL) and triglycerol (TG) levels were measured before and after the experiment.

Results: The glucose levels in both groups were raised. However, the increase in the fasting glucose levels of the experimental group was significantly less than those in the control group ($p< 0.05$). On the other hand, levels of total cholesterol, LDL and triglycerides in the control group increased while those in the experiment group decreased significantly ($p< 0.05$). HDL level was increased in experimental group where as it decreased slightly in control group ($p< 0.05$).

Conclusion: Natural honey significantly limits the rise in blood glucose along with a significant decrease in the levels of total cholesterol, LDL and triglycerides, and increase HDL in young healthy adults. It is suggestive of the fact that honey is one of the best foods for improving blood glucose and lipid profile in young healthy individuals and can be beneficial in the prevention of diseases like diabetes, cardiovascular diseases, hyperlipidemias and obesity.

The type 1 interferon response induced by different lineages of Mycobacterium tuberculosis

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Type 1 interferons are renowned for their anti-viral properties, but they are also induced by a variety of bacterial pathogens, including *Mycobacterium tuberculosis*. The role of type 1 interferons in the immune response to *M. tuberculosis* is still debated and the method of such induction still unclear, with the ESX-1 secretory system and the cytosolic NOD 2-Rip2 receptor pathway hypothesised as important for initiating such a response. Additionally, a previous study based on the hypervirulent strain, HN878 (a member of the East Asian lineage), has suggested that the virulence of a strain of *M. tuberculosis* may be associated with the level of type 1 interferon induced. In this study, we infected murine bone marrow derived macrophages with heat-killed *M. tuberculosis* strains of three different lineages: the Indo-Oceanic, East Asian/Beijing and Euro-American lineages. We found that macrophages have the ability to recognise heat-killed *M. tuberculosis* due to the levels of TNF-a and IL-12p40 produced in response. Furthermore, we identified that out of the three lineages tested, only the heat-killed strains of the Euro-American lineage induced the expression of type 1 interferon genes, with peak induction of IFN-b mRNA at 6 hours. Two possible mechanisms could explain these findings. Firstly, the Euro-American strains may have more heat-stable components of their ESX-1 secretory system than the other lineages. Secondly, due to expected denaturing of the proteins of the ESX-1 system, the Euro-American strains may have a novel, as yet unrecognised, ESX-1 independent pathway of type 1 interferon induction.

Neutrophil responses to Diesel Exhaust Particles are dependant on host-mediated factors

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Diesel exhaust particles (DEP) are a major component of air pollution and have been shown to provoke inflammation. Peripheral blood neutrophils (PBN) have a major role in the innate immune system and have been shown to be involved in this inflammatory response. We investigated how DEP induce neutrophilic inflammation.

Preliminary experiments demonstrated that DEP (50mg/ml) caused an increase in Interleukin 8 (IL-8) production in BEAS-2B/ monocyte cocultures. Light microscopy analysis of cytospins showed that supernatant from these cocultures increased PBN survival at 20 hrs, suggesting that DEP may be pro-inflammatory to PBN. We hypothesised that DEP would directly effect PBN in key activation assays. Light microscopy analysis of cytospins revealed that DEP 50 mg/ml did not significantly alter PBN survival alone or in the presence of 5% peripheral blood mononuclear cells, 2%, 1% or 0.5% purified monocytes. Preliminary experiments indicated that DEP 50 mg/ml primed PBN to release increased IL-8 in response to LPS 1 and 0.1 ng/ml. PBN treated with DEP 50 or 200 mg/ml did not significantly increase reactive oxygen species (ROS) generation measured by flow cytometry using dichloroflourescein. However, phagocytosis of fluorescent latex beads was increased by co-incubation with DEP 50 mg/ml, measured by flow cytometry. Timelapse microscopy and cytospin analysis indicated that while monocytes efficiently phagocytosed DEP, neutrophils did not.

We conclude that DEP 50 mg/ml modulates neutrophil function both directly (priming phagocytosis) and indirectly (modulating survival through actions of other cells), but that neutrophils do not respond to DEP in the same manner as monocytes.

The effect of isolated adipocytes on the human placenta and subsequent changes in the obese state

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Background: Numerous epidemiological studies implicate obesity as an independent risk factor in the development of adverse outcomes in pregnancy.

Aim: To explore the effect of whole adipocyte secretome on placental explants.

Methods: Mature adipocytes were isolated from subcutaneous and omental adipose tissue taken from normal BMI (20 to 25; n=4) and obese (over 30; n=4) patients at the time of Caesarean Delivery using a modified Rodbell method. Stromal cells from corresponding adipose tissue were isolated as controls. Conditioned media was collected after 24h of cell culture in serum-free media. Placental explants were cultured in conditioned media for 24, 48 and 72 hours before collection of the supernatant and explants for analysis.

Results: Normal and obese adipocyte-conditioned media significantly up-regulated mRNA encoding the inflammatory cytokines IL -6 and TNF-α in placental explants as compared with stromal-conditioned controls ($p<0.05$). Adipocyte-conditioned media also significantly reduced levels of hCG secretion by placental explants compared with controls by at least 2 fold at every time point ($p<0.0001$), despite no differences in cell viability. This effect was most significant in placental explants treated with adipocyte-conditioned media from obese omental adipose tissue compared with media from normal BMI omental adipose tissue (74.5% reduction over 72h; $p<0.05$).

Conclusion: Adipocyte secretome could impair placental function and induce inflammatory changes through the regulation of gene expression. Both a quantitative and qualitative change in secretome from omental adipose tissue in the obese state may be implicated in altered placental function leading to adverse pregnancy outcomes.

Obtaining stem cells from adipose tissue. Experimental studies

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Background: The frequency of back pain symptoms is comparable with the prevalence of upper respiratory tract infections. It is postulated that degenrative changes might be prevented by using stem cells to regenerate the intervertebral discs.

Objective: The aim of this study was to obtain mesenchymal stem cells from subcutaneous fat tissue from rat.

Methods: Adipose tissue was collected from subcutaneous area of Wistar rats. Isolated tissue was mechanically fragmented and digested by colagenase. During culturing, cells proliferation progress was monitored using microscope. Immunohistochemical staining was used to identify mesenchymal stem cells. Specific antibodies directed against rabbit beta-1 integrin - CD29 and CD45 were used followed by detection with secondary antibodies (anti-rabbit) labeled with fluorescein (microscopic examination) or horseradish peroxidase (western blot).

Results: We observed significant growth potential of adipose derived cells. Immunohistochemical labeling and western bloot confirmed the presence of CD29 antigen expression and the lack of CD45 antigen. In the early stage of culturing the most intense growth of cells and the highest expression level of CD 29 antigen was observed. In subsequent passages both, cell growth intensity and expression level of CD29 antigen decreased.

Conclusion: Our studies demonstrated the possibility of obtaining mesenchymal stem cells from adipose tissue which gives hope for a quick and easy way of these cells isolation. However, the effectiveness of the procedure requires further studies. It is necessary to determine the capability of adipose derived mesenchymal stem cells to differentiate toward chondrocytes and other cell lines.

Can mutations in the receptor moiety of a Growth Hormone Ligand-Receptor Fusion modulate bioactivity?

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Hypothesis: We are investigating development of long-acting growth hormone analogues for states of growth hormone (GH) deficiency. GH circulates bound to the cleaved, extracellular portion of its receptor which acts as a binding protein (GHRe). A ligand-receptor fusion of GH with GHRe acts as a potent, long-acting GH agonist (Wilkinson et al., Nat Med 2007). These ligand receptor molecules form head-tail dimers which effectively increase molecular weight and reduce clearance. However dimerisation may also reduce the bioactivity of these molecules by reducing bioavailability of GH. We hypothesise that a mutation in the GHRe portion (Tryptophan 104 > alanine) which has been shown to prevent GH binding would also prevent dimerisation. It is anticipated that this mutation will increase the bioavailability of GH in the GH-GHRe molecule by preventing dimerisation.

Method: The W104A mutation has been produced by PCR and cloned into a vector allowing expression of histidine-tagged GH-GHRe. Recombinant DNA was expressed in CHO cells. ELISA and Western Blot analysis was used to determine levels of production and examine dimer formation.

Results: Wild type and mutant (W104A) GH-GHRe fusion molecules were successfully cloned and transiently and stably expressed in CHO FlpIn cells. The constructs containing the W104A mutation were expressed at comparable levels to wild type molecule. Native PAGE demonstrates the lack of dimer formation in W104A mutants and GH Bioassays confirm superior bioactivity in W104A mutant.

Conclusions: The W104A mutation does not affect expression of GH-GHRe fusions, prevents dimer formation and increases bioactivity.

The effect of insulin on oxidant-induced inhibition of the PMCA and cell death

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Acute pancreatitis involves inflammation of pancreatic acinar cells characterised by aberrant intracellular calcium [Ca2+]ic signalling and premature activation of enzymes leading to its autodigestion. Previous studies have shown that hydrogen peroxide (H2O2) causes inhibition of the plasma membrane Ca2+-ATPase (PMCA) and a Ca2+-overload response characteristic of acute pancreatitis suggesting oxidative stress plays a key role in the pathophysiology of pancreatitis. The exocrine pancreas and endocrine pancreas are anatomically and functionally linked. In certain models of pancreatitis, the majority of the acini showed signs of acute pancreatic inflammation, while the periinsular acini remained intact suggesting that insulin secreted by the Langerhans islets protect the surrounding acini. The aim of the present study was to investigate the role of insulin in protecting against oxidant-induced PMCA inhibition and cell death. This was achieved using collagenase digested rat pancreatic acinar cells. PMCA activity was measured using an in situ [Ca2+]ic clearance assay. [Ca2+]ic clearance was measured using fura-2 imaging. Cell death was measured using a trypan blue exclusion assay. H2O2 caused a concentration-dependent inhibition of the PMCA activity. Moreover, pretreatment with 100nM insulin significantly attenuated this H2O2-induced PMCA inhibition. These data suggest that insulin protects against oxidant-induced inhibition of the PMCA. We also investigated the protective potential of insulin against oxidative stress-induced cell death. These esults were inconclusive. Further studies may help elucidate the mechanisms by which insulin attenuates H2O2-induced PMCA inhibition. This may then help in the future development of drugs that can attenuate the pathological course of acute pancreatitis.

Characterisation of the Urinary Metabolic Profile of Liver-Fluke Associated Cholangiocarcinoma using Magnetic Resonance Spectroscopy in a Thai Population; A Pilot Study

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Cholangiocarcinoma (CCA) incidence is increasing worldwide whilst mortality rates and detection efficacy remain very poor, with no current adequate diagnostic biomarkers or other suitable diagnostic modalities with an adequate sensitivity and specificity. We present a ^{1}H NMR spectroscopy urinalysis on Thai CCA patients that accurately separated cancer patients and healthy controls in small cohorts. Urine samples from 3 well-matched cohorts were collected from a Thai population in Khon Kaen, Thailand. In this area CCA is nearly wholly attributable to liver-fluke infestation giving a uniform aetiology for analysis. Using an 11.7T nuclear magnetic resonance system the urine was analysed from 3 separate cohorts consisting of: 5 pre-resection CCA patients; 3 post-resection CCA patients; and 20 healthy Thai controls. Multivariate statistical analysis was used to compare pre-resection CCA and healthy controls in the form of principal components analysis (PCA) and partial least squared discriminant analysis (PLS-DA) with a sensitivity and specificity of 100%. Metabolites that contributed most strongly to the multivariate models were creatinine, citrate, hippurate, glycine, phenylalanine, alanine and trimethylamine N-oxide, with urinary levels of hippurate and citrate showing significant differences ($P<0.05$). These key metabolites were also considerably different in pre- and post-resection CCA. The findings validate further research into this area, especially with the significance of previous urinalysis findings on diseases such as hepatocellular carcinoma. These urinary CCA biomarkers are indicative of tumour effects on physiology, energy production, and aberrant chromosomal methylation, and furthermore if validated in larger studies have the potential to be developed as simple urinary screening tests.

Influence of a Self Assembled Monolayer on the Sensor Response of a Protease Sensor

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Self assembled monolayers used in the formation of stable films to create sensor devices for proteases to detect biomarkers of periodontal disease were explored. Alkanethiol monolayers with the head functional groups OH and NH2 were assembled onto gold metal substrates separately. Hydrogels were formed via cross links between aldehyde groups in oxidised dextran and the peptide sequence (AAPVAAK) Ala-Ala-Pro-Val-Ala-Ala-Lys and then spread on to the self assembled monolayers. The aim of the experiment was to see whether degradation of the hydrogel films would occur as a result of action of HNE (Human Neutrophil Elastase Enzyme) on the AAPVAAK cross links and to find out which functional group monolayer provided the most stable sensor device. Degradation was monitored using simultaneous QCM and Electrochemical Impedance techniques using the Frequency Response Analyzer and Network Analyzers respectively. Initially the stability of the films using the two different monolayers was determined by the effect of pH 7.5 charge transfer buffer (which contains no enzymes) on the polymer films. Impedance and QCM Impedance values changed in the presence of charge transfer buffer only suggesting instability of both sensor structures. Addition of HNE did show further changes in readings suggesting that HNE does have an effect on AAPVAAK and hence can cause degradation of the hydrogel. In conclusion the study shows a potential relationship between AAPVAAK and HNE which can be utilized in the development of a biosensor for the detection of periodontal disease, provided that a method of creating a more stable monolayer can be found.

The Effect of Zinc on Fenestrae Formation in Endothelial Cells

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Age-related macular degeneration (AMD) is the commonest cause of irreversible blindness in people over 50 in the developed world and accounts for 50% of those registered blind or partially sighted in the UK. A key feature is reduced permeability of Bruch's membrane associated with deposition of extracellular material called drusen. This interrupts nutrient and waste diffusion between fenestrated choriocapillaris of the eye and outer retina, causing photoreceptor degeneration and blindness.

Zinc deficiency is linked to AMD and zinc supplementation is one of few treatments available, however its mechanism of action remains unknown. Preliminary experiments in our laboratory suggest zinc plays a role in fenestrae formation in endothelial cells. We hypothesise zinc increases permeability of the choriocapillaris, thus improving debris clearance from Bruch's membrane and zinc deficiency in AMD reduces fenestrations which exacerbates deposition.

We aim to confirm effects of zinc on fenestrae formation by immunolabelling fenestral diaphragm component PV-1 to observe sieve-plates in bEND-5 endothelial cells incubated with zinc at different concentrations and durations. Actin cytoskeleton, zinc and intracellular organelle distribution patterns were also studied.

Results confirmed fenestration with zinc treatment from 90 minutes and sieve-plate proportions appeared to increase as incubation time increased. Above the optimal concentration of 125uM, cells showed evidence of toxicity. Cytoskeletal structure was maintained throughout. Zinc and lysosomal studies demonstrated similar distributions, but zinc was also present in sieve-plates. These observations advocate future studies into how zinc may slow the progression of AMD by improving permeability of choriocapillaris.

Raman Imaging for Cancer Diagnosis using Clustering Analysis based on the Pearson Correlation Coefficient

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Recent advances in Raman spectroscopy, an optical-based technique which analyses photons scattered by a sample surface, have generated new interests in the field of optical diagnosis and characterisation of biological tissue. In few cases, differentiation between cancerous and benign tumours from human patients was shown to be possible using principal component analysis on the collected Raman spectra. However, this simple approach has been limited by a number of factors such as the lack of images, namely the ones found in conventional histology. Thus, in this study, using the rapid Streamline Raman imaging capabilities of a Renishaw's inVia Reflex spectrometer, we have mapped with high resolution, the Raman signature of a number of different samples. To extract meaningful chemical information from these large datasets, we have developed an automated clustering approach based on the Pearson correlation coefficient. Using this Raman analysis, we have successfully differentiated the various components from samples containing a mixture of 1 to 6 µm fluorescent beads of different emission wavelengths: 460 nm (blue), 515 nm (green) and 620 nm (carmine). Subsequently, we have clustered the different biochemicals of both stained and unstained human breast tissue sections.

This study demonstrates a novel non-invasive method to differentiate different biochemicals of human tissue, which could have a substantial future clinical impact, as it may become a useful adjunct to the pathological diagnosis of cancer.

Oestrogen Receptor-negative Progesterone Receptor-positive Breast Cancer: A Re-evaluation Study

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The occurrence of oestrogen and/or progesterone receptors in breast carcinomas plays a crucial role in the prognosis and treatment of disease. Consequently breast cancer can be subdivided into phenotypes on the basis of combined receptor status to provide a more explicit prediction of outcome. However, the validity of one such subtype, the oestrogen receptor-negative, progesterone receptor-positive tumour, is greatly disputed as to whether it is inherent in nature or a product of artefactual error.

The study utilised contemporary methods of immunohistochemical analysis for both steroid receptors to attempt to verify the expression of this dubious phenotype. This was performed on cases classified as such by prior assays (n=32) using an array of antibodies with a focus on the oestrogen receptor due to the frequency of false negatives reported in literature. Additionally, real time-polymerase chain reaction investigating the presence of oestrogen receptor mRNA was used as a complementary tool in determining receptor expression.

Although the latter method was not successful, immunohistochemistry revealed a substantial decline in the presentation of such carcinomas whereby most cases exhibited alternative phenotypes. Furthermore cases determined “oestrogen receptor-negative progesterone receptor-positive” (n=5) under clinical thresholds for positivity (<1% staining) demonstrated weak estrogen receptor expression.

Such evidence suggests that incidence of the oestrogen receptor-negative progesterone receptor-positive breast carcinomas may well be a product of assay insensitivity. Concurrently, this elicits how the issue of technical error and subsequent inter-variation of results has hindered the process of reaching a universal definition of this phenotype for the clinical setting.

The Role of 99m-Tc Sestamibi Scanning in the Pre-operative Localization of Abnormal Parathyroid Glands in Patients with Primary Hyperparathyroidism

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Background Primary hyperparathyroidism is one of the most common endocrine conditions. Surgical management is often necessary, yet the methods used to localize the abnormal gland pre-operatively are controversial. The aim of this study was to establish whether one of the most commonly used methods, 99M-Tc sestamibi scanning, is accurate enough to be useful in the pre-operative localization of parathyroid pathology in patients with primary hyperparathyroidism.

Methods A retrospective case-note review of 258 patients (199 female; mean age 61.1 ± 13.1 years) with primary hyperparathyroidism who underwent parathyroidectomy between February 2003 and July 2010 was conducted. Patients who presented with hyperparathyroidism as part of Multiple Endocrine Neoplasia type 1 (n=4) were included.

Results Post-operatively, mean serum corrected calcium and parathyroid hormone (PTH) levels fell significantly ($p<0.0001$). A cure rate of 57.9% was achieved based on PTH levels taken 24 hours post-operatively. 87.2% of patients had a pre-operative 99M-Tc sestamibi scan. The technique had an overall sensitivity of 94.4% and a Positive Predictive Value of 95.8%. The rate of localization to the correct side was 81.8% and in 49.3% of patients, the scan could correctly localize the precise abnormal gland.

Conclusion 99m-Tc sestamibi scanning is useful in the pre-operative planning of parathyroidectomy for primary hyperparathyroidism. This has implications for the surgical procedure carried out, making unilateral neck exploration possible. This reduces the postoperative complications associated with bilateral neck exploration and results in shorter hospital stays. Clearly, surgical experience is also important in improving the accuracy of parathyroidectomy, as is combining imaging techniques.

Audit to assess how well investigations are handed over from the medical take to the wards at the Bristol Royal Infirmary

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Background: At the BRI, medical patients are admitted under the take-team before subsequently being transferred to the ward-teams. GMC guidance highlights the importance of effective handover for safe and efficient patient care[1]. This audit was designed to assess, and subsequently improve, the clarity of written investigation handover from the take team, in order to improve patient safety and satisfaction.
Method: Thirty-eight patients admitted via the medical take to two medical BRI wards during March 2011 were retrospectively audited. Information recorded in admission pro formas regarding the planning, request status and results of investigations, was compared with equivalent data available at the time of the post-take ward round on the ICE computer database used for investigation request and reporting at the BRI. The standard was 100% recorded handover.
Results

- Whether or not a planned investigation was requested was not documented for 62% of investigations.
- Of those investigations planned and requested, only 53% were handed over as requested.
- 14% of investigations requested on ICE were not recorded as planned.
- 5% of investigations not requested were documented as requested.
- 13% of investigation results available on ICE by the post-take ward round were not documented.
- 11% of planned investigations were neither requested nor handed over as needing to be.

Conclusion: Handover of investigations from take- to ward- teams was found to be poor overall. This is likely to increase patient stay and impede quality of care, as well as creating extra work for ward doctors. A more efficient and reliable method of handover is therefore required. It is proposed that an investigations handover grid will be added to the medical pro forma prior to re-auditing.

[1]GMC: Good Medical Practice 2006

HIV testing in all children of HIV positive women

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Background: Undiagnosed HIV infection leads to a significant risk of increased morbidity and mortality in children. The testing of children of HIV-positive adults should be taken as a matter of urgency. The aim of this study is to establish the HIV status of children of HIV-positive women attending HIV outpatient follow up clinic.

Method: This is a retrospective cohort study of HIV-positive women who were pregnant between 2006 and 2010. We reviewed if any children of these women were tested for HIV.

Result: There were 50 HIV-positive women with a total of 54 pregnancies. 3 newborns were tested HIV-positive. A total of 46 live siblings were eligible for HIV testing. Of 46 siblings, 16 children (35%) were not tested. Of these 16 children, one child had no valid reason for being untested.

Conclusion: One child was identified untested for HIV status as his mother failed to bring him to the HIV follow up outpatient clinic. The adult HIV team had been reminded to contact the mother and encourage her to bring the child for HIV testing. In the future, any children <2 years old or symptomatic should be offered HIV testing as soon as possible as this group of children carries higher risk of morbidity and mortality associated with delayed diagnosis. As for older children, we should respect mother's wish to wait for the result of HIV testing of her newborn and then only arrange blood test for older siblings on same day of the newborn's deferred BCG.

Audit of early medical terminations of pregnancy (EMTOP) in an area of high ethnic diversity and socio-economic deprivation

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Women in Newham are at high risk for abortion, given the majority immigrant population, multiparity and high prevalence of sexually transmitted infections. Abortion is an expensive, time consuming and emotionally stressful approach to managing fertility. Nationally, whereas overall rates are decreasing, early medical terminations (EMTOP) are increasing. This audit set out to determine local trends and demographics with regard to EMTOP demand, and conformity to national guidelines.

The initial audit prospectively studied 100 cases in 2008; re-audit was performed retrospectively in 2010 (357 cases). Among the data audited were demographics, contraception, previous abortions, timescale and complications.

Initial audit highlighted waiting times in excess of RCOG requirements, high termination failure rate, incomplete documentation and unreliable contraceptive choices. Therefore, clinic capacity was increased, documentation discussed and EMTOP protocol modified. Re-audit revealed 97% EMTOPs within approved time periods, failure rates meeting national standards and a 25% increase in correct documentation. However, also found was a twofold increase in EMTOPs performed in <20 year olds (contrary to national trends), and a threefold increase in those requesting repeat abortion. Contraceptive choices were still suboptimal, with 1/3 of patients 'undecided' about future contraception, and only 1/3 considering the use of long acting reversible contraceptives.

This audit illustrates improvements that modest service alterations can achieve. It also raises a new question: is there an increasing tendency in the teenage population to use EMTOP as an alternative family planning method? Concerted efforts should focus on educating women at termination to ensure adequate contraception throughout their remaining reproductive years.

Abdominal x-rays in the acute setting: How are we using them?

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Background: The National Radiation Protection Board estimated that a single abdominal x-ray would expose a patient to thirty-five times more radiation then a chest x-ray. In 1976 the Royal College of Radiologists working party was established to promote effective use of radiology. The Royal College of Radiologists first published guidelines in 1988 to ensure safe use of radiology. The guidelines of 2003 provide specific clinical situations for the acceptable use of abdominal x-rays. The aim of this audit is to establish how we are using abdominal x-rays in the acute setting and whether we are requesting them appropriately.

Design: A total of 110 patient records were included over a two-week surgical on-call period.
The parameters recorded were as follows: Diagnosis (provisional and definitive); Investigations (initial radiological investigations and further); grade and specialty of the requester.

Results: The results showed that 40 patients out of 110 had no radiological investigations on admission, 45 had abdominal x-rays, 7 had a CT KUB, 5 had an abdominal USS and the remainder had other radiological investigations. 73% of the requests made were acceptable, 27% were not Obstruction was the most common provisional diagnosis made (18 cases). Of these cases, only 7 cases were true obstruction. 21 patients had further radiological investigation following an abdominal x-ray.

Conclusion: Recommendations made included wider distribution of the RCR guidelines within the hospital. Education of junior staff as to when it is appropriate to request an abdominal film and whether an abdominal film is necessary if further imaging is required.

Audit Report reveals lack of follow-up for HBsAg-positive pregnant women and their contacts in Thames Valley

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Chronic hepatitis B is an important public health issue due to its high infectivity and ability to cause significant morbidity. In this cohort study 201 HBsAg-positive pregnant women were identified between January 1st 2008 and December 31st 2009 in the Thames Valley area. They were investigated regarding follow-up of their sexual and household contacts and the referral of the index case to a gastroenterology specialist.

Methods included identifying HBsAg-positive pregnancies by laboratory results and requesting information from GPs regarding case referral to gastroentologists, sexual and household contact screening and vaccination and evidence that TVHPU advice letters were received by GPs. Letters, telephone calls and faxes were implemented to request the information

Among the 201 women only 107(64%) were referred to a gastroentologist. 323 contacts were identified of which 146(45%) completed vaccination, 11(3%) had incomplete vaccination, 119(34%) were registered with the cases' GP but had not been immunised and 57(18%) sexual contacts were not registered with the practice and thus their follow-up was unknown. Of those registered at the same GP but not immunised, 67% were children and 31% were sexual contacts. The study prompted immediate positive reactions in which many of these contacts were subsequently screened and vaccinated and previously un-referred cases were referred to a Gastroentologist.

The study highlighted that there is incomplete follow-up of chronic hepatitis B carrier mothers and their contacts indicating a need to improve collaboration between the TVHPU and local GPs in a proactive approach to appropriate follow-up.

Ward based troponin

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At GWH a ward based troponin test is used in the Acute Assessment Unit (AAU) to expedite discharge. It is a simple blood test performed on the ward that gives a troponin, CKMB and myoglobin result in 20 minutes compared to over two hours for a laboratory based troponin. This test costs nearly ten times that of a lab based. Each week the AAU spends up to £500 on this test. Concerns were raised whether usage is always appropriate so the use of this test been audited and re-audited after a period of education.

Two retrospective audits were conducted of 50 consecutive patients from July – August 2010 and in April 2011. Limited guidance already existed however only 72% of patients achieved same day discharge. New guidance was drawn up stating that a ward troponin was only performed if it facilitated rapid same day discharge.

The guidelines were re-audited 6 months later showing a large improvement; with 94% of tests now compliant with new guidelines.

This audit has benefitted the trust by improving the usage of an expensive but useful ward based test. Twenty percent fewer ward tests are being ordered using the new guidelines. Tests are now only used when the added speed can directly benefit hospital discharges. We should all strive in these times of increasing austerity to evaluate our practice and look for cost savings while maintaining patient best interests and safety.

Dendritic cell and Regulatory T cell interactions in chronically inflamed liver

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Background: Interactions between CD4+CD25+ regulatory T cells (Tregs) and dendritic cells (DC) are important in regulation of immune tolerance. Liver DCs display a unique tolerogenic phenotype, and in chronically inflamed liver parenchyma are found in close proximity to Tregs, but the effect of their interactions is unknown

Aims: This in vitro study examines effects of interactions between Tregs and DCs derived from blood or isolated from liver tissue.

Methods: Tregs were isolated from peripheral blood. DCs were generated from peripheral blood monocytes, and matured with lipopolysaccharide; or isolated from liver provided by the University Hospitals Birmingham liver transplant service. Tregs were co-cultured with DCs, and phenotype was assessed by flow cytometry. After transwell culture allowing only diffusion of soluble factors, Tregs were titrated in to suppression assays.

Results: Co-culture with immature blood-derived DCs led to a significant decrease in the proportion of cells with Treg phenotype. However mature blood-derived DCs maintained Treg phenotype, and significantly increased suppressive function after transwell culture. Livers from which DCs were isolated were grouped into non-autoimmune (healthy donor liver, alcoholic liver disease) and autoimmune (primary biliary cirrhosis, primary schlerosing cholangitis). Non-autoimmune DCs failed to maintain Treg phenotype, whereas autoimmune DCs significantly better maintained Tregs, and also maintained Treg function after transwell culture.

Conclusions: Mature DCs seem to maintain tolerance via Tregs while also driving inflammation. In the liver, Tregs are only maintained by DCs when there is chronic autoimmune pathology, suggesting that there is a tolerogenic network operating, perhaps to prevent further damage.

A Quality Improvement Project- Improving the Quality of Weekend Handover in Surgical Firms at Frenchay Hospital, North Bristol NHS Trust

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Objectives: It was noted that handover at the weekends among general surgical firms at Frenchay Hospital needed improvement as anecdotally there had been occurrences where important tasks were not performed or recorded by the on-call weekend staff. Our aim was to improve the quality of weekend handover, thus ensuring better patient safety.

Methods: The existing weekend handover system involved an unpopular weekend sticker and an electronic handover sheet of variable format (Excel/Word). Through the course of four PDSA (plan-do-study-act) cycles we changed the format of the sticker. We then converted all patient and handover lists to a unified Excel format in a further PDSA cycle. After each cycle, we conducted a questionnaire of junior doctors and then modified the handover format accordingly. We collected data on the percentage of jobs done during the weekend as requested by the handover system over a 14 week period

Results: The baseline score (the percentage of jobs done during the weekend as requested) before effecting the changes was 65% and through the course of 5 PDSA cycles, this rose to 89%. A questionnaire given to all surgical junior doctors demonstrated that the new system was universally more popular and effective that the previous system.

Conclusion: Through relatively small and simple changes in practice, junior doctors were able to demonstrate a large change in clinical outcomes, thus improving the standard of weekend patient care and its safety.

Delirium- The Assessment of at Risk Patients

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Delirium is characterised by disturbed consciousness, cognitive function or perception, which has an acute onset and fluctuating course. It affects up to 30% of all elderly patients and is associated with significant burden and poor outcomes including an increase in length of stay and mortality. Fortunately it can be prevented and treated if dealt with urgently.

AMTS (abbreviated mental-test score) is a 10-point test used to rapidly assess elderly patients' cognitive function, where <8 is significant for confusion.
The aim of the audit was to aid recognition of delirium and to provide guidance on the importance of assessing cognition in elderly patients.

In 2010, 500 in-patients over 65 years from a UK hospital were retrospectively analysed to identify if cognition was documented and whether this was based on their AMTS, and if other investigations were performed including urine dipstick, rectal examination (if faecal impaction was suspected) and CT head if clinically indicated.

Of the 500 patients, 155 had developed delirium and this was identified in the notes. However, only 77% of these had a documented AMTS. 55% of delirium patients had a documented dipstick result. Of the total patients, only 215 (43%) had an AMTS completed.

The audit led to AMTS and investigation documentation to be introduced onto the clerking pro-forma to screen patients over 65 years. AMTS score will also provide a baseline to patients' cognition. Simple investigations such as urine dipstick should be obtained to aid a management plan. Healthcare staff were reminded of the importance of documentation.

Caring for adolescents with HIV

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Background: In 2009, 13, 861 16-24 year olds were living with HIV in the UK. The unique psychosocial development during adolescence demands a multi-faceted approach to healthcare. Limited studies are available to inform practice.
Aims: 1.Characterise the population of adolescent HIV+ patients accessing CUH GUM services. 2. Identify unique treatment challenges. 3. Identify differences between patients with vertically vs. horizontally-acquired HIV.

Method: Retrospective case note review of all HIV positive patients aged 16-24 years using the CUH GUM services.

Results: 46 patients met our inclusion criteria. The median age was 23, 70% were female and 52% were Black African. The commonest mode of transmission was unprotected heterosexual intercourse (57%). 57% of patients were on HAART therapy, for 70% this was their second regimen. Overall adherence was good: 14% of the total cohort had 'poor' adherence. However in the 'transitioners', 72% had poor adherence. There was a high incidence of alcohol, recreational drug use and mental health problems. 46% of adolescents had lost one or both parents. 42% of patients were sexually active, of whom only 30% had a regular partner

Conclusions: This group has a high incidence of psychosocial problems and complex medical needs, which would be best addressed by specialist adolescent services. Sexual and reproductive health promotion should be integral to this. Transitioners (24%) are more likely to be: symptomatic, with advanced disease at diagnosis, and exposed to multiple HAART regimens with poor adherence. These key differences could be best addressed in a tailored 'transitioner' clinic.

A near gastro-catastro phe

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A previously well 10 year-old girl presented with sudden, severe, persistent rectal bleeding and syncope. Despite having numerous investigations which included an abdominal ultrasound, abdominal x-ray, chest x-ray and laparotomy, the cause of bleeding remained unknown and she became critically ill. A CT angiogram was performed once she was clinically stable, which showed multiple bleeding points in the mid-jejunum consistent with angiodysplasia. She was not a suitable candidate for vascular embolisation, as there were multiple bleeding points over a large area and the vessels supplying this area were too narrow, she was therefore managed surgically. Intraoperatively the small bowel was visualised by endoscope and areas of potential bleeding were isolated and tested. A 30cm length of abnormal bowel in the mid-jejunum was resected and a primary anastomosis was performed. She was transferred to PICU for postoperative management. She was discharged 5 days after admission.

This case raises a number of interesting discussion points due to its unusual nature. Firstly, it is extremely rare to find angiodysplasia in the jejunum, especially in children. Secondly, it is usual for angiodysplasia to present with major rectal bleeding that causes profound hypotension and loss of consciousness requiring massive fluid resuscitation (11870ml in total of colloid, crystalloid and blood products over 4 days).

This is a fascinating case study that highlights the importance of considering angiodysplasia as a differential diagnosis for an acute persistent rectal bleed in children and the management required to prevent a potentially fatal outcome.

Evaluating saccadic latency as a novel diagnostic tool for minimal hepatic encephalopathy in patients with liver cirrhosis

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Minimal hepatic encephalopathy (MHE) affects up to 80% of patients with liver cirrhosis. Although asymptomatic, MHE impairs daily living and is treatable. There is no definitive diagnostic test but psychometric tests are commonly used. These are resource-intensive, and MHE is not routinely screened for in relevant patient groups despite its clinical significance. We evaluated the usefulness of saccadic latency, the time between appearance and fixation of a visual target, as a novel diagnostic tool for MHE in patients with liver cirrhosis. Using a saccadometer, we measured saccadic latency in 17 patients with liver cirrhosis and in 15 age-matched controls. Participants also completed 4 psychometric tests (NCT-A, NCT-B, digit symbol test, block design test). MHE was diagnosed in 12 patients based on at least 2 abnormal psychometric results (as recommended by the Working Party, 1998). Analysing saccadic latency, we found no significant differences in promptness, μ, among the groups, but significantly greater variability, σ, in the MHE+ patients (1.3±0.1) compared to MHE- patients (1.0±0.1; p=0.048) and controls (1.0±0.07; p=0.01). Based on ROC curve analysis, a cut-off of σ>1.09 gave a diagnostic sensitivity of 75% and specificity of 80%. The aspects of cognitive impairment that manifest as changes in σ remain poorly understood but could be due to impairment of the neuronal attentional system as seen in patients with frontal lobe lesions. In conclusion, saccadometry is an easily-administered, quick and reliable tool which could potentially be used to screen patients with liver cirrhosis to identify candidates for further testing.

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Should Society Take Precedence Over Individuals and Do Scientists Need More Autonomy In Modern NHS?

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ABSTRACT

Traditionally doctors decided what research was acceptable to conduct on their patients and whether the risks justified the benefits. Patients now-a-days, however, are less likely to accept the orthodox idea that the doctor is omniscient and always right; instead, they demand for the autonomy to decide for themselves what procedures they are prepared to consent to and what treatments they are willing to receive. One of the characteristics of medical research, counter-intuitive though it may be, is that it is not always intended to directly benefit the individuals participating in it. Healthcare professionals working within the National Health Service (NHS) in the United Kingdom (UK) have an obligation to carry out research as part of their function to continually improve the quality of healthcare provided as well as for continuing professional development. Many times the researcher is confronted with a dilemma: questions like, "*How do I conduct research on individual patients in an ethical manner but also advance the frontiers of medical science?*", and, "*What is my role in the well-being of the society as a whole?*" are ones that the inquisitive investigator poses. This article debates such issues and reasons why, in certain circumstances, the interests of the society as a whole should be given precedence over individual patients providing that they are not disadvantaged or harmed in any way. Finally, it also argues that a pragmatic paradigm should be adopted and healthcare professionals should be given more autonomy within the NHS to conduct research for the betterment of future generations.

BACKGROUND

In past centuries, society mainly relied on the discretion of the medical profession to decide whether the potential benefits to future patients and to society as a whole justified exposing patients and healthy volunteer to the risks of healthcare research. Patients now-a-days, however, are less likely to acquiesce to the orthodox idea that the doctor is omniscient and always right. Instead, they demand for the autonomy to decide for themselves what procedures they are prepared to consent to and what treatments they are willing to receive1. In the latter part of 20th century, radical changes in the roles of autonomy and authority, advances in medical technology, and vibrant (and sometimes vociferous) debates about what constitutes right and wrong have rendered choices that doctors and their patients once considered self-evident complicated2.

Health care professionals working within the National Health Service (NHS) framework in the United Kingdom (UK) have an obligation to conduct research as part of their function to continually improve the quality of healthcare provided and for continuing professional development. Hence the ethical issues related to research are relevant to all in the healthcare sector who wish to fulfil these stipulated requirements. Moreover, there is an increasing recognition that the introduction of a novel procedure or therapeutic, without full evaluation or comparison with existing methods, may result in ineffective and sometimes harmful treatments being used3.

One of the characteristics of medical research, counter-intuitive though it may be, is that it is not always intended to directly benefit the individuals participating in it. Its aim, rather, is to procure more knowledge about the cause of disease and the functioning of the human body in relation to pathology; develop new treatments or compare existing treatments with each other to discover which is more efficacious and cost-effective. It may be known from the outset that at least some of the participants in the research will not directly benefit themselves. So does this mean that they have an absolute right not to take part because they are not directly reaping the rewards or do they have a duty, although unsolicited, to participate, providing that it is

not harmful, since the medical profession would obtain new knowledge from which future patients and indeed society would benefit?

This article debates such issues and argues why, in certain circumstances, the interests of the society as a whole, in our opinion, should be given precedence over that of the individual providing the intervention in question is not disadvantageous or harmful in any way. Pertinent issues including confidentiality and the role of ethics committees are also discussed. Finally we reason why researchers need more autonomy in our modern NHS for the betterment of future generations.

The National Health Service

The NHS in the UK is a state-run health care system, funded through taxation and works on the principle of providing universal and comprehensive healthcare at the point of delivery. It is increasingly apparent that the demand for health care now exceeds the capacity of the national economy to sustain it, as a result of greater expectations, improved technology, increasing longevity of life and a burgeoning morbidity rate in an aging population. This means that the NHS is ineluctably subject to resource constraints. Clinicians and managers attempt to balance medical needs and financial prudence which poses major ethical dilemmas. Hence it is generally accepted that there must be structured and explicit rationing.

So what is the role of research in our modern NHS apart from advancing the frontiers of medical innovation? Cost-benefit analysis attempts to provide a balance-sheet of the costs and benefits to society over time, all expressed in today's money terms, of investing in a particular service. Numerous retrospective case-control studies and trials are carried out in the NHS to find ways wherein the benefits outweigh the costs. Physicians are expected to put the medical needs of their patients above all other considerations. However, conflicts of interest arise in clinical practice when practitioners become involved in arrangements that introduce other considerations that are potentially incompatible with the best interests of patients[4].

This inevitably leads to the dilemma: Does the clinician/ researcher act in the best interests of his patients or does he have a role in promoting the well being of the society as a whole? Does he adopt a *prima facie* or a utilitarian approach and also simultaneously advance the frontiers of medical science? Could the traditional 'moral high ground' of clinicians, 'altruism, activism, beneficence, and non-maleficence' fit in a modern NHS with only finite resources?

Herein lies one of the fundamental ethical issues in modern medicine: how can physicians fulfil their moral obligations as fiduciary agents for individual patients while being shrewd stewards of the finite pool of resources?[5] In the area of resource allocation we sometimes provide less than the best treatment for one patient in order not to disadvantage another patient excessively. Justice demands balancing the interests of different patients: is it very different if we offer a patient now, in the context of a large clinical trial, a treatment that is not, on the evidence, the very best, on the grounds that this will benefit other patients in the future?

The Declaration of Helsinki

When publishing reports of experimentation, journals have a duty to define what constitutes medical research of the highest quality and to include the ethical conduct of trials in this definition[6]. The Declaration of Helsinki charges journals with this important responsibility, stating: "*Publishers have ethical obligations. . . . Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication*."[7] It follows that editors of journals should specify on all published trials if informed consent and ethics committee approval was obtained or why these were waived [6]. This duty is supported by the International Committee of Medical Journal Editors (ICMJE) [8].

Despite this duty, in 1997, on the 50th anniversary of the Nuremberg Code[9], there was mounting evidence that journals were not fulfilling their commitment to these guidelines.[10-13]–Data at the time[10] and further documented since[14] suggested that articles reporting ethical protections were of higher methodological quality than those that did not.

Yank and Rennie analysed articles of clinical trials published before and after 1997 (July 1995 to December 1996 and January 1998 to June 1999) in the major journals Annals of Internal Medicine, BMJ, JAMA, The Lancet, and The New England Journal of Medicine[6]. Sixty articles per journal per period were randomly selected and included in the study and assessed for rate of reporting on informed consent and on ethics committee approval [6].

Yank and Rennie concluded that the major medical journals have improved their reporting on informed consent and ethics committee approval; however, 9% of studies still report neither[6].

CONFIDENTIALITY

Confidentiality is a vital part of the understanding on which the doctor-patient relationship is based and is a central ethical pillar of clinical practice among all healthcare professionals. Individual clinicians, according to their conscience and guided by statute and ethical training, will vary in the limits they apply to confidentiality. The World Medical Association issued the Declaration of Helsinki in 1964, [15] with subsequent

updates,[7] to establish international regulations for human experimentation.

It specifically identified 2 protections: that all participants in trials should understand the risks, benefits, and alternatives of the experiment and, following this, should enrol in the trial under their own free will, by giving informed consent, and that a disinterested party unconnected with the trial, termed the ethics committee or institutional review board, should have approved the experimental protocol after assuring its appropriateness of design. Article I.6 of the Declaration of Helsinki (World Medical Association 2004)[16] states: "*Every precaution should be taken to respect the privacy of the subject and to minimise the impact of the study on the subject's physical and mental integrity and on the personality of the subject*".

Respect for the privacy of the subject is demonstrated by obtaining their informed consent before releasing any confidential information about them and by taking all reasonable efforts to minimise the risks of a breach of confidentiality during a study. This, however, may not always be possible. In epidemiological studies involving the scrutiny of thousands of computerised records, it might be impracticable to seek the permission of each individual patient and may even be unethical if it causes needless anxiety for a large number of unaffected individuals. If individual consent is not to be obtained, the World Health Organisation (WHO) epidemiological guidelines[17] state that: '*An investigator who proposes not to seek informed consent has the obligation to explain to the ethical review committee how the study would be ethical in its absence*'. However, the Royal College of Physicians[18] (s.8.24) takes a different view. It advises that so long as the same strict code of confidentiality is observed when medical records are used for research purposes as in standard clinical practice, it may not always be necessary to ask the patients permission first[18]. It further says that, ethical review is not always essential if no patient contact is involved[18] (s.6.23). So does this account to breach of confidentiality? What about accessing patient information from computerised case registers and other databases where the researcher is not the patient's doctor or not a member of the team providing treatment?

Section 60 of the Health and Social Care Act 2001 was introduced to allow healthcare professionals and medical organizations to use patient identifiable information for the support of essential research activity within the NHS without the consent of patients[19]. Its main goal was to support medical research that was in the interests of patients or the society, where consent could not be obtained or where anonymised information will not suffice. However, concerns were soon raised over the loss or abuse of rights by some patient groups, consumer groups, and civil rights groups. Therefore, safeguards have been introduced and advisory groups such as the patient information advisory group (PIAG) have been created to prevent the use of these powers for trivial or inappropriate purposes[20].

This leads to the crucial question: Could the patient's records be used for research purposes as long as the patient's confidentiality is strictly maintained? In a retrospective case-note study involving 1,000 patients assessing the role of prophylaxis in the prevention of venous thrombo-embolism after minor surgeries (e.g., unilateral hernia repair), it might be impractical to obtain the consent of all individual patients. If at the end of the study it is found that there is no role for venous thrombo-embolism prophylaxis in minor surgeries, then isn't there huge cost containment for the NHS? Does this not then blatantly support the argument that society should take precedence over the individual, at least in this scenario?

ETHICS COMMITTEE APPROVAL

Traditionally doctors decided what research was acceptable to conduct on their patients or healthy volunteers and whether the risks justified the potential benefits. If the doctors who wish to conduct research into a particular condition are recognised experts in its treatment, are they not then the best people to decide what is acceptable for their patients? Whilst this may very well be the case, there is still a need to ensure that overzealous researchers do not get so carried away with making a valuable contribution to science, and improving the lot of patients in the future to the extent that they fail to adequately ensure the safety and comfort of patients today.

Scientific research is permitted in the Western world to advance medical knowledge but concern for the safety of the patient/volunteer/human being must never be relinquished in consideration of the potential benefits to be gained[21]. The ethics committee thus has an important moral and social responsibility. One of the important duties of the ethical committee formulated by the Royal College of Physicians (RCP)[18] (s.1.5-1.7) states: "*Patients must be protected from undue risk of injury, distress or discomfort. They have a right to know what is being done to them and why, and their freedom of choice, confidentiality and privacy must be respected...*"[18] (s. 5.24).

However, with the implementation of recent new ethical regulations both within the ethics committees and the NHS, even minor, non-invasive, non-harmful trials need the approval of ethics committees. It takes a

painstaking amount of time and effort by the researchers, many of them practicing clinicians, to accurately and comprehensively fill in these detailed ethical approval forms. This undoubtedly robs invaluable time both for the clinicians and for the commencement of the trial. Although it should be considered mandatory to get ethics committee approval for major trials involving invasive procedures or introducing new treatments, wouldn't it be prudent for research involving review of patient notes, laboratory assays, hospital database, minor clinical trials, and non-invasive monitoring to be left to the discretion of the senior clinicians?

The authors of a paper published in JAMA conclude that they did not know whether patients have benefited from having informed consent or ethical approval as safeguards or whether describing them in articles helps at all. Nevertheless, they do maintain that transparency in the reporting of science has inherent benefits.[13] They assert that the reporting of informed consent and ethics committee approval attests publicly—in a forum where the methods can be openly challenged or discussed—to a minimum level of ethical consideration. They feel that there is certainly a moral imperative to assure participants in trials that meticulous attention is being paid to their safety.

Yank and Rennie state that patients have died in studies that failed to adequately provide protection[22-24] News stories, not surprisingly, have questioned the ethical conduct of medical research.[22-24] These events "*have shaken the public's confidence in our ability to govern ourselves*." [25] In describing the federal government's response, Shalala [26]stated, "*Clinical researchers and the institutions that support them must, without exception, maintain the public's confidence in our work, our competence, and most important, our ethics*."

DISCUSSION

Since the 1960s, the spectre of a patient led consumer movement in health care has gradually evolved. Many health care professionals see this as a detriment to high standards, regarding their professional judgement and erudition as better than any service users' perception in judging the quality of care. On the other hand, consumerism in health care can be seen as a welcome antidote to paternalism and to the indiscriminate use of patients as research fodder. The days of omniscience, authoritarianism and the supercilious attitude of the doctors aloft and aloof in their ivory towers are now confined to the history books.

Similarly, research ethics is under scrutiny, particularly in the light of the current debates over the revision of the Declaration of Helsinki. The declaration states: "*Concern for the interests of the subject must always prevail over the interests of science and society*". This seems generally to be taken to imply, for example, that when a patient takes part in a clinical trial the treatment within that trial should be in his or her best interests. Such interests should never, on this view, be compromised for the sake of those patients in the future who might benefit from the trial results. RCTs, for example comparing the effectiveness of two treatments, should only be undertaken if there is "equipoise"[11]. The "best interests" of the patient are widely seen as the bedrock of medical practice. However, the best interests of the individual patient have, of course, long been compromised for the sake of other potential patients – in infectious disease control, to cite but one example and it is ludicrous to deny that we have consequently made quantum leaps in our antimicrobial arms race.

More autonomy should be given to the researchers and a broader approach needs to be adopted rather than the bigoted and myopic views of some groups. An absolutism approach may not be helpful in the complexities and mosaicism of today's healthcare world. The government and other regulatory bodies have to take adequate steps and enforce laws to ensure that bureaucracy does not hamper genuine research which would be severely deleterious for the survival of the NHS and the well-being of society as a whole. Although individual patients should not be used as a fodder for research, a civilised society should understand and appreciate their role in contributing towards medical research. It should not be forgotten that we also have a duty towards the health of future generations. Indeed, as Babington exhorted, 'Every generation enjoys the use of a vast hoard bequeathed to it by antiquity and they transmit that hoard, augmented by fresh acquisitions, to future ages...'

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The Portrayal of Mental Illness in Film and its Application as a Learning Tool in Medical Education

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Introduction

'If you really want to understand a man you have to slip into his shoes and walk around in them…'
Atticus Finch, To Kill a Mocking Bird

Figure 1: Medfest 2011 (with permission from Kamran Ahmed, Rory Conn, Peter Byrne)

Film offers an unrivalled medium for entertainment but also a unique interface for public education. Indeed public opinion is strongly influenced by vivid images in the form of documentaries and feature films[1]. Film can also, as alluded to in the epigraph of this article, provide viewers with an insight into the psyche of people with psychopathology so that we may *"Slip into their shoes and walk around in them".* By virtue of cinema, we can learn more about what mental illness is like from the inside and this in turn can help us to better understand what it is like to have a psychiatric disorder, be that the narrowing of repertoire in Autism as depicted by Dustin Hoffman in *Rainman* or Schneider's First Rank Symptoms of Schizophrenia as portrayed by Russel Crowe in *A Beautiful Mind…*

With the above in mind, it should come as no surprise that film is utilized in the field of medical education. Indeed, over the last three decades mental educationalists have attempted to use film as an educational tool for teaching medical students and psychiatry trainees for a number of mental health conditions and scenarios. This remit includes personality disorders, assessment of mental state, response of others to the mentally ill and the relationship between the therapist and the patient; especially on issues of transference and counter-transference[2].

The Role of Film as a Learning Tool in Medical Education

A key advantage of films as an approach in teaching mental illness is that their use does not involve encroaching on the confidentiality of a real patient. In addition the 'patient' can be seen interacting with others encompassing them thus giving a clearer understanding of the impact of the illness on others. Unlike clinical consultations in myopic settings focusing on symptoms and treatment which are time-limited, this gives a wider picture on the lives and interactions of people with mental illness with those around them[2].

The use of cinema in postgraduate psychiatry training has been gaining increasing acceptability, but its potential for use in undergraduate psychiatry has received little attention in the literature hitherto. Special Study Modules (SSMs) in undergraduate medical education have developed in response to the General Medical Council's recommendations. St George's, University of London offers a 'Psychiatry and Film' SSM for medical students on the 5-year MBBS course[3]. A similar SSM is also run in King's College London (KCL). A paper by Datta reports on the rationale behind and medical students' responses to an SSM for third year medical students at KCL. In summary, the medical students in this study were very receptive to the use of film as an educational tool and were able to understand both the strengths and limitations. The participants found the module enjoyable, and subjectively rated their knowledge of psychiatric topics and the history of psychiatry as significantly improved[4].

These findings do provide provisional support for the use of film as an educational tool in undergraduate psychiatry however more systematic research is needed to elucidate the potential role of cinema in undergraduate psychiatric education[4].

Film as a Therapeutic Tool

In recent years in the United Kingdom film has been not only been used as an educational tool for medical students and psychiatry trainees but also as a therapeutic tool for service users. For example, researchers on marital strife have suggested that relationship therapists recommend service users to watch a film that specifically revolves around the theme of disharmony amongst partners. The couple is then invited to return for a further therapy session in order to have a detailed discussion about the film in a facilitated environment which may yield new insights and consequently ameliorate discord[2].

An example of a film with a theme on marital disharmony is the 1994 motion picture *When a Man loves a Woman* starring Andy Garcia and directed by Luis Mandoki. It tells the story of an airline pilot, Michael Green (Garcia), and his wife, Alice (Ryan), a school counselor, who ostensibly have a wonderful life living with their daughters in San Fransisco, until the truth about Alice's alcohol dependence reveals itself and threatens to destroy everything. What is especially interesting about the film is that it is based on the real-life experiences of one of the two scriptwriters, Al Franken, who is now a United States Senator. Al Franken's wife struggled with alcohol dependency whilst their two children were young and this placed a tremendous strain on their marriage as well as on the upbringing of their children. *When a Man Loves a Woman* is especially valuable in its portrayal of the far-reaching effects that alcohol addiction can have on married couples and their children[5].

Cinematherapy

The term *cinematherapy* has been coined and refers to using film as a therapeutic tool with service users to deal on issues such as relationship disharmony and identity crises. Recently, films have also been used for character building and as a means to make apparent the benefits of virtuous character traits[6]. Niemiec et al have used positive psychology models portrayed in film to illustrate and inculcate a number of strengths such as wisdom, knowledge, courage, humanity and justice. Such an approach also looks at matters such as love, kindness, citizenship, hope, humor and spirituality, which can also be developed using models from films. Although some of these models are fictional they can nonetheless still be utilized as the morals they convey can be explained, understood and applied in the real world[2].

Film, Policy and Society

Policy makers are not oblivious to the influence that film has on the public and the ministry for health has utilized motion picture for promoting public health campaigns. Not withstanding this, film has also had an influence on policy making. For example, the portrayal of electroconvulsive therapy (ECT) and the associated negative connotations were seen most powerfully in films such as *One Flew over the Cuckoo's Nest*, which influenced public attitudes to the extent that there were changes in the law regarding the use of ECT in several countries leading to a reduction in the number of ECTs actually being given[2].

In addition, the role of how substance abuse is portrayed, including nicotine and alcohol, has led to changes in consumption of these substances. In some countries governments have restricted the depiction of smoking in films and have also recommended that film actors reduce their smoking in public to protect impressionable members of society[2]. These are but some of the examples of the dynamic relationship between policy, society and film.

The 'Negatives' of Film

Regarding film and its application to medical pedagogy, this point is moot. It has been posited that in cinematherapy patients do not have the medical acumen and/or expertise to filter out the pseudo-psychiatry. This may lead to misinterpretation, which has been attributed to adverse consequences. In 1995, for example, Sarah Edmonson and Benjamin Darrus murdered two people and in a statement claimed that they were inspired by Oliver Stone's motion picture *Natural Born Killers*. The same film was also allegedly an influence for the perpetrators of the infamous Columbine school massacre, with the phrase "going NBK" in the journal entries of Eric Harris and Dylan Klebold signaling the start of their killing spree that tragically ended 13 lives.

The above does illustrate that films may have a negative influence on its audience. Service providers must be aware of this; this awareness will allow them to guide the

cinematherapist to diligently identify suitable films, especially with more impressionable service users, and to explore the piece with enough detail with the patients so as to avoid misunderstanding and corruption of an effective form of therapy.

One Flew Over the Cuckoo's Nest: the Archetype of the Portrayal of Mental Illness in Film

By the end of the 1950s psychiatry had reached the zenith of its prestige in the American imagination. Washington, D.C.'s St. Elizabeth's Hospital, with more than seven thousand patients became the bastion of segregating the mentally ill from the community for successful treatment. The 1948 adaptation of Mary Jane Ward's novel *The Snake Pit* depicted the psychiatrist as the savior of a woman suffering in a mental institution. Indeed, the portrayal of psychiatrists in mid 20th century film as knights of reason and order rescuing damsels in distress from the fire-breathing dragons of their minds was in vogue[7].

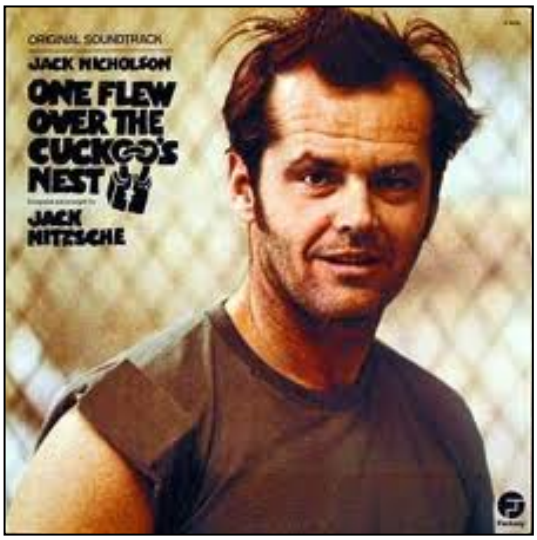

Figure 2: Jack Nickleson as Randle McMurphy in Ken Kesey's *One Flew over the Cuckoo's Nest* (Google images)

But by 1960, the dragons had become the psychiatrists and the institutions of psychiatric care themselves. Budapest-trained psychoanalyst Thomas Szasz, in The Myth of Mental Illness (1960) turned on his own training and called the idea of psychiatric illness "scientifically worthless and socially harmful.' Michael Foucult's magnum opus Madness and Civilization (1961), provided a narrative on the inception of the asylum and contended that the modern concept of madness was a cultural invention of control; the mad who had once been an accepted part of society and life's folly became seen as threats, separated into asylums, and silenced[7].

Despite the prestige and influence of these seminal books in intellectual circles, none of them had the widespread impact of a novel that was begun in 1960 by a twenty-four-year-old writing student who was working the graveyard shift at a mental hospital and participating in government-sponsored drug experiments. Ken Kesey worked on the mental ward in the Menlo Park Veterans Hospital near Stanford University, and became sympathetic to the patients and began to question the boundaries that had been created between sane and insane. In *One Flew Over the Cuckoo's Nest*, Kesey turned the mental ward into a symbol of the tricks afoot in postwar American society[7].

Medfest: a Celebration of the Fruitful Collaboration between Film and Psychiatry

(with permission from: Kamran Ahmed, Rory Conn, Peter Byrne).

MedFest was founded in 2011 as the UK's first ever Medical Film Festival and is run by a group of Trainee psychiatrists under the auspices of the Public Education Committee of the Royal College of Psychiatrists. The purpose of Medfest is to explore the relationship between medicine and cinema. Medfest 2011 explored '*The Image of Doctors in Film'* and was warmly received at 9 Universities throughout the nation. The festival in 2012 was entitled '*HealthScreen: Under-standing Illness through Film*' and toured 16 universities throughout the United Kingdom. The aim of the 2012 festival was, *'To stimulate debate of the social, political and ethical implications of portrayals of health and illness on our screens'*[1]. Indeed when viewed through a romantic or sensationalistic lens, the lack of veracity in the inaccurate portrayals of psychopathology in film can perpetuate myths, propagate falsehoods and promote stigma. But when correctly presented, films with a medical theme have the potential to inform the public, empower patient groups and dispel prejudice[1].

An example of a film that accurately portrays mental illness would be the 2004 box office motion picture *The Aviator*, directed by Martin Scorsese with Leonardo DiCaprio playing the American billionaire magnate Howard Hughes. Scorsese actually consulted an expert in obsessive compulsive disorder, Dr Jeffrey M. Schwartz MD, an Associate Research Professor of Psychiatry at the UCLA School of Medicine and a medical advisor to the UK's national Obsessive Compulsive Disorder charity OCD-UK, on every aspect of DiCaprio's portrayal throughout the filming. The painstaking work that went into this enterprise did not go unnoticed as *The Aviator* went on to garner 5 Academy Awards[8].

Figure 3: Medfest 2012 (with permission from Kamran Ahmed, Rory Conn, Peter Byrne)

MedFest's panelists are selected from a broad range of backgrounds and include; doctors, filmmakers, medical ethicists, playwrights, social scientists and celebrities with an interest in medicine, particularly mental health. The audience MedFest primarily aims to gauge with is medical students, but a wide range of health professionals, as well as members of the public and indeed patients are also invited to attend the enlightening events[1]. Indeed, the heterogeneity of attendees in previous festivals is indicative of how broad and diverse Medfest's appeal is.

MedFest was the brainchild of Dr Kamran Ahmed who, amongst his other accomplishments, was the winner of the prestigious Morris Markowe award in Psychiatry for his essay *'Beards and Bow Ties'.* Dr Ahmed sees strong parallels between his works as a psychiatrist and the art of film making and story-telling. As a movie buff, Kamran is fully aware of the impact that portrayals of doctors in film and the media have on public perceptions His short film (which was an adaptation of his award winning article accessible on YouTube) was, in the words of the prestigious medical journal The Lancet, *"A charming animated short film… that sets out to dispel the many myths that apparently prevail about psychiatrists*[9]*."*

The inauguration of Medfest is a celebration of the fruitful collaboration between doctors and film. Indeed, the Art of Medicine has a long history in film and was one of the first professions to make it onto the big screen at the inception of cinema which was towards the end of the 19th century. For better or for worse, it has survived the ravages of time and has been there ever since; but why this should be the case is the question that begs to be asked. Doctors will touch most people's lives in some way or another, yet they work in a realm that is for the most part obscure from the public's eye. Perhaps artistic representations of medicine allow people, to some extent at least, to get behind the scenes, while the definitive themes of medicine—namely life and death—provide scriptwriters with ample material to derive their inspiration from[2].

Conclusion

Our exposition has revealed that film can be used as an effective learning tool as well as a therapeutic one. Medical pedagogy can be replete with tedium however due to the entertaining nature of film this mode of percept has utility in the realm of medical education since it can appeal to students of knowledge. Moreover, festivals like Medfest offer an opportunity for people to augment their humanity by providing an insight into psychiatric illness through film and discursive debate by esteemed and eclectic panelists. Further research, however, in the field of film, mental health and medical education is recommended by the authors.

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Elective Opportunities in Lebanon

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Lebanon: Historical Background

Unbeknown to many, Lebanon is the mother of Europe. Legend has it that many, many centuries ago, Europa, the daughter of the king of Tyre (a city in the South of Lebanon) was carried away by Zeus who appeared to her in the form of a bull, and with her he scoured the continent that now bears her name[1].

Lebanon is famed for being a Holy Land, for the Gospels tell us that Christ came to Tyre and Sidon, preached there and performed many miracles. According to scripture, Jesus performed his first public miracle in the Lebanon, converting water into wine[1]. In 2012, Pope Benedict visited the Lebanon which is home to a considerable Christian population.

Lebanon: a Tourist's Paradise

Lebanon was and remains renowned for boasting a spectacular opulence. You can go skiing down the convoluted slopes of the snow capped summits in *Fareiya*, or you can bask in the glory of our irresistible beaches on the coasts of the Mediterranean Sea. Perhaps you would like to sip on a freshly prepared cocktail of fruit juices whilst perched on a chair on our illustrious promenades where the ancients would barter frankincense and silk with merchants from far and wide? Beirut is a melting pot, a mosaic of cultures from all four corners of the globe and a city of endless delight. It is a modern and thriving city for commerce and also a center for scholarship with universities and hospitals of international repute.

Lebanon is renowned for championing freedom of expression as evidenced in the following quote by the Columbia University Scholar Edward Said:

Everything seemed possible in Beirut, every kind of person, every idea and identity...

Indeed, our lands have produced some of the most mystic and romantic poets known to humankind.

Today Lebanon is bustling and boisterous with tourists eager to assimilate our heritage, a country that is home to one of the wonders of the world (the Jeita grotto), a nation that hosts the magnificent Roman ruins in all its majesty and grandeur (Baalbeck the city home to the world's largest Roman temple complex), a state that has a dazzling capital city. It should come as no surprise then that in 2009, the New York Times ranked Beirut the No. 1 travel destination worldwide due to its unique nightlife and hospitality[2].

The Lebanese Medical Students' International Committee (LeMSIC)

The Lebanese Medical Students' International Committee (LeMSIC) is an apolitical, non-religious, not-for-profit student-run organization that represents medical students in Lebanon. It is a full National Member Organization (NMO) of the International Federation of Medical Students' Associations (IFMSA)[1].

The IFMSA is an independent organization that represents medical students' associations, embracing more than 1,000,000 students in 101 countries worldwide. It was founded in May 1951 and operated by medical students for the purpose of serving them[1].

The IFMSA is officially recognized as a Non Governmental Organization (NGO) within the United Nations (UN), and is also recognized by the World Health Organization (WHO) as the International Forum for medical students. Its mission statement is:

...to *offer future physicians a comprehensive introduction to global health issues, to develop culturally sensitive students of medicine intent on influencing the transnational inequalities that shape the health of our planet...*[1]

LeMSIC was founded in the 1960s by proactive medical students enrolled in the American University of Beirut. Unfortunately, with the onset of the Lebanese civil war, all the committees' activities ceased. They were reactivated in 1997, with the launching of the Exchange Program[1].

LeMSIC is recognized both nationally and internationally, and has expanded to embrace more than 300 medical students in its various standing committees[1].

Aims and Scope of LeMSIC

The primary purpose of the elective scheme in Lebanon is to provide medics with an insight into the provision of healthcare services in a developing nation in the Mediterranean region. For example, with the provision of healthcare being free at the point of delivery in the UK and very much a private enterprise in the Lebanon, an elective in Lebanon enables UK medical students to compare and contrast the disparate healthcare systems (i.e. universal healthcare vs private healthcare).

Lebanon has been politically stable for the past six years, even at present whilst insurrections and uprisings are rife in the Arab world. Yet the ramifications of the Lebanon-Israel wars (one of which was dubbed, '*The Grapes of Wrath'* after John Steinbeck's Pulitzer Prize winning novel) and the exodus of Palestinians into Lebanon since the 14th of May 1948 when Israel declared sovereignty allows medics on the elective scheme in Lebanon to learn more about the far-reaching effects of conflict and disaster, and also about humanitarian efforts under the auspices of the United Nations and non-governmental organisations such as Medical Aid for Palestinians and *Medicine sans Frontiers.*

With the vast majority of clinicians proficient in Arabic, French and English, prospective students needn't be concerned about any language barriers amongst the healthcare personnel (Lebanon was once a French colony and hence spoken French is ubiquitous in Beirut).

Exchange Conditions of LeMSIC

NB: The following information is by no means exhaustive. The author recommends that readers use this article for reference only. For a complete guide on the application process please visit the website:

http://www.lemsic.org/files/LeMSIC%20Exchange%20Conditions.pdf

Students who are interested in conducting placements in Lebanon through LeMSIC should have commenced clinical training. English is the language of instruction and it is obligatory that applicants are proficient in this language. An English Language Certificate from the exchange student's university is required with all applications. If it transpires upon arrival that the student's capacity to converse and comprehend English is mediocre at best, the student will be refused. Clerkships are for one month duration (calendar month). Exceptions are dependent upon availability. LeMSIC expect students on the scheme to proactively participate in departmental activities[3].

Exchange students are not covered by malpractice insurance in Lebanese hospitals. Thus, they are mainly observers. They are, however, required to attend and actively participate in all ward rounds, bedside teaching, conferences, and case discussions. They are also allowed to examine patients under supervision. Exchange students are required to attend a minimum of 6 hours per day, Monday through Friday, excluding holidays[3].

The specialties that are available to exchange students are listed below:

1. Anesthesiology
2. ENT-Head and Neck Surgery
3. Family Medicine (for final year medical students)
4. Internal Medicine:
   a. Cardiology (for final year medical students)
   b. Endocrinology
   c. Gastroenterology
   d. Hematology/Oncology
   e. Infectious Diseases
   f. Nephrology/Hypertension
   g. Pulmonary Medicine
   h. Rheumatology/Geriatrics
   i. Neurology
5. Obstetrics and Gynecology
6. Ophthalmology
7. Pathology and Laboratory Medicine
8. Pediatrics
9. Surgery
   a.General Surgery
   b.Vascular Surgery
   c.Paediatric Surgery
   d.Orthopaedic Surgery
   e.Plastic Surgery
   f.Urology
   g.Cardio-thoracic Surgery and Cardiac Supportive Unit

Clinical placements through LeMSIC are available only via the American University of Beirut Medical Centre. An alternative elective scheme AESOP offers electives in the capital of the South of Lebanon Sidon (see the article entitled AESOP). LEMSiC can provide students with placements throughout the year except for between May 1 and June 15[3].

Each application must be presented at the March general assembly for July/August/September and at least 3 months prior to arrival for other months of the year. LeMSiC cannot guarantee acceptance for applications that do not meet these deadlines. The American University of Beirut application form is the most important document in LeMSIC without which no student is accepted. The AUB application should be submitted with all the other documents during the March meeting with no exceptions. It should be signed and stamped by the dean's office of the student's original university. THIS DOCUMENT IS MANDATORY. It can be accessed through the following link[3]:

http://www.aub.edu.lb/academics/fm/visiting/fm-visiting.pdf

A list of all the other necessary documents that must be submitted to LeMSiC is available at the following website:

http://www.lemsic.org/files/LeMSIC%20Exchange%20Conditions.pdf

It is an absolute must to have health insurance during one's stay in Lebanon. LeMSiC cannot accept responsibility for any student who does not have medical coverage. LeMSiC offers free board and lodging in furnished apartments in the vicinity of the hospital which is in the heart of West Beirut. Meals will be offered at the hospital's cafeteria on a daily basis (weekends included) three times a day[3].

The Social Program is 100% free. It is, however, only available during the months of July and August. During the rest of the year, activities would be available and offered by local students on a personal basis. The social program consists of 4 full days of site-seeing and outdoor activities in addition to a large variety of recreational facilities, clubs and events on AUB campus[3].

A visa can be acquired on arrival at the airport for students who are bearers of a passport of the following countries:

Australia,Canada,EU countries,Japan,South Korea, Switzerland and USA.

Students coming from other countries need to get their visas from the Lebanese Embassy in their country.

If needed and upon request LeMSiC can arrange to contact the Lebanese embassy to facilitate the visa procedure. A note to be made is that students who have an Israeli visa on their passport have to apply for the visa at the Lebanese Embassy in their country 2 months prior to the date of their clerkship[3].

Conclusion

Students who have conducted their elective placements in the Lebanon have thoroughly enjoyed the experience (with one student stating in a feedback form that it was a life-changing experience). As well as gaining an insight into how the healthcare system in the Lebanon functions they also had the truly incredible opportunity to experience the fascinating culture of Lebanon. For more information please refer to the LEMSiC webpage:

http://www.web.lemsic.org/index.php?option=com_content&view=article&id=7&Itemid=139

References:

1. Lebanese Medical Students' International Committee. http://www.web.lemsic.org/
2. Zach Wise and Miki Meek/The New York Times (11 January 2009). "The 44 Places to Go in 2009 – Interactive Graphic". *The New York Times.* .Available [online]: http://www.nytimes.com/interactive/2009/01/11/travel/20090111_DESTINATIONS.html. Retrieved 21 December 2010
3. Exchange of Conditions of LEMSiC: http://www.lemsic.org/files/LeMSIC%20Exchange%20Conditions.pdf

Elective Opportunities in Lebanon: The Abouzahr Elective Scheme of Phoenicia (AESOP)

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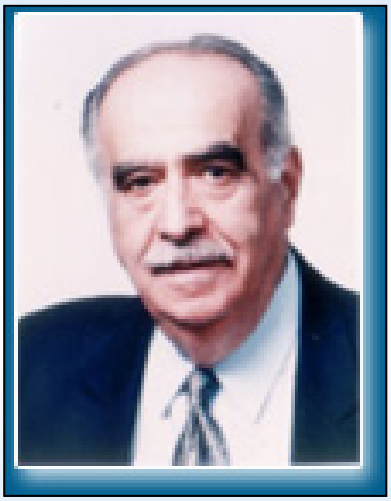
Labib Medical Center (LMC): Introduction

Labib Medical Center (LMC) is one of the leading hospitals in the Middle-East founded in 1974 by the late Dr. Labib Kamel Abouzahr. LMC is situated in the ancient Phoenician port of Sidon, the capital of South Lebanon.

Dr Labib Abouzahr Sr

Basic Medical and Surgical Training: American University of Beirut 1943
Surgical Specialty Training: Fordham Hospital, New York, USA
Chief Surgeon and CEO of LMC
Lasting legacy to the present day for having transformed the landscape of medical services in the Lebanon



Dr Labib Abouzahr Sr

Through the unrelenting efforts of Dr. Abouzahr and with the assistance of an eclectic group of highly qualified internationally trained physicians LMC grew from a 52 bed hospital in 1974 to a 125 bed hospital at present. Despite the fact that the number of inpatient beds in LMC is relatively small the range of specialties that are available at LMC is as broad as that of any tertiary center in the United Kingdom (see below).

Professor Labib Abouzahr Jr (son of the late Dr. Labib Abouzahr senior) is the CEO and chief of staff incumbent of LMC. Students who wish to undertake AESOP will be under the tutelage of Professor Abouzahr, who has a long and illustrious career as a medical educationalist in Canada (see below).

Professor Labib Abouzahr Jr

- MD degree American University of Beirut
- Residency training in General Surgery and Cardio-Thoracic Surgery at the University of Toronto
- Fellow of the Royal College of Physicians & Surgeons of Canada (FRCSC) with certification in General Surgery (1994) & Cardiothoracic Surgery (1997)
- Attending surgeon at Sunnybrook Health Sciences Centre & Lecturer at the University of Toronto, 1998-9
- Assistant Clinical Professor, McMaster University & Hamilton Health Sciences, 1999-2005
- CEO & Chief-of-Staff at Labib Medical Center (2005-)
- Founder and Chief of Cardio-Thoracic Surgery unit at Clemenceau Medical Center (Affiliated with Johns Hopkins International) (2005-)
- Teaching awards (for teaching students & residents) from University of Toronto & the Canadian association of General Surgeons

Professor Labib Abouzahr Jr

Mr Mouin Abouzahr is a graduate of the prestigious American University of Beirut and is the Admistrative Director of LMC. Mr Mouin is currently spearheading LMC's campaign to forge a Global Health partnership with a leading medical school in the United Kingdom.

Mr Hazem Badih FRCSi is a graduate of the Royal College of Surgeons of Ireland and consultant vascular surgeon. Mr Badih completed his specialist training in St Vincent's University Hospital in Ireland under the supervision of Professor Lord Ara Darzi. Mr Badih is also a potential supervisor medics on AESOP receive tutelage from.

The Abouzahr Elective Scheme of Phoenicia-AESOP

In keeping with LMC's mission statement of creating an environment that is conducive of education, the Abouzahr Elective Scheme of Phoenicia (AESOP) was launched in 2004 and has gone from strength to strength ever since its inception. AESOP was first conceived when I was in the Lebanon providing medical assistance to displaced, disenfranchised and destitute Palestinian patients in LMC.

After having been introduced to the CEO incumbent of LMC Professor Labib Abouzahr, arrangements were made to meet with him in Knightsbridge, London and it was during this meeting that I learnt a little more about the man behind the title. Professor Labib exudes serenity and panache and one cannot but feel a sense of calm when in his presence. He is cultured, erudite and his vivacity for life is communicable (Indeed it is these very attributes that make Professor Abouzahr the ideal elective supervisor to have). It was during this lively meeting that Professor Abouzahr cordially invited medics to complete their elective placements in his hospital.

The AESOP scheme provides medical students and junior doctors with accommodation in the hospital premises, daily meals and sponsorship to international academic conferences in the dazzling capital of Lebanon, Beirut. To date, six Manchester medics have been on the elective scheme in Lebanon and the feedback that we have received has been exceptionally positive (as evidenced below).

AESOP is currently available only to medical students registered in UK medical schools however plans are underway to expand this global health initiative to involve medical students from other parts of the world. Flights from England to Lebanon are in the range of £350-£450 and a direct flight is approximately five hours in duration. LMC is situated in the city of Sidon which is a 45 minute drive away from Beirut. British citizens can obtain a visa in Beirut International Airport free of charge; citizens from other countries must contact the Lebanese Embassy for Visa enquiries. AESOP provides students with clinical placements for up to four weeks in the following specialties:

Anesthesiology	Dermatology	Emergency Department
Cardiac Surgery	Critical Care Medicine	ENT
Cardiology	General Surgery	Gynecology
Colon & Rectal Surgery	Hematology	Infectious Diseases
Maxillo-Facial Surgery	Neonatology	Nephrology
Neurology	Neurosurgery	Obstetrics
Oncology	Ophthalmology	Orthopedic Surgery
Pathology	Pediatrics	Plastic Surgery
Radiology	Rheumatology	Thoracic Surgery
Urology	Vascular Surgery	

Qualitative Testimonial on the Elective Scheme in Lebanon

"*We had such an amazing experience … an NHS trained consultant paediatrician, spent most mornings providing us one-to-one teaching in his private clinic on common presentations in the neonate.. We also got to see rare conditions we had only ever read of, such as leishmaniasis*

...However, we did not leave Lebanon without seeing the beauty and splendour of the country & people. Our hosts proved to be the most hospitable people we could have ever hoped for.

All in all, it was definitely a life changing experience, where I met people with the kindest of hearts & I owe a lot to the organisers for making the experience worthwhile!"

Dr Javeria Khan, CT1 Doctor

Conclusion

AESOP is ideal for those medics who wish to conduct their elective placements in the vibrant country of Lebanon however in a hospital that is outside the hustle and the bustle of Beirut. Despite the fact that LMC is not in the capital city, the services that are rendered and the facilities that are available contend with leading hospitals in Lebanon's largest city. The city of Sidon itself is peaceful yet there is always something to do be it paying a trip to the ancient Crusader Castle, or mingling with the natives in the interminable streets of the old souks. Add on top of that LMC's friendly and hospitable environment, AESOP is a learning opportunity medics really can't afford to miss.

In order to register your interest in AESOP or for any further information, please don't hesitate to contact me: ahmedzakaria@doctors.org.uk

LMC website: http://www.labibmedicalcenter.com/

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An Introduction to Cardiology

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Introducing Cardiology...

Cardiology is an exciting and highly competitive branch of medicine which is concerned with the identification, assessment and management of diseases affecting the heart and blood vessels. Therefore, an in-depth knowledge of the pathological processes and cardiovascular physiology and pharmacology are required for those wishing to proceed in this rapidly evolving speciality.

Cardiology is at the very forefront of cutting-edge research. This is especially true for interventional cardiologists where increasing numbers of new techniques are becoming available for the treatment of cardiac diseases, such as coronary artery stenting and percutaneous valve replacement.

Life as a Cardiologist

The variety in the cardiology workload ranges from highly acute, life-threatening illnesses such as myocardial infarctions and dangerous cardiac arrhythmias, to chronic diseases such as cardiac failure. Likewise, cardiology encompasses all ages from pre-natal management to the provision of end-of-life care.

Due to the wide variety of patients seen in this speciality, the workload of the cardiologist is highly dependent on the type of services provided by a centre and the specialist interests of that individual. Many cardiologists will sub-specialise, with some of the largest areas including congenital heart disease, interventional cardiology, heart failure, cardiac devices, electrophysiology and cardiac imaging. In larger centres, there may be opportunities to further sub-specialise within a sub-specialty.

The amount of elective and emergency work varies depending on the centre and sub-specialisation. With current NICE recommendations stating that ST-elevation myocardial infarctions should undergo primary percutaneous intervention, interventional cardiologists in an acute centre should expect to do increasing amounts of on-call. This is in comparison to electrophysiologists, who may find their on-call workload slightly less demanding.

A typical day is likely to vary in accordance with an individual job plan but cardiologists are involved with acute take of cardiology emergencies, out-patient clinics and in-patient reviews. It should be noted that cardiologists do not work alone and must liaise within a multi-disciplinary team, including cardiac physiologists, nurses, cardiac surgeons, anaesthetists and GPs in order to maximise patient management.

Despite the large workload, cardiology can be a highly rewarding speciality which enables doctors to make a marked difference to patients' mortality and quality of life.

Facts and Figures

Candidates for ST3 cardiology must first complete two years of core medical training or acute care common stem, during which time they must pass their membership examinations for the Royal College of Physicians.

ST3 competition for cardiology is the highest of any medical speciality with 6.46 applicants to each post in 2011. Due to the high level of competition, it is sometimes recommended that potential applicants should do a higher post graduate degree such as an MD or PhD.

From ST3-ST5 cardiology trainees are required to obtain the core competencies as part of teams at both district general hospitals and specialist centres e.g. echocardiography, cardiac catheterisation and pacing. Trainees may also elect to train in cardiology and general internal medicine combined and provision is made for this in the training programme.

ST6-ST7 trainees will undertake general cardiology work in conjunction with advanced specialist modules of their choice.This includes options such as Interventional Cardiology, Electrophysiology, Non-invasive Imaging, Adult Congenital Heart Disease or Heart Failure.

The Future

The continuing emergence of new catheter technologies continues to move cardiology in to a new age. NICE is in the process of assessing a new technique to treat aortic stenosis which involves trans-catheter aortic valve implantation. This new procedure would allow patients who are at too much risk to undergo surgery, to receive vital treatment for a condition that would otherwise impact significantly on the patient's quality of life.

Advancement in the field of heart failure management including technological advances in implanted cardiac devices and mechanical assistance devices will undoubtedly benefit the growing number of elderly people suffering from cardiac failure. We also look forward to the exciting new research into cardiac cell therapy in the form of cultured autologous myoblasts injections into the myocardium and the use of autologous bone-marrow derived stem-cells. The continuing quantum leaps in cardiology make this speciality perhaps one of the most enticing areas in the medical profession to pursue.

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An Introduction to Cardiothoracic Surgery

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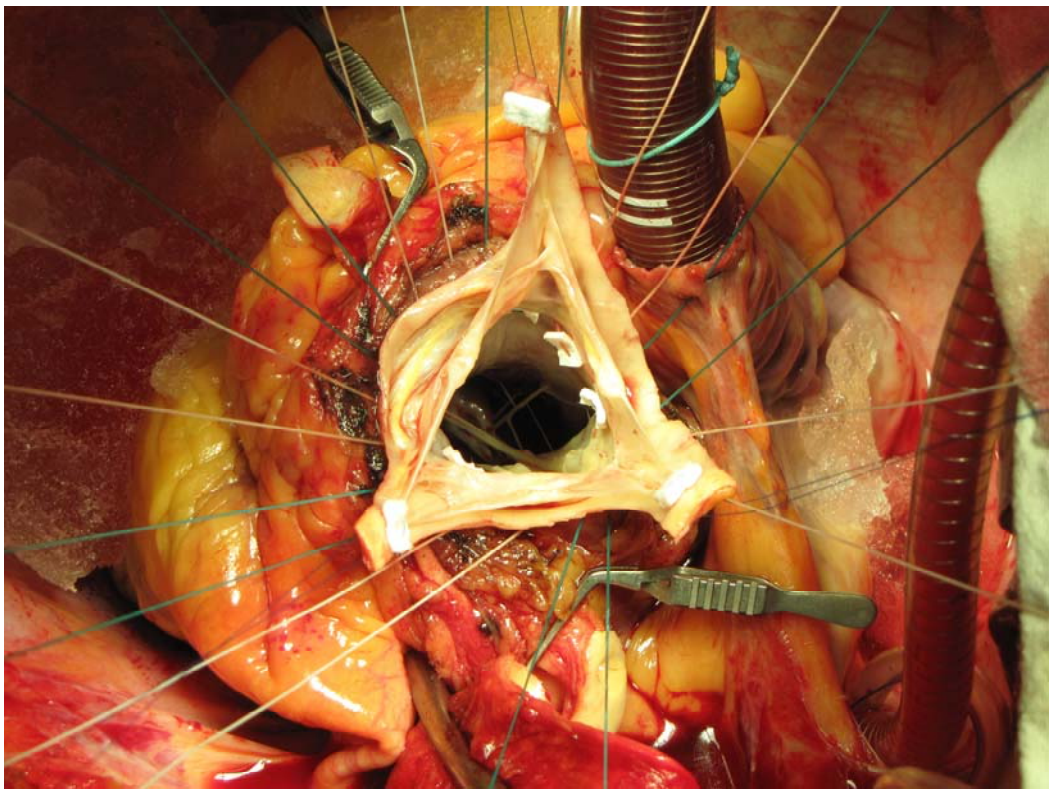


Introducing Cardiothoracic Surgery…

Cardiothoracic surgery is an exciting and challenging surgical speciality which provides treatment of diseases affecting the heart and lungs and, in some centres, the oesophagus.

The first successful cardiac operation was in 1953 and since then cardiac surgery has rapidly expanded to include numerous operations. The most common operations include coronary artery bypass grafting (CABG), valve replacement or repair, pneumonectomy and lobectomy.

In this specialty, life and death tread on a thin wire. There is nothing minor about complications, so there is a great deal of focus on improving the safety of the surgery. Cardiothoracic surgery is not just a specialty but a lifestyle that requires commitment, physical dexterity and mental strength, and requires sacrifices throughout in order to perform the long and frequently complex operations.

Life as a Cardiothoracic Surgeon

A day in cardiac surgery begins from the previous day. In simple terms, it does not end! Surgeons start the night before by reviewing their patients and are expected to go through their patients as thoroughly as possible, despite having seen them in clinic. On a typical operating day itself, surgeons would start with reviewing in-patients on the ward. The ward rounds are short, precise and focussed.

Due to the length of the operations, patients will typically be sent for early in the morning and will often be in the anaesthetic room by 8am. During this time it is important for surgeons to be available in the unlikely event that they quickly decompensate in the anaesthetic room and emergency cardiopulmonary bypass needs to be implemented.

Operating time varies from operation to operation and team to team, but an average CABG may take four to six hours. Cardiac surgery is a team based effort with surgeon as the lead and with ultimate responsibility for the outcome. However, it is a busy theatre and on a standard day there will be at least seven people in attendance including theatre nurses, anaesthetists and perfusionists who operate the cardiopulmonary bypass machine. Typically, two operations will be performed in the day.

Following their surgery, patients must be assessed in the intensive care unit which is run in conjunction with anaesthetists. Pre-operative patients for the following day must then be reviewed on the wards. The days are often long and finishing times may be highly variable but the work can be highly rewarding for those involved. This is because cardiac operations have been shown to increase survival for a given set of clinical conditions.

In general, operations are elective but there is still some emergency work and in-patients may need to be re-opened should there be a complication. Due to the specialist expertise required should a cardiac surgery patient deteriorate, a senior registrar is always resident on site and will be responsible for all patients in intensive care, the ward and emergency setting. The on-calls are about 1:7 as a registrar and consultant.

Although cardiothoracic surgeons will frequently perform just a few operations on a regular basis, the different surgeries performed over a career will be wide and varied. There are also options for sub specialisation including aortic surgery, transplantation (including of artificial hearts), congenital cardiac surgery and oesophageal surgery.

In addition to operating days and on-call, a cardiac surgeon will also be involved with seeing post-operative patients and potential pre-operative patients in outpatient clinics. The surgeon's attendance is also required in multi-disciplinary discussions with interventional and non-interventional cardiologists.

Thoracic surgery life style is more sedate and family friendly compared to cardiac surgery. Out of hours calls as a registrar and consultant are minimal and the on-calls as a registrar in pure thoracic centres are non-resident. Most of the thoracic on-call work is related to trauma. Oesophageal surgery, which constituted a major bulk of thoracic surgery, has partly moved to upper gastrointestinal teams but is still done in some thoracic units.

In addition to on-calls thoracic surgeons must see patients in pre-operative clinics and liaise with a multi-disciplinary team including physicians, radiologists and oncologists.

Thoracic private practice has increased over the years whilst cardiac has steadily declined but does still remain. There is also scope to work abroad with the North American association of thoracic surgeons who are predicting a significant shortage of cardiothoracic surgeons by 2015-2016. UK-trained cardiac surgeons are often in high demand internationally.

Training

Cardiothoracic surgery is a highly competitive speciality. Potential cardiothoracic surgeons must compete for core surgical training posts prior to advancing to specialist training. In 2010, there were 22 ST3 posts in the UK, with 6 applications per post.

Training in thoracic surgery is coupled with cardiac surgery, and requires a minimum of two years of cardiac surgery and 4 years of thoracic surgery. The choice in choosing a pure thoracic theme comes early in the career and the training is themed accordingly. The examination for fellowship for thoracic surgery is the same as cardiac but is set to become uncoupled in the years to come.

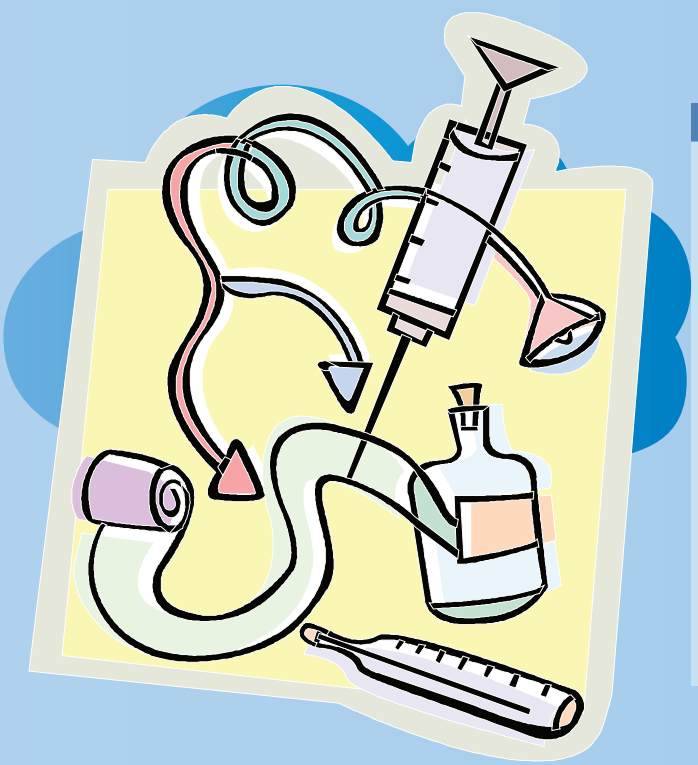
The Future

In the UK and North America, cardiothoracic training has always been coupled together. However, with time, recent advancements in lung malignancy and increasing volumes of work, thoracic surgery has established itself as an entity, so that more and more units are recruiting specialist thoracic surgeons.

Cardiac surgery has rapidly evolved over the past 50 years. Two exciting developments in cardiac surgery include minimally invasive cardiac surgery and the transplantation of artificial hearts. Minimally invasive surgery has been performed routinely in other surgical specialities for some time e.g. laparoscopic and arthroscopic work. It is now starting to be utilised in cardiac surgery as well. Most notably it has been utilised for mitral valve replacements and CABGs.

Fewer hearts are available for organ transplantation at a time when heart failure is increasingly prevalent. Artificial hearts cannot, as yet, fully replace the function of the heart in the long term but have been used as a bridge prior to transplantation. The use of these mechanical hearts and the ability to maintain life is an exciting new development in cardiothoracic surgery.

Test your knowledge with **WJMER** quarterly quiz…



Theme: Upper Gastrointestinal Surgery

Question

A 45-year-old gentleman is brought into the Emergency Department with severe abdominal pain. He reports going to a stag party and consuming in excess of 45 units of alcohol. The pain is in the epigastric region, excruciating (10/10 in severity) and is associated with nausea and vomiting.

For the clinical scenario described above, choose the LEAST appropriate investigation to assess the severity of disease:

A. Serum amylase
B. Serum calcium
C. Blood glucose
D. Age
E. White cell count

Theme: General surgery

Question

A 13-year-old boy presents with sudden-onset, severe pain in his left testicle radiating to the lower abdomen, and vomiting. On examination, the left testicle is swollen, erythematous and lying in a transverse plane, slightly higher than the right testicle. It is exquisitely tender to palpation.

For the clinical scenario described above, choose the most appropriate diagnosis:

A. Epididymo-orchitis
B. Testicular torsion
C. Strangulated inguinoscrotal hernia
D. Varicocoele
E. Testicular haematoma

Test your knowledge with WJMER quarterly quiz…

Theme: Upper Gastrointestinal Surgery

Answer: See below

Explanation

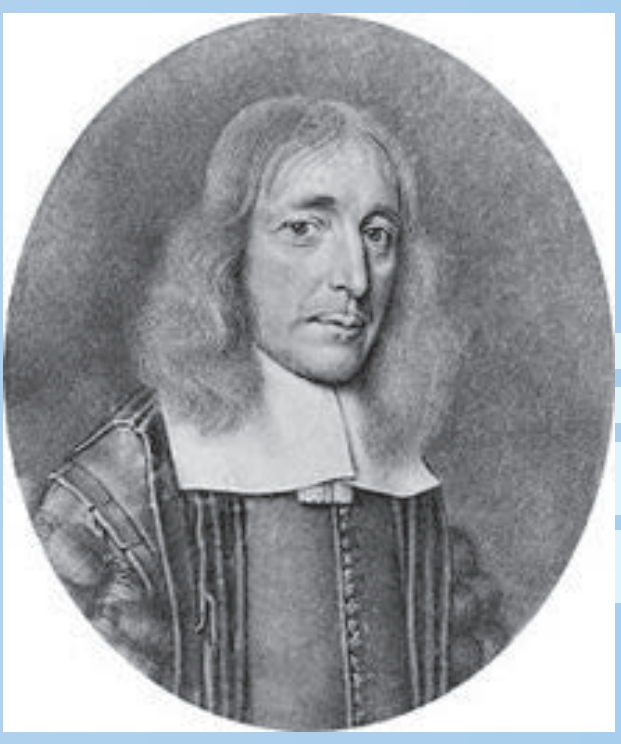
This patient presents with acute pancreatitis secondary to alcohol intoxication. Although amylase is useful in the diagnosis of pan-creatitis, it is not useful for assessment of its severity. A useful mnemonic for markers of severity in pancreatitis is : PANCREAS (P – PaO2 < 8kPa, A – Age > 55 years, N – Neutrophils > 15 x 10^9/L, C – Corrected calcium < 2 mmol/L, R – Raised urea > 15 mmol/L, E – Elevated LDH > 600 iu/L, A – Albumin < 30 g/L, S – Sugar(BM) < 10 mmol/L). If 3 or more of the criteria are satisfied, the episode of pancreatitis is labelled as severe. The above features make up the Glasgow criteria which are valid only after 24-48 hours after onset of symptoms. Alternatively, severity scores such as APACHE II can be used prior to 24 hours.

Theme: General Surgery

Answer: See below

Explanation

Sudden-onset and swelling in the testicle is strongly suggestive of testicular torsion in a patient of this age – it is a surgical emergency not to be missed. Pain may be referred to the groin and lower abdomen (due to involvement of the T10 nerve, which sup-plies the lower abdomen as well as the testes), along with nausea and vomiting. The torsion occurs around the spermatic cord when there is an anatomically abnormal and may follow a history of mild trauma. An example of such anatomical anomaly is the 'bell-clapper' testis, where the testicle is not anchored to the scrotum posteriorly by the gubernaculums ligament (as it normally is), leaving it to swing freely like the 'clapper of a bell'. In torsion, the testis may be high-riding and lying transversely within the scrotum, although this may not always be apparent. Irreversible infarction of a twisted testicle occurs within 6-12 hours; so af-fected patients should be taken to theatre for surgical exploration without further investigation. Surgery involves untwisting of the testicle and bilateral fixation (orchidopexy) of the testes to the tunica vaginalis to prevent further torsion. Bilateral fixation is advocated as anatomical anomalies of the testes that predispose to torsion usually occur bilaterally.



Who is this famous anatomist?

Hint 1: Born in 1621

Hint 2: Was the founding member of the early Royal Society

Hint 3: He was a pioneer research into the anatomy of the brain, nervous system and muscles

Hint 4: He is associated with the circle of arteries that supply blood to the brain and the surrounding structures

Answers: SBA 1 - **A**, 2 - **B**; Famous Faces: **Thomas Willis** (as in Circle of Willis)

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