



*Special Edition*

# WJMER

World Journal of Medical Education and Research

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

## Abstracts from Doctors Academy Events:

'Winner of Winners' presentations -  
5<sup>th</sup> International Medical Summer School, 2013

3<sup>rd</sup> International Academic and Research Conference, 2013

- Dental-derived Stem Cells and Whole Tooth Regeneration: An Overview

- A Career in Child and Adolescent Psychiatry

- Post Operative Surgical Care



- Ulceration of the Lower Limb: An Introduction to Medical and Surgical Intervention



## Selected best articles from 2012-13

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

Stem Cell Treatments for Huntington's Disease

Operating Theatre: Essential Concepts and Procedures

The Use of Geometric Morphometrics as a New Method to Analyse Glenoid Bone Loss after Shoulder Dislocation

Role of Cloud Computing in the Provision of Healthcare

Management of Major Trauma: A Malaysian Perspective



### Introduction

The World Journal of Medical Education and Research (WJMER) (ISSN 2052-1715) is an online publication of the Doctors Academy Group of Educational Establishments. Published on a quarterly basis, the aim of the journal is to promote academia and research amongst members of the multi-disciplinary healthcare team including doctors, dentists, scientists, and students of these specialties from around 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. We envisage an incessant stream of information flowing 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 editions. We are honoured to welcome you to WJMER.

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Doctors Academy has an online repository consisting of 100s of questions with correct answers & detailed explanations for questions in multiple choice, extended matching, single best answer and short answer formats. In addition, there are questions and answers related to clinical images, radiology, osteology and data interpretation. Other useful resources include applied surgical anatomy, focused clinical history and examinations, and a quick exam revision guide. Candidates can also view numerous clinical presentations and watch videos of many clinical examinations and skills. Mock exams with feedback of the performance will provide the candidates with a focussed revision of the topics. The questions, written by an experienced group of clinicians and clinical academics from Doctors Academy, are based on past exams and have been carefully created and formatted to suit the requirements of undergraduate medical and dental students, doctors appearing for entrance and medical licensing exams, and postgraduate trainees undertaking relevant speciality exams.

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## WELCOME

We are delighted to bring you the *Special Edition (2013)* of the World Journal of Medical Education and Research (WJMER) as a print version. We are pleased and humbled to inform our readers that we have successfully brought out three quarterly issues since its launch last year and this special edition is intended to both celebrate this success as well as provide the readers with the abstracts from our flagship annual conference.

This edition proudly brings to you an array of selected articles that include the complexities and promises offered by dental stem cell research, an insight into the intriguing world of child and adolescent psychiatry, and career options in pathology and psychiatry. Articles about post-operative care and management of lower limb ulceration will be educational for the students and young doctors, whilst also informing the experienced clinicians on current practices.

The carefully chosen articles from 2012 to 2013 include Stem Cell Treatments for Huntington's Disease and Antigen Microarrays for Rapid Screening of Autoimmune Diseases. In keeping with the ethos of WJMER in promoting the global transfer of knowledge, we have also included a highly informative and instructive article on trauma management from Kedah, Malaysia, that aims to encourage the reader to reflect on, among other matters, first principles and the universality of medical knowledge.

We have incorporated within this edition the top abstracts from the prestigious *Future Excellence 3<sup>rd</sup>* International Academic and Research Conference (IARC) 2013, Manchester, United Kingdom. The conference under the auspices of Doctors Academy, supported by University of Sheffield and Royal College of Physicians and Surgeons of Glasgow, provide a unique platform for junior doctors and medical students to share interesting clinical observations and innovative ideas with fellow colleagues, and encourage exchange of information and the transfer of knowledge from all corners of the globe. A total of 470 abstracts were submitted, and after several rigorous rounds of judging by a mix of senior clinicians and scientists from all over the UK, a handful was selected to present their work.

We hope that you find this edition informative and enjoyable to read.

With very best wishes,

**Ms. Karen Au-Yeung, BSc (Hons), MB BCH, MRCS**

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## Table of Contents

Introduction	<b>i</b>
Welcome	<b>ii</b>
Table of Contents	<b>1</b>
Antigen Microarrays for Rapid Screening of Rheumatoid Arthritis and Other Autoimmune Diseases Ms. Sophie Wing	<b>3-10</b>
Stem Cell Treatments for Huntington's Disease Dr. Jason Seewoodhary	<b>11-13</b>
Operating Theatre: Essential Concepts and Procedures Mr. Karl Walsh, Dr. Jemma Boyle	<b>14-27</b>
The Use of Geometric Morphometrics as a New Method to Analyse Glenoid Bone Loss after Shoulder Dislocation Mr. Thomas Key, Professor Lennard Funk	<b>28-34</b>
Role of Cloud Computing in the Provision of Healthcare Ms. Anusha Bamini, Professor Sharmini Enoch	<b>35-38</b>
Management of Major Trauma: A Malaysian Perspective Dr. Kashfil Tengku, Dr. Narisa Damanhuri, Dr. Jazree Jamaluddin	<b>39-52</b>
Dental-derived Stem Cells and Whole Tooth Regeneration: An Overview Dr. Prashant Chetal, Dr. Pratima Bhutani, Dr. Deepak Bhutani, Dr. B.R Chetal	<b>53-56</b>
A Career in Child and Adolescent Psychiatry Dr. Kiruthika Sivasubramanian	<b>57-59</b>
Ulceration of the Lower Limb: An Introduction to Medical and Surgical Intervention Ms. Natalie M Roberts, Ms Karen Au-Yeung	<b>60-65</b>
An Introduction to a Career in Psychiatry Ms. Mayura Damanhuri, Dr. Neel Halder	<b>66-67</b>
Post Operative Surgical Care Ms. Naima Poonja, Miss Laura Derbyshire	<b>68-74</b>
Introducing a Career in Pathology Mr. Gursevak Singh, Dr. Anne Marie Kelly	<b>75-76</b>
Abstracts from The International Academic and Research Conference	<b>77-146</b>



# The Royal College of Surgeons of Edinburgh Future Surgeons: Key Skills

For Medical Students & Foundation Year Trainees

26<sup>th</sup> October (Saturday) 2013, 27<sup>th</sup> October (Sunday) 2013,  
25<sup>th</sup> January (Saturday) 2014, 29<sup>th</sup> March (Saturday) 2014,  
31<sup>st</sup> May (Saturday) 2014, 25<sup>th</sup> October (Saturday) 2014  
Christie Hospital, Manchester

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- » Practical course with a high tutor-to-participant ratio
- » Delivered using a series of tutor demonstrations and hands-on sessions where participants work on animal tissue
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## Best Six Articles from 2012-2013 (Article - 1)

## Antigen Microarrays for Rapid Screening of Rheumatoid Arthritis and Other Autoimmune Diseases

**Ms. Sophie Wing**

Final Year Medical Student

Department of Immunology, Queen's Medical Centre, Nottingham

*Address for correspondence:*Ms. Sophie Wing: [mzyicsw@nottingham.ac.uk](mailto:mzyicsw@nottingham.ac.uk)**INTRODUCTION****Rheumatoid Arthritis**

Rheumatoid Arthritis (RA) is a chronic and extremely disabling disease, primarily characterised by extensive synovial inflammatory attack, leading to progressive autoimmune destruction of cartilage, ligaments and occasionally bone<sup>1-4</sup>. Approximately 580,000 patients in England and Wales suffer from this multi-factorial disease<sup>2</sup>, costing the UK an estimated £3.8-4.75 billion per annum<sup>4,5</sup>. As the complexity of the disease aetiology is still relatively unidentified, the disease remains incurable<sup>6</sup>.

**Diagnosis**

In 2009, NICE guidelines advocated the importance of early RA diagnosis, as Disease Modifying Anti-Rheumatic Drugs (DMARDs) significantly enhance prognosis if started early in disease progression<sup>4</sup>. This led to the 2010 American College of Rheumatology diagnostic criteria<sup>7</sup>, as previous 1987 criteria depended heavily upon clinical presentation, which is equivocal in early stages<sup>8,9</sup>. It also relied upon detection of Rheumatoid Factor (RF)<sup>9,10</sup> that, despite being highly sensitive, is poorly specific. (Approximately 60% of Sjögren's Syndrome patients and 5% of healthy populations are sero-positive<sup>3,11</sup>.) Hence, novel laboratory diagnostic techniques evolved with a greater sensitivity, specificity and ability to detect RA before irreversible joint destruction occurs<sup>3,12</sup>.

A prime example is testing for anti-citrullinated protein antibodies (ACPA) against a synthetic peptide termed cyclic citrullinated peptide (CCP). These are well recognised serological markers of RA presenting years before symptom onset<sup>13</sup>, and are virtually absent in healthy individuals and other rheumatic diseases<sup>14</sup>: this is because inflammatory processes in RA release Peptidylarginine Deiminase (PAD) enzyme into the synovium. PAD converts arginine subunits of membrane proteins into citrulline and researchers believe this post-translational modification alters protein antigenicity, triggering autoimmune processes<sup>8</sup>.

Research is currently investigating the spectrum of citrullinated proteins involved in pathogenesis and their relationship with certain ACPA isotypes and classes/subclasses<sup>11,15-18</sup>.

Recent ACPA ELISAs have the ability to be, as a minimum, equal to RF sensitivity (82%) with an even greater specificity (98%)<sup>11</sup>. Consequently, ACPA assays have emerged as a superior diagnostic test to RF and have been incorporated into the 2010 American College of Rheumatology criteria<sup>7,19</sup>. However, current ELISA techniques limit the possibility of screening worldwide arthritis populations for all ACPA isotypes and specificities, due to time-scales and costing. For this reason, there is emerging potential to develop an improved technique with this capability.

**Protein Microarrays**

Advances in technology have brought protein microarrays to the forefront as a validated method of autoantibody detection and have so far shown very promising results<sup>16,20,21</sup>. They can simultaneously detect multiple autoantibodies and ACPA isotypes in a single assay, whilst maintaining similar sensitivities and specificities to current ELISA methods<sup>22</sup>. By aiding diagnosis and management, monitoring response to therapeutics and identifying disease subgroups or novel autoantigens<sup>21</sup>, microarray potential in the world of immunology is far superior to current methods.

**Research Proposal**

The project aim is to investigate a new method of screening for autoantibodies in the serum of autoimmune patients, including RA, to aid patient categorisation.

Protein microarrays will particularly assess the significance of known autoantigens, second generation cyclic citrullinated peptides (CCP2), citrullinated proteins and their non-citrullinated counterparts. Antigens will be robotically printed onto microscope slides alongside

control proteins. The assays will screen donated patient sera for autoantibodies and, in terms of RA, the project will hope to observe ACPA in patient sera. Only a tiny volume of patient serum (less than 5µl, compared to 5ml required with ELISA21) will be required to simultaneously screen for autoimmunity against a wide range of autoantigens.

### Objectives

- 1) To analyse protein microassay potential of diagnosing RA in early stages.
- 2) To determine whether protein microarrays can provide useful information in other autoimmune conditions.
- 3) To establish the possibility of creating biomarker profiles that relate to disease severity, course and prognosis.
- 4) To discover if protein microarrays have the ability to classify patients into disease subgroups.

### EXPERIMENTAL PROCEDURES

#### Chemicals and Reagents

All chemicals and reagents used in the following experiments were purchased from SIGMA ALDRICH CHEMISTRY®, USA and stored at room temperature, unless otherwise stated. Experiments were also carried out at room temperature, unless otherwise stated.

#### Antigens

CCP2 was printed in both PBS and in Dimethyl Sulfoxide (DMSO) solvent to aid correct peptide formation, along with a range of citrullinated proteins and their non-citrullinated counterparts. Citrullination was performed prior to this study.

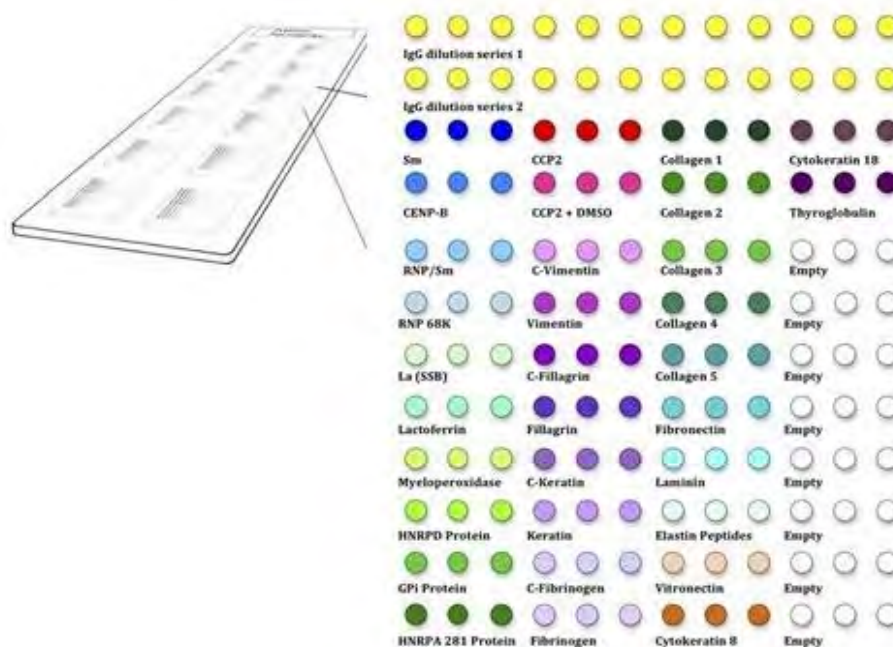
Various other antigens covering a wide range of autoimmune diseases were also printed alongside putative Chronic Obstructive Pulmonary Disease (COPD) biomarkers - as both COPD and RA are linked with smoking, it has been questioned whether COPD biomarkers act as autoantigens in RA<sup>11</sup>(Figure 1).

Stock antigen samples were diluted using a 5 times stock solution of PBS-Trehalose-Tween20 buffer (0.5mls PBS, 0.5mls Trehalose and 2µl Tween20) to give 10 µl of a of 0.1µg/µl concentration. Samples with unknown stock concentrations were assumed to be at a concentration of 1mg/ml, and samples with very weak stock concentrations were not diluted. Calculations were produced to ensure the buffer used in every sample was at a 1 times concentration.

#### Printing Proteins

Each sample was transferred into a 384 well microtitre plate and printed onto PVDF coated slides by means of a Genomic Solutions Microgrid II 610 Arrayer with use of a silicon PETC (partially etched through channel) pin (PARALLEL SYNTHESIS TECHNOLOGIES, USA). Three triplicate spots of autoantigens were printed in each grid to monitor reproducibility. Two rows of a 2-fold serial dilution of human IgG (with the same diluent and buffer as above) were also printed per grid to serve as a positive control.

In each case, proteins were robotically printed in a 12x12 grid with each spot approximately 150 microns in diameter. Sixteen identical grids (roughly 6x6mm each) were printed onto each slide in an 8x2 array (Figure 1).



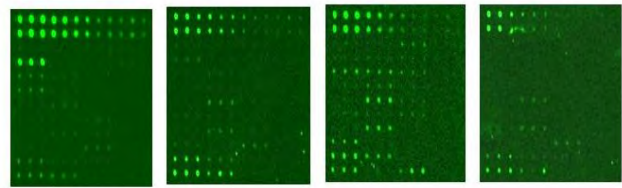
**Figure 1:** Autoantigens were printed in 12 X 12 squares, in the adjacent format, onto PVDF-coated slides using a microarrayer

### Probing Slides

- 1) Slides were inserted into a Grace-BioLabs 16-well plastic slide gasket
- 2) One hundred micro litre (100µl) of 0.2% I-block (0.05 grams of I-block pellets dissolved in 25mls of Phosphate Buffered Saline-Tween 20[PBS-Tween]; stored in a fridge) was added to each well [NB. A 1 litre stock solution of PBS-Tween was previously prepared using 10 PBS tablets dissolved in 1 litre of distilled water and 500µl of 100% Tween20].
- 3) Slides were covered with cling-film and left to shake for 1 hour at room temperature
- 4) Each well was washed with PBS-Tween 3 times, each for 5 minutes
- 5) One hundred micro litre (100µl) of patient serum (1:100 with Antibody Diluent) was added to each well
- 6) Slides were covered with cling-film and left to shake for 1 hour
- 7) Each well was washed with PBS-Tween 3 times, each for 5 minutes
- 8) One hundred micro litre (100µl) of biotinylated anti-human IgG antibody (1:1000 in Antibody Diluent) was added to each well
- 9) Slides were covered with cling-film and left to shake overnight in a coldroom at 4°C
- 10) Each well was washed with PBS-Tween 3 times, each for 5 minutes
- 11) One hundred micro litre (100µl) of Streptavidin-IR780 (1:5000 in PBS-Tween) was added to each well
- 12) Slides were covered with silver foil and left to shake for 30 minutes
- 13) Each well was washed with PBS-Tween 3 times, each for 5 minutes
- 14) Slides were briefly washed with distilled water, immediately dried with dry nitrogen gas and scanned using a Licor Odyssey Infrared Scanner (School of Biomedical Sciences) to obtain digital images for analysis
- 15) Primary data acquisition (spot identification, feature and background measurements) was performed using Molecular Devices Genepix Pro V6.25 software within the Post-Genomic Technologies Facility, A floor, West Block, QMC

### Patient Serum

Thirty patient sera samples were probed onto two PVDF coated slides. The samples encompassed a wide range of autoimmune diseases, including the same patient over time, whilst receiving treatment and during a flare of symptoms. Three RA, 11 SLE, three Palindromic Arthritis (PA), two Scleroderma, two Myositis, four Wegener's Granulomatosis and five Sjögren's Syndrome samples were tested (**Figure 2**). Wells 15 and 16 on one of the slides were probed with I-block instead of primary antibody to serve as control wells.



**Figure 2:** Florescent images obtained from Sera Test. Reading left to right, images obtained were from 0946 Scleroderma, 0954 SLE, 1071 Palindromic Arthritis and 0934 RA sera samples. Refer to **Figure 2** for a layout of autoantigens.

### Analysis

Graphs were created using Prism 5.04 (GraphPad Prism Inc)<sup>23</sup>. Comparison of sample profiles was undertaken using MeV 4.6 (Institute for Genome Research)<sup>24</sup>. Due to the small number of samples available, statistical analytical methods were limited. Hierarchical Clustering Algorithms using Pearson's Correlation were successfully created to determine the propensity of samples from similar disease diagnoses to cluster together.

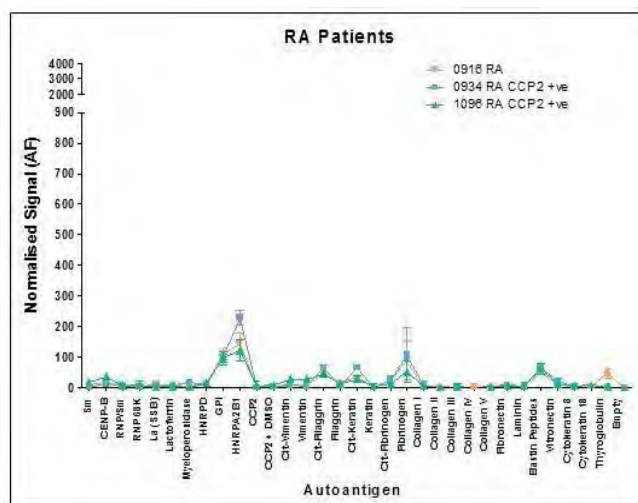
### RESULTS

#### IgG Dilution Series

Signals were detected consistently and as expected with the IgG dilution series, validating the techniques and methods used.

#### Sera Test

Of the three RA samples tested (**Figure 3**), results obtained suggested negligible autoantibody titres throughout. CCP2 peptides produced weak signals, despite two samples known to be CCP2 positive. Subsequent testing later indicated that the CCP2 peptide



**Figure 3**



did not bind successfully onto the PVDF slides, limiting analysis potential. Small signals were obtained with citrullinated Filaggrin and Keratin, yet not with citrullinated Fibrinogen or Vimentin. In relation to the putative COPD biomarkers, low signals were obtained.

PA patients appeared to have similar autoantibodies to RA, but to different citrullinated proteins (Vimentin, Keratin and Fibrinogen) and with higher autoantibody titres (Figure 4). As PA is associated with ACPA<sup>25</sup>, comparing Graphs A and B may suggest that PA is serologically more reactive than RA, yet similar in terms of autoantibody targets.

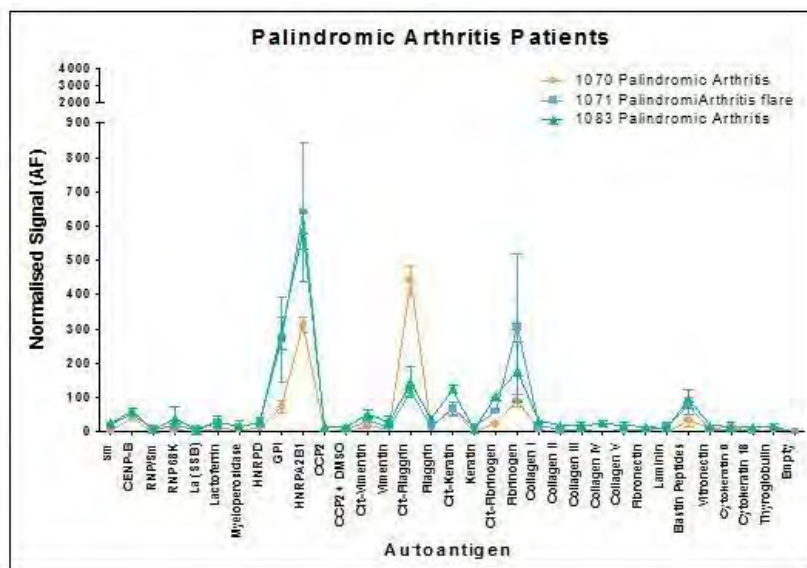


Figure 4

Autoantibody responses were largely similar between the two Scleroderma patients (Figure 5).

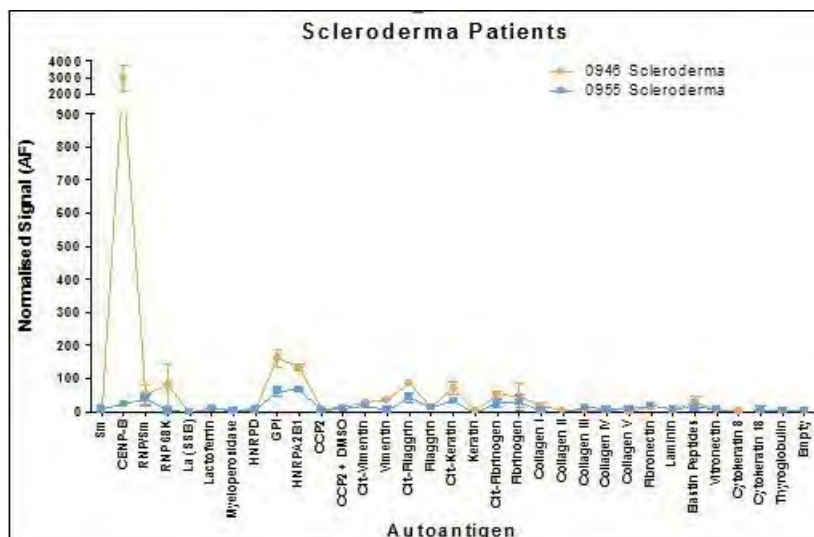


Figure 5

SLE responses (Figure 6 and 7) are much more varied between individual patients than all other diseases tested. As expected, RNP/Sm, RNP 68K and La(SSB) gave several high signal values<sup>26</sup>. Samples 0903 and 0954 were taken from the same patient over time and results demonstrate a 2-fold increase in autoantibodies to Cytokeratin 8. In total, three patients with alleged inactive forms were tested: sample 1067 had relatively low signal values across the range of autoantigens, whereas the remaining two samples (0903 and 0918) had comparatively high signal values. When comparing sample 0903 with an active sample taken from the same patient (0954), it is clear that inactive signal intensities are far smaller than in the active sample. This highlights the relationship between autoantibody titre and clinical presentation in SLE.

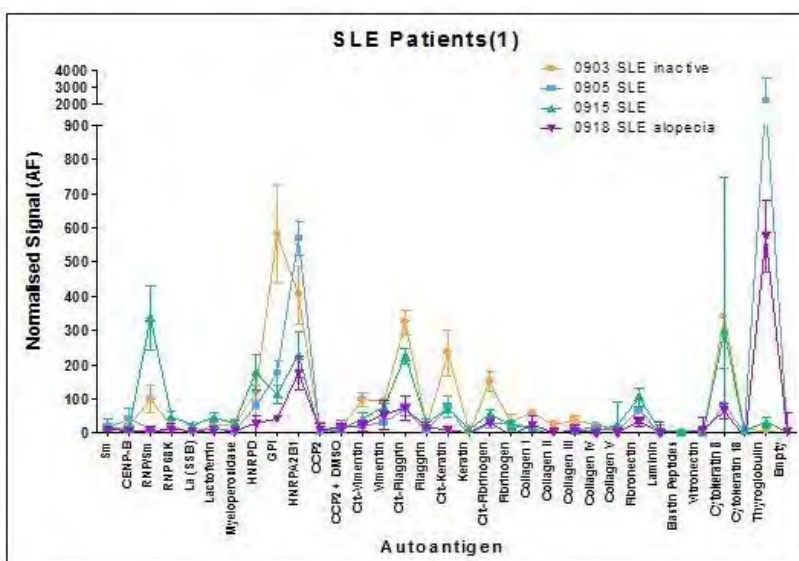


Figure 6

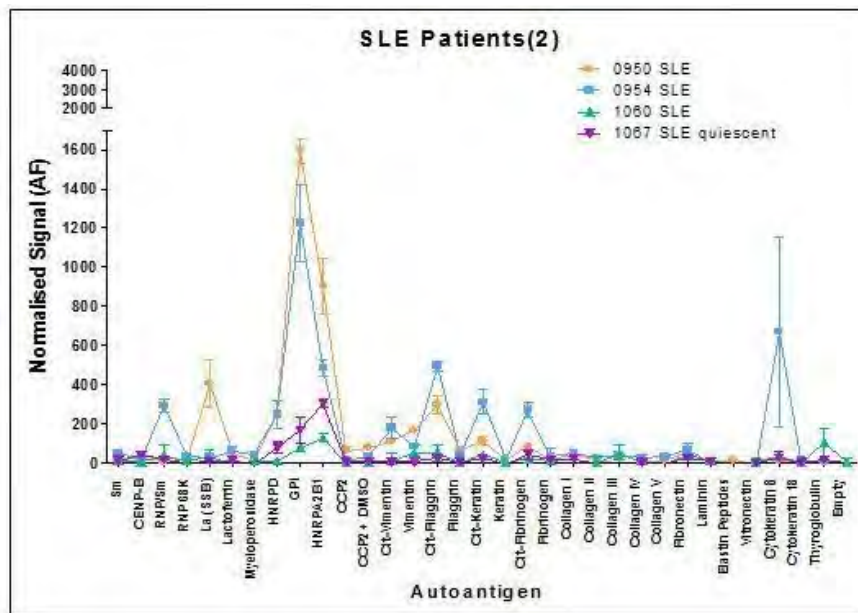


Figure 7

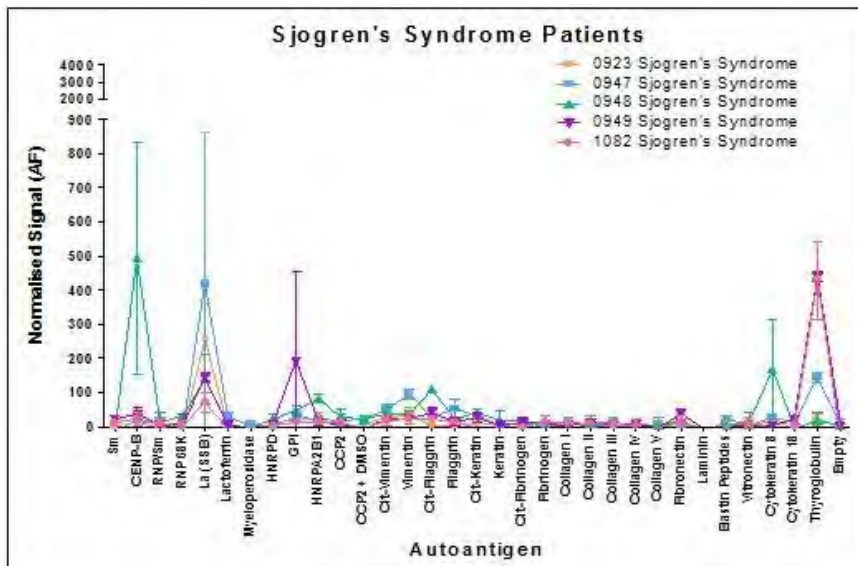


Figure 8

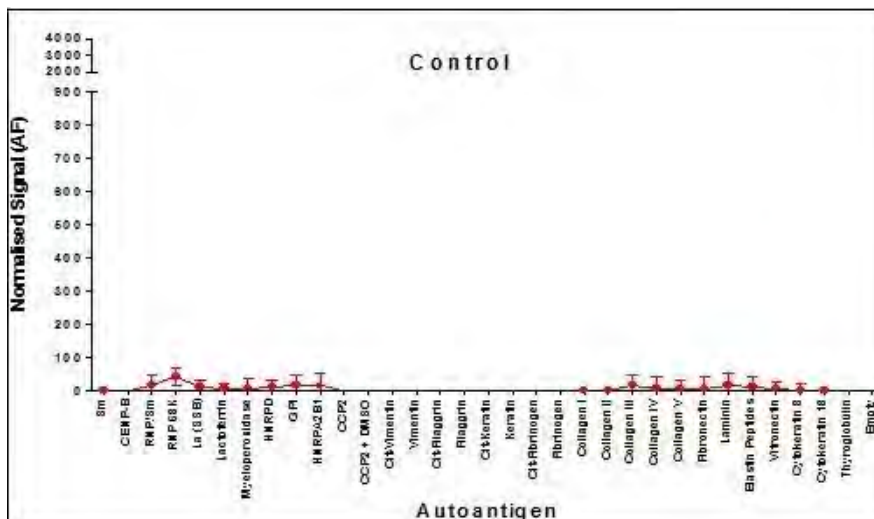


Figure 9

Sjögren's Syndrome data (Figure 8) also illustrates variation between individual patients. As evidence suggests<sup>2,6</sup>, autoantibodies were present against both CENP-B and La(SSB), yet signals were absent against RNP/Sm or RNP/68K.

Figure 9 demonstrates the very small signals generated in the absence of primary antibody. Consequently, any signals above 1 standard deviation of the mean control values have been considered as positive signals.



Analyses comparing differences between several autoimmune diagnoses reveals the true potential of microarrays for diagnosis, classification and recognition of specific biomarker profiles that relate to evolution of new diseases and subsets. **Figure 10** is a cluster representation of the patterns recognised between samples. The majority of RA and PA samples cluster together, highlighting strong similarities between the autoantibody profiles of these two conditions. In terms of the autoantigens, there is a strong cluster of antibodies towards Fibrinogen and Elastin Peptides in both RA and PA samples, indicating a possible role for these antigens in the two disease pathogeneses. In addition, there appears to be two distinct clusters of SLE samples that have distinguishably different autoantibody profiles, and all of the Sjögren's Syndrome samples clustered together.

## DISCUSSION

### Analysis of Sera Tests

Hierarchical Clustering Analysis allows comparisons to be made between related autoimmune diseases (*i.e.*, PA and RA). Further work may aid in understanding similarities between disease aetiologies or what makes them pathologically distinguishable. Incorporating many autoantigens into an assay alongside full utilisation of patient clinical data can lead to novel associations and may identify new disease subgroups (for example, two possible SLE subgroups).

Microarrays also have a potential role in monitoring treatments. Comparative analysis of patients over treatment periods were made and current research indicates there is often a relationship between autoantibody titre and clinical presentation. By monitoring titres before and during treatment, scientists can potentially discover new drug mechanisms and there is a possibility to tailor treatments to an individual's own needs if current regimens are ineffective.

Although evidence associates both RA and COPD with smoking, it would be highly unrealistic to associate RA with COPD in terms of autoantibody targeting from this study; further testing with more samples is needed.

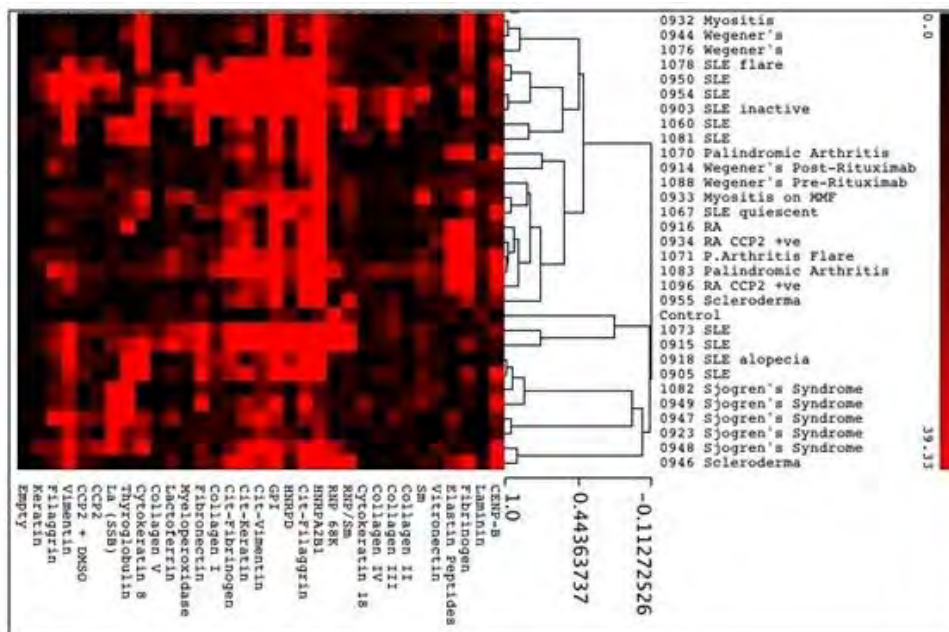


Figure 10

### Limitations

Patient samples available to carry out this study were limited. Future research should involve screening with a more even spread of samples on a wider scale. Another limitation was to only use an IgG secondary antibody. Microarrays allow simultaneous detection of multiple antibody isotypes by incorporating multicolour fluorescent detection with anti-isotype specific secondary antibodies<sup>21</sup>. Incorporating this would help identify associations between isotype and pathogenesis, a concept currently under investigation in RA<sup>15,18</sup>.

### Future Work

- To permit testing for even more autoantibodies, additional antigens can be added to the microarray: many spots remained empty and the design can compress to 20x20 grids. Hueber *et al.* describe an interesting concept, however, that despite best efforts, the number of autoantigens on an array will never be representative of the vast number of expressed proteins in a synovial joint<sup>16</sup>.
- Recall antigens that the majority of individuals have immunity towards (*i.e.*, Epstein - Barr virus), can be added to act as positive controls, as is currently undertaken in Paediatric ELISAs.
- It has been argued through three hypotheses ('Citrulline Specific', 'Peptide Specific' and 'Antigen Specific'<sup>11</sup>) that CCPs are not representative of the citrullinated epitopes that exist in vivo. There is, therefore, a growing importance to discover and include the exact citrullinated epitopes acting as ACPA targets to develop more effective and sensitive assays<sup>19</sup>.

- ❑ Sera samples from healthy individuals would allow a full comparison between disease and non-disease states and give scientists clues as to the role of tolerance towards certain antigens in autoimmune conditions.
- ❑ Results should be compared to current ELISA techniques. This would indicate whether identical results can be achieved within a reduced time and costing scale.

### Conclusion

Microarrays compress multiple assays into a small space equivalent to a single well of an ELISA, allowing simultaneous testing for autoantibodies to multiple autoantigens in a very confined area. The procedure demonstrates a proof of purpose, with a promising potential to allow accurate diagnosis of RA and other autoimmune conditions. With improvement, there seems to be the capability of diagnosing RA in early stages, complying with NICE guidelines<sup>4,7</sup>. Biomarker profiles can

be generated that may relate to symptom severity, treatment response or disease classification and progression<sup>21</sup>. The new method is less time-consuming and less costly, yet maximises patient data collection to unprecedented levels. The minimal volume of blood required also has great significance in terms of seriously ill patients and children. There is a potential to develop the technique further using microfluidics devices, which could take the test into GP clinics. Microarrays could also aid in diagnosis of 'mystery' autoimmune conditions, through elimination of possible candidate diseases or the creation of novel biomarker profiles. It is evidently clear, therefore, that protein microarrays have pivotal future roles in many aspects of immunology.

### Acknowledgements

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## References:

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## Best Six Articles from 2012-2013 (Article - 2)

## Stem Cell Treatments for Huntington's Disease

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Dr. Jason Seewoodhary: [seewoodharyj@hotmail.com](mailto:seewoodharyj@hotmail.com)**Keywords:***Stem Cells; Huntington's disease; Transgenic Animal Models; RNAi; Transplantation*

This review will critically consider the evidence that supports the use of stem cells in the management of Huntington's Disease (HD) including that provided by animal models.

HD is a chronic progressive neurodegenerative condition associated with motor, cognitive, and psychiatric symptoms. It has a prevalence of 4-8 per 100,000 and is caused by an autosomal dominant mutation in the Huntingtin gene (HTT) located at 4p16.3, which codes for the protein Huntingtin. Part of the HTT gene contains a repeated trinucleotide sequence of the bases CAG, which encodes a polyglutamine chain; the diagnosis of HD is confirmed by the detection of an expansion of >36 CAG repeats coupled with a positive family history and characteristic clinical features. Patients become symptomatic between approximately 35 - 44 years and the average survival time is 15 to 18 years thereafter<sup>1</sup>.

Unfortunately current licensed treatments for HD are limited to symptom control and palliation. Stem cells offer a new dimension that provides insights into: understanding the genomics and proteomics of HD potentially identifying drug targets; providing a cellular HD model to validate gene therapies such as those based on RNAi; and providing a source of human striatal cells for transplantation. Such principles have been applied to animal models of HD. These will be discussed in turn.

Both human embryonic stem- (ES) and induced pluripotent stem- (iPS) cells from affected donors have been used as cellular models to understand the molecular mechanisms of HD<sup>2</sup>. Mutant HD ES cell lines with CAG expansions in the adult-onset range of approximately 40-51 repeats and iPS cell lines, which include some with CAG triplet repeat lengths associated with juvenile onset HD, are available from laboratories.

Studies<sup>3</sup> using these cell lines have reliably reported the replication of known molecular pathological mechanisms although the relevance of these findings is limited for two reasons. Firstly "age equivalence", that is discrepancies in the chronobiology of the in vitro ES- and iPS cells, which are immature in relation to "developmental age" compared to the in-vivo situation in HD patients whereby the disease process is developmentally more mature having a late clinical age of onset. This may be important as RNA processing may be controlled differently in the embryo relative to adults and gene expression could be dependent upon developmental age. Secondly, human HD ES- and iPS cell lines provide a disease specific cellular model that is inherently biased towards cell autonomous mechanisms. Therefore, validating transcriptomic results from HD ES- and iPS- cells in vitro by comparison against transcriptomic results of the in vivo model in the HD patient is not clear-cut.

HD-specific iPS cell neural derivatives have been used for assaying new drugs that disrupt cell-autonomous mechanisms of HD. These cells can be used to validate gene therapy and provide an ideal alternative to the 'gold standard' that is HD brain tissue, which is difficult to obtain and limited to post-mortem samples. RNAi using shRNA and small synthetic oligonucleotide RNA molecules targeted against mutant HTT mRNA silences the HTT gene by inhibiting its translation<sup>4</sup>. In a mouse HD model this resulted in improved motor symptoms and longevity<sup>5</sup>. HD-specific iPS cell neural derivatives are now being used to escalate validating gene therapy even further via "allele specific RNAi", which involves using synthetic oligonucleotides to suppress translation of mutant HTT leaving normal levels unaltered. The results of these trials are awaited<sup>6</sup>. This may be limited by varying levels of basal HTT gene expression in different neural cell types.

ES-, adult- and iPS- cells can all be used as a source of striatal cells for transplantation in HD. These will be discussed in turn.

Recent evidence from a rodent model showed that human ES-cell derived striatal grafts produced neural precursors capable of differentiating into DARPP-32 expressing (a dopamine receptor marker) GABAergic neurons<sup>7</sup>. These extensively integrated into host neuronal circuits contributing to dopaminergic and glutamatergic neurotransmission within the midbrain and cortex respectively with a resultant functional rescue of motor deficits. The ES-cell derived striatal grafts showed no evidence of tumorigenesis at 16 weeks post-transplantation.

Adult stem cells have been used as a source of striatal cells for transplantation in HD. In a rat model of HD, adipose-derived stem cells from human subcutaneous tissue transplanted into the striatal border were found to improve behavioural symptoms and slowed striatal degeneration<sup>8</sup>. Further evidence has shown that intra-striatal transplantation of homotypic foetal tissue improved functional symptoms in HD patients<sup>9</sup>. However, adult stem cells have a limited role in cell transplantation for HD due to a lack of donor tissue. Furthermore, there are logistical difficulties associated with the acquisition and preparation of foetal stem cells and thus very few patients have benefited from foetal stem cell transplantation. The results of large on-going clinical trials looking at the role of foetal stem cells in HD are awaited.

Transplanted iPS cells derived from a patient with juvenile onset HD carrying 72 CAG repeats regenerated GABAergic striatal neurons and when transplanted into a rat model of HD significantly improved behavioural symptoms<sup>10</sup>. Limitations included: the iPS cells had a lower neuronal differentiating capability compared to ES cells; and the hope of iPS cells providing a cure for HD was hindered by the post-transplantation observation that iPS cells are prone to proteasome inhibition with subsequent development of HD pathognomonic features. The aforementioned evidence embodies the importance of transgenic animal models in developing stem cell treatments for HD with the aim that stem cell derivatives can, in the first instance, repair the brain of HD transgenic animal models and then ultimately that of human HD patients. The criteria of what constitutes a reasonable transgenic animal model of HD should include: age and time-dependence, that is demonstrating a gradual and progressive decline in striatal neurons; an ability to measure the motor, cognitive and behavioural impairment associated with HD; and demonstrable pathognomonic hallmarks of HD such as polyglutamine neuronal inclusions and striatal degeneration. These

principles are exemplified by the R6/2 transgenic mouse model of HD, which is created by transfecting exon 1 of the human HD gene containing expanded CAG triplet repeats into the murine germ line<sup>11</sup>. These transgenic mice replicate many features of human HD. Tests such as the fixed speed rotarod test can measure functional impairment due to motor deficits and similar tests exist for quantifying cognitive and psychiatric symptoms. Post-mortem studies on the brain of R6/2 transgenic mice have identified polyglutamine neuronal inclusions that existed before symptom onset. These neuronal inclusions occurred prior to any selective neuronal cell death being identified<sup>12</sup>.

A study looked at the effects of transplanting the C17.2 neural stem cell line into the lateral ventricle of R6/2 transgenic mice<sup>13</sup>. Trehalose was co-administered to inhibit polyglutamine aggregate formation. The effects of this combined treatment on the R6/2 transgenic mouse model included: reduced polyglutamine aggregate inclusions; reduced striatal volume and ubiquitin-positive aggregation; and increased life expectancy. Motor function improved as measured by behavioural evaluation.

In addition to transplantation therapy, R6/2 transgenic mice have been used as a model for screening other therapies for HD. These novel therapies include: antagonism of histone methylation and deacetylation, caspase inhibition, inhibition of excitotoxicity, inhibiting oligomerization and misfolding of protein aggregates, environmental fortification, improving metabolic symptoms including hyperglycaemia, transglutaminase inhibition, antioxidant medications, genetic manipulations, and restoring neurogenesis. Results from phase I and II clinical trials on these new drug discovery targets have been disappointing with no clinical interventions tested in murine models significantly delaying HD progression<sup>14</sup>.

The results of studies using transgenic HD animal models are limited in their application. R6/2 transgenic mouse models express, as a third allele, fragments of or full length HTT protein. As the cause of striatal degeneration in HD involves both "a toxic gain of function" of the mutant HTT and "a loss of function" of the normal HTT, transgenic mouse models such as R6/2 fail to 'model' the pathology and clinical phenotypes that result from the loss of human wild-type HTT and the expression of full-length mutant HTT. Furthermore, xenotransplantation experiments involving transgenic mouse HD models are capricious, which makes extrapolating the significance of results to human HD patients difficult. Differences in size of the human striatum relative to the rodent striatum considerably changes the extent of proliferation of neuronal stem cell derivatives needed and the spatial



ability of graft-derived neurites to integrate into host neuronal circuits and contribute to dopaminergic and glutamatergic neurotransmission within the midbrain and cortex respectively. Finally as the age of onset of HD in humans is approximately 35-44 years, the short two-year lifespan of a mouse limits its usefulness as a transgenic HD model.

In summary, stem cells have offered a hope, which has now turned to an expectation that developing curative therapies for HD are within the realms of possibility. However, until a credible and tested human stem cell neural model of HD is created then the discrepancies between promising data from experimental animal models and clinical studies will continue to be a barrier that hinders the search for a cure.

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Best Six Articles from 2012-2013 (Article - 3)

## Operating Theatre: Essential Concepts and Procedures

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### Introduction

The aim of this article is to introduce to the reader the basic but essential concepts that are part of an operating theatre set-up. As a medical student or as a junior doctor, these vital concepts are seldom explained by the busy surgical team. A firm knowledge of the basic principles will enable the student/ junior doctor to become an active participant in theatre and be able to understand the purpose and pitfalls of surgical methods. The basic concepts described within this article include: sterilisation, laminar flow, patient positioning, how to scrub for theatre, principles of tourniquet usage, diathermy, radiography and the different types of instruments used is some of the common surgical procedures.

### Sterilisation

This is the most fundamental and crucial component in an operating theatre setting but frequently doesn't come to the attention of the surgical team. Sterilisation is the process whereby all viable micro-organisms are destroyed.<sup>1</sup> In practical terms it is measured by the probability of one single micro-organism surviving on 1 million items. The term 'sterilisation' refers to equipment and not human skin.

There are numerous methods available to sterilise surgical equipment. One such method involves the use of an autoclave. This is a piece of equipment that pressurises steam to approximately 134 degrees Celsius. The use of steam in this manner is an effective method for killing bacteria, mycobacterium tuberculosis, viruses and heat resistant-spores. The total sterilisation cycle lasts around 30 minutes. The autoclaves are regularly checked by independent organisations to reduce the risk of infection.<sup>1</sup>

Another method of sterilisation is incineration. This is a process whereby all materials are completely destroyed by the use of heat. This is used when a patient is suspected of having a transmissible spongiform encephalopathy (TSE), or when equipment comes into contact with high-risk tissues such as the brain, spinal

cord or the eyes which increase the risks for patients to develop TSE. Therefore incineration destroys the pathogen and also the material it may have been transmitted onto. This prevents future cross contamination and hence sterilisation.<sup>1</sup>

A dry heat of 160 degrees Celsius is an effective method of sterilising non-aqueous liquids, air tight containers or ointments. However, this should not be used with non-stainless metals which have fine cutting edges. Finally, the use of chemical sterilisation with sterilising agents such as ethylene oxide, glutaraldehyde and peracetic acid can be employed.<sup>1</sup>

### Theatre Set-up Including Laminar Flow

The theatre environment must be controlled in order to limit cross-contamination with micro-organisms. This involves measures such as controlling the temperature, humidity and air circulation within the theatre.

Air circulation can be controlled by vertical or horizontal laminar flow systems. Laminar flow involves a continuous flow of filtered air which passes through ventilators into the operating theatre. The system ensures that no air can travel back into the room. The air is filtered to reduce airborne micro-organisms which may cross-contaminate the sterile field. Studies have shown that the use of laminar flow reduces the rate of post-operative sepsis.<sup>2</sup>

Increasing the number of cycles of filtered air reduces the quantity of air-borne pathogens. With conventional operating theatres, one can expect 20-30 air changes per hour. This results in airborne micro-organisms typically in the order of 150-300 colony forming units/m<sup>3</sup>. Laminar flow operating theatres have up to 300 air changes per hour. One can expect airborne micro-organisms to be in the order of 10 colony forming units/m<sup>3</sup>.<sup>3,4</sup>

The process was first pioneered in the 1960s by Charnley and was proven to result in a reduced number of post-operative wound infections. Normally, the temperature of the theatre is within the range of 20-22 degrees Celsius. If the temperature falls below 21 degrees Celsius, the patient is at risk of hypothermia during prolonged

procedures. For neonates, children and elderly patients, higher temperatures will be required for longer procedures. Another example is if a patient requires extensive debridement for the management of a large, dermal burn. In this instance, the temperature in theatre will be raised as burned patients can develop hypothermia.

### Patient Positioning

During an operation, it is imperative that the patient is positioned correctly for a number of reasons. Firstly, the surgeon needs adequate and comfortable access to the anatomical site. The correct positioning is vital to minimise any trauma to anatomical structures. Furthermore, the position should not cause any unnecessary restriction on the patient's respiratory system. Some of the additional factors which need to be taken into consideration when positioning a patient include age, weight and the presence of comorbidities such as paraplegia.

Poor positioning may lead to nerve injury. For example, brachial plexus injury can result from stressing the patient's upper limb. Common fibular or saphenous nerve damage may be acquired from poorly positioned leg supports. Careful positioning of the patient onto a comfortable operating table is important for maintaining patient safety.<sup>5</sup>

Pressure ulcers may also occur due to poor positioning of a patient. These tend to develop when the patient's own weight stresses a particular area of tissue for a prolonged period of time. Pressure ulcers are more likely to develop the longer the operation continues. Gel pads are commonly used to avoid pressure ulcers to vulnerable anatomical sites.<sup>5</sup>

There are numerous surgical positions. Each position imposes risks to anatomical structures.

### Supine

This is the most frequent position used for most surgical operations, and involves the patient being laid flat on their back (Figure 1). Some of the most prominent pressure points in this position include the heel, the occiput and the sacrum.

Severe hypotension may arise if the Inferior Vena Cava is compressed against the vertebral bodies (particularly in pregnant or obese patients). Gastric regurgitation may occur, particularly in patients with a pre-existing hiatus hernia. The eye is at risk of direct or indirect trauma from the operating light causing corneal drying. This may occur within ten minutes of exposure, if not prevented appropriately.<sup>5,6</sup>

C8 and T1 nerve roots of the brachial plexus are predisposed to compression as these nerve roots are in close relation to the first rib, clavicle and the humerus. The risk can be reduced by preventing the patient's arm



Figure 1: The Supine Position.

from being abducted more than 90 degrees and keeping their forearm in pronation.<sup>5</sup>

### Lithotomy

The lithotomy position involves the patient's legs being separated, with the hips flexed and the knees in varying degrees of extension. The legs are then supported by stirrups (shown in Figure 2). This position is utilised in gynaecological and urological surgery.



Figure 2: The Lithotomy Position.

Extreme flexion of the hip joints can cause neural damage by stretch (obturator and sciatic nerves) and by direct compression (femoral, peroneal and saphenous nerves).<sup>5,6</sup> The sites of direct compression are listed in Table 1.

Calf compression in the lithotomy position predisposes the patient to venous thromboembolism and compartment syndrome. The risk is increased if the patient's calves are held in this position for a prolonged period of time. Foot stirrups reduce the compression on the calves; however there is little evidence to show that this reduces the risk of compartment syndrome.<sup>5,8</sup>

### Lateral

The lateral position involves the patient being laid on their side, usually with their arms stretched out perpendicular to the body. Their back is supported and the arm is rested on a pillow or an over-arm rest to prevent compression of the axillary neurovascular bundle (Figures 3 and 4). The lower limbs are usually flexed, with

some sort of padding between the legs to prevent saphenous and peroneal compression. This position is used for surgical access to the spine, the posterior skull or for renal procedures<sup>5</sup>.



**Figure 3:** The Lateral position. The overhanging arm is supported by a rest and a pillow is placed between the legs.



**Figure 4:** The lateral Position (Posterior aspect). A support rests against the patient's posterior trunk to hold the patient in place.

Problems which can be encountered with this position include excess pressure on the side of the face, shoulder and breast. This position may also compromise lung

expansion as the lateral surface of the ribs rest against the operating table.

#### Prone



**Figure 5:** The Prone position. Ideally, two pillows should be placed on the chest and pelvis allowing the abdomen to move during respiration. The same effect can be achieved using a Montreal mattress or a Wilson frame to avoid compression on the abdominal wall.

Whilst in the prone position, the entire anterior surface of the face, trunk and lower limbs face the operating table (Figure 5). This position is particularly useful for some types of spinal surgery.

Problems with this position include excess pressure on: the ocular orbit, the breasts, the genitals and the dorsum of the feet. Padding should be placed over the orbital ridges and a pillow placed over the chest and the pelvis to prevent pressure ulcers.

Pressure on the abdomen can compress the Inferior Vena Cava, reducing venous return and poor cardiac output. Ideally forearm support pads should be in place to limit the risk of ulnar nerve compression against the medial epicondyle of the humerus. There is also a risk of compression of the axillary neurovascular bundle against the humerus.<sup>5</sup>



Position	Pressure Sore Sites	Possible complications	Neural Damage	Mechanism of Neural Damage
Supine	Occiput Sacrum Heel	Inferior Vena Cava compression (obese, pregnant) Corneal Drying Gastric Regurgitation Severe hypotension	C8, T1	Direct compression at first rib, the clavicle and the humerus
Lithotomy	Calf Heel	DVT risk from calf compression	Obturator Nerve & Sciatic Nerve	Stretch forces from hip flexion
			Femoral Nerve	Direct compression at the inguinal ligament
			Peroneal Nerve	Direct compression at the neck of the fibula.
			Saphenous Nerve	Direct compression at the medial condyle of the tibia.
Lateral	Face Shoulder Breast	Compromise lung expansion	Peroneal Nerve	Direct compression at the neck of the fibula
			Saphenous Nerve	Direct compression at the medial condyle of the tibia.
			Brachial Plexus	Compression at the Axilla
Prone	Orbit of the Eye Breast Genitals Dorsum of the feet	Compromise lung expansion  Poor Cardiac Output	Ulnar Nerve	Compression of the Cubital tunnel
			Axillary Nerve	Indirect compression against the humerus

**Table 1:** Summary of the complications from different surgical positions.

### Preparing for Theatre

The scrubbing procedure reduces the cross contamination of micro-organisms that exist on the surgeon's hands, finger nails and forearms. Micro-organisms are removed by the combination of strong cleansing agents, including betadine and chlorhexidine, and a systematic cleaning procedure.

Prior to the surgical scrubbing procedure itself, you must change from normal clothes into scrubs, which are usually found in the theatre changing rooms according to size. You also need to put on theatre shoes. Most theatre staff will wear special clogs, however, if you don't have a pair of your own there are usually plenty of spares in the changing rooms – just ensure that you choose a pair without someone else's name in, as there is nothing more embarrassing than being accused of wearing your consultant's favourite shoes!

Next, you should remove all of your jewellery. The only acceptable jewellery to be worn in theatre is a plain wedding band. Some people may wear earrings, but ideally these should be removed as there is the risk of them falling out.

Once changed you should put on a theatre hat, prior to

leaving the changing rooms. This should completely cover the hair. Once you get into the theatre, you will also need to put on a face mask. The most important point with the face mask is to ensure that you mould the firmer part around your nose, and ensure that it is comfortable. There is nothing worse than an uncomfortable mask for the duration of an operation, which you are unable to touch once scrubbed.

Another piece of protective clothing which is not always used is eye protection. These can come as separate pieces of equipment, or attached to the face mask. Many people will not use eye protection but it is strongly recommended, especially during operations with a lot of potential for blood exposure such as in vascular and orthopaedic procedures.

Scrubbing should take place in a designated scrub room within the theatre. At the start of a list, the scrubbing procedure should last for about 3-5 minutes. This time does not account for rinsing time. During the procedure, it is important that no contact is made with non-sterile objects. If the arms or forearms come into contact with non-sterile objects, the scrub procedure must restart. It is therefore advised that at all times during the procedure



the arms and forearms are carefully manoeuvred.

The surgical gown is packaged so that the person who is scrubbing in comes into contact with the inside of the gown whilst putting it on. After scrubbing, the hands must not come into contact with the outside surface of the gown. If this occurs, the gown will be considered as contaminated and must be discarded.

Whilst scrubbed in, the hands should be raised 20-30 degrees above the elbows, and must always be kept above waist height. The scrub person's hands are considered to be contaminated if the hands fall below the waist line. The areas of the surgical gown which are considered to be sterile are the sleeves and the front of the gown above waist height.

### Surgical Scrubbing

Before starting to scrub in, it is essential to ensure that you have all of the equipment that you are going to need. This is because once you are sterile you are not allowed to touch anything non sterile. You should ensure that you have your theatre hat, face mask and eye protection on, and that your surgical gown and gloves are prepared to put on.

You should turn on the taps and make sure that the water is of an adequate temperature. You want it warm enough to lather up and remove dirt, but not so hot that it is unbearable for the length of time that you are required to wash your hands under it. There are two types of hand wash to choose from. The first of these is a chlorhexidine-based product, which may be referred to as "Hibiscrub". The alternative is an iodine-based product which might be referred to as "Betadine". The soap dispensers have levers attached to them so that once you have started to wash you are able to use your elbows to dispense the cleansing solutions. Once you commence washing, you should not use your hands to adjust the taps or dispense the cleaning solution.

If you are scrubbing in for the first time that day, you should scrub for approximately 5 minutes. This can then subsequently be reduced to 3 minutes. For the first minute, you should wash your arms and hands and then rinse. It is important to clean in a distal to proximal direction. For example, after washing your hands, you should then continue cleaning from your wrist down to your elbow. Once you have wash down to both elbows (as seen in Figure 6) you should then rinse. Whilst rinsing, you should tilt your hands up from your elbows and run your arms through the water in one direction. You should not pass your arms back and forth through the water.

You should then repeat this general wash for the second minute. During the third minute, you should clean your nails thoroughly using a nail pick and a nail brush

provided as shown in Figures 7 and 8). The fourth and fifth minutes should concentrate on washing the hands. This involves making sure that you wash the dorsum and palms, in between the fingers and the wrists thoroughly. If you require more hand wash it is important to press the handles using your elbows as shown in Figure 9.

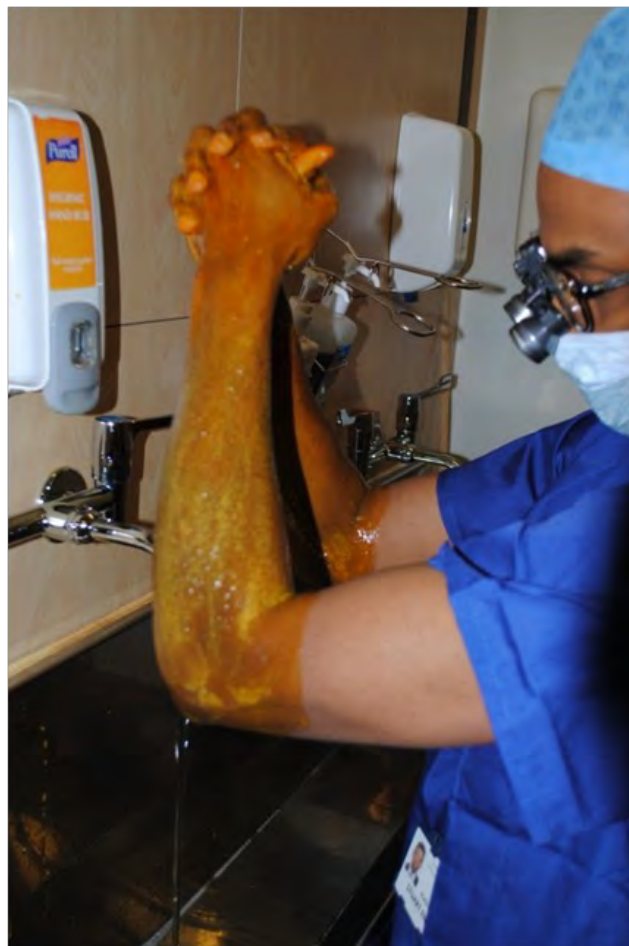


Figure 6: Arms should be scrubbed to the point of the elbows.



Figure 7: A nail pick is used to clean under the fingernail.



**Figure 8:** The tips of the fingers are cleaned using a nail brush.



**Figure 10:** Putting on gloves. Keep your hand within the surgical gown whilst donning the surgical gloves.



**Figure 9 :** The elbow should be used to press down on the lever to dispense cleaning agent.

Once this process is complete, you should turn the taps off using your elbows only. Your arms should be positioned with your hands directly above your elbows, so that your elbow joint is forming a 90 degree angle. You should let the water drip off your arms, rather than shaking them.

Hands and arms are dried using sterile towels. You must dry one arm at a time, ensuring that you dry from hand to elbow continuously downwards, rather than returning to any sections. Once you reach the elbow, the sterile towel should be disposed of, and a new towel used for the other arm.

Now that the arms and hands are sterile, it is time to put on the surgical gown and gloves. You pick up the gown using both hands and allow it to open, ensuring that it does not touch anything else. As you are opening the gown the arm holes will become visible and you should slide your arms inside them, but keep your hands within the sleeves. A member of theatre staff will then pull the gown onto your shoulders and fasten up the ties at the back.

Keeping your hands inside the sleeves at all times, you should proceed to open up your sterile gloves and put them on (shown in Figure 10).

The cuffs of the gown should be covered with the gloves because they are not water-resistant.

Finally, you must close the back of your gown. On the front of the gown, you will notice that there are some ties with a small piece of card attached to them. You should keep hold of the shortest tie, and hold the card in your hand. Give the card to a colleague, without touching them, and rotate in a circle to close the gown. Take hold of the longer tie, and secure the ties together with a knot.

Once the operation is complete, you are able to remove the protective clothing. You should start by removing the surgical gown first, followed by the gloves, and finally the mask. All should be disposed of in the appropriate bins. You should then wash your hands.

#### **Skin preparation and draping**

Prior to any surgical procedure, the patient's skin must be prepared in order to reduce the numbers of microbes on the skin surface. The cleansing solution used for this purpose needs to target a broad-spectrum of microbes, and must be fast-acting and tolerated by the patient. The patient's allergy status and surgeon's personal preference also have to be taken into account.

The main skin preparations used are either betadine or chlorhexidine, as used for surgical scrubbing. These are available in either aqueous or alcoholic preparations. The skin preparation is applied using sterile equipment starting from the centre and moving outwards.

The purpose of surgical draping is to create and maintain a sterile field. Different drapes will be used dependent on the anatomical site and the positioning of the patient.

#### **Surgical Tourniquet**

A pneumatic tourniquet is used in theatre to reduce the amount of blood loss whilst operating and also to help maintain a clear field of vision without blood obstructing the wound site. An image of a pneumatic tourniquet cuff is shown in Figure 11.





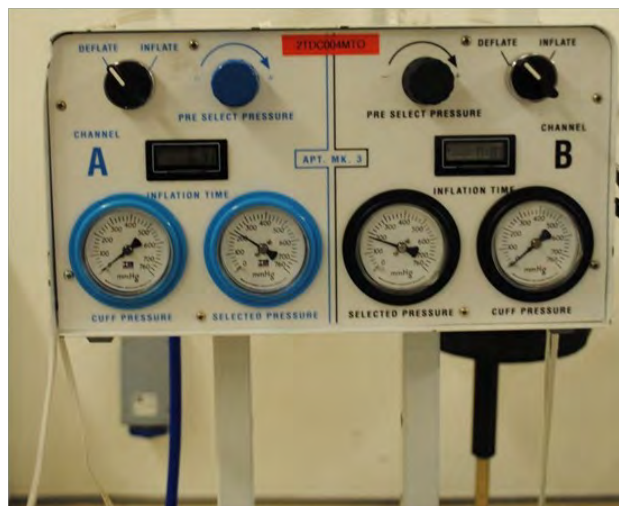
**Figure 11:** Pneumatic tourniquet.

Padding is placed around the arm where the tourniquet is to be placed (Figure 12). This is to protect the skin from trauma from the pressure of the tourniquet cuff. In local anaesthetic procedures, the patient may not tolerate the tourniquet for more than 20-30 minutes at a stretch. However when the patient is under general anaesthetic, tourniquets can be applied for longer (see below).



**Figure 12:** Padding is placed around the arm before the tourniquet is put on the patient's limb.

Tourniquets are applied at different pressures depending on the site of use and the age of the patient. In paediatrics, tourniquets are applied to children at a systolic pressure range between 140-250mmHg in the lower extremity and 155-190mmHg in the upper extremity.<sup>9</sup> In adults, there are two approaches for setting the tourniquet pressure. Tourniquets can be set to a fixed pressure (typically 250mmHg for the upper limb and 300mmHg for the thigh). Tourniquets may also be set at a fixed pressure above the systolic arterial pressure (100mmHg greater in the upper limb or 100-150mmHg greater at the thigh).<sup>10</sup> The tourniquet pressure is controlled by a tourniquet machine (Figure 13). The duration of time for which the tourniquet is to be applied is monitored by theatre staff. In principle the pressure and time of tourniquet usage should be kept at a minimum. Tourniquet use is monitored carefully because prolonged use can result in muscle fibre necrosis and micro-vascular injury leading to 'post-tourniquet syndrome'. This is when the patient has a swollen, pale, stiff limb. There is weakness however there is no paralysis.<sup>10</sup>



**Figure 13:** Pneumatic Tourniquet machine.

Tourniquet use is contraindicated at sites of vascular grafts and also in patients with pre-existing deep vein thromboses. Another important complication of prolonged use is tourniquet paralysis. It has been reported that in the upper limb, the median, ulnar and radial nerve distal to the elbow are vulnerable to tourniquet paralysis which can take up to 210 days post operatively to recover.<sup>11</sup>

The literature recommends that tourniquets are released for approximately 20 minutes after tourniquet application of 90-120 minutes. This is the point where ATP stores are depleted. The release of the tourniquet reduces the risk of ischaemic and neurological injury. The tourniquet is released for approximately 20 minutes and is then reapplied. At the end of an operation the tourniquet time should be documented.<sup>10,12</sup>

Tourniquet use can elicit pain in areas of muscle mass. There are various theories about the actual physiological mechanism of pain attributed to tourniquet application. One theory is that the ischaemia causes the release of local inflammatory mediators such as prostaglandins. This increases the excitation of local pain fibres. Another theory is that compression of the tourniquet continuously stimulates slowly conducting, unmyelinated, cutaneous C-fibres. Large nerve fibres are more susceptible to compression at the tourniquet site than these smaller C-fibres. The compressed larger nerve fibres are unable to inhibit the post-synaptic effect of the smaller C-fibres at the dorsal horn. This lack of inhibition of C fibres leads to the experience of tourniquet pain.<sup>10,13</sup>

#### Electrical Powering in theatre

A rigid clinical pendant system (Figure 14) is an integral part of the operating theatre. The pendent accommodates a number of electrical socket outlets, Anaesthetic Gas Scavenging Systems (AGSS) terminal units, data sockets and audio visual connectors. It can also be used to connect power drills (such as K-wiring, and a number of power saws used in orthopaedic procedures such as knee replacements).



**Figure 14:** A rigid Clinical Pendant System.

### Surgical diathermy

Surgical diathermy requires the use of frequencies within the range of 400kHz – 3MHz. Low frequencies are not suitable as they can cause neuromuscular stimulation. High frequency currents enable enough energy to pass through to the tissue in order to heat up the particular area of tissue.

Monopolar diathermy involves an active electrode held by the surgeon which receives the high frequency current from a diathermy generator. Monopolar diathermy requires a complete circuit to be formed. The circuit consists of an arc between the active electrode, the patient's tissues and an active plate which is positioned underneath the patient. The circuit is completed by being connected back to the generator.

The monopolar diathermy device is able to cut through tissue via a continuous current or coagulate via a pulsed current. Tissue is cut through processes of initial dessication (cellular water is vaporised) and rapid tissue heating causing cells to destruct. Coagulation is possible as the pulsed signal seals the blood vessels without causing tissue disruption. In order to cut, the yellow button is pressed to produce a continuous output from the diathermy generator. In order to coagulate, the blue button is pressed to produce a pulsed output from the diathermy generator (Figures 15 and 16).

Monopolar diathermy can lead to burn complications. If a patient is not in full contact with the active plate then an

incomplete arc exists. If the patient were to be in contact with a metal object, for example an intravenous drip stand or electrocardiogram electrodes, then this would complete the arc and result in a burn injury at the site where contact is made.



**Figure 15:** Monopolar diathermy device. The yellow button cuts and the blue button coagulates.



**Figure 16:** A diathermy generator.

Bipolar devices (Figure 17) are used for coagulation purposes and they do not require an active plate. Current passes from each limb of the forceps and heats the tissue held between the two limbs. Bipolar devices are unable to cut through tissue. This is because there is no active plate and so a continuous arc cannot be formed between the electrode and the tissue, but instead between the two limbs of the forceps. Bipolar devices also cannot cut as the heat generated is insufficient to cause explosive vaporisation. For safety purposes the bipolar device is active once a foot pedal is pressed by the operating surgeon. Only when the foot pedal is pressed the device is able to be used (Figure 18).



**Figure 17:** A Bipolar diathermy device (forceps).

There are known complications of diathermy use in patients with a cardiac pacemaker in-situ. If diathermy is used near to a cardiac pacemaker, there is the chance that it may accidentally lead to contact between the active electrode and the pacemaker. If this happens, it may result in myocardial damage and lead to a cardiac arrest. Furthermore, the diathermy current can affect the circuits of the pacemaker which may lead to arrhythmias.<sup>15</sup>





**Figure 18:** A Bipolar foot pedal.

Finally, it is also important to take care with the application of alcohol gel when diathermy is going to be used. This is because alcohol gels are highly flammable and so if they are used at the site of a surgical wound, the diathermy could potentially ignite the gel and the skin underneath and surrounding it. If alcohol gel is applied, it should be placed away from the surgical site, or rubbed thoroughly into the patient's skin.<sup>10</sup>

### Radiography

Radiography is used within many surgical specialties. X-rays are useful diagnostically as they allow the surgeon to image the bone during a surgical procedure. However X-rays are a source of ionising radiation. Overdoses of ionising radiation can lead to serious effects ranging from a mild burn to malignant diseases like leukaemia.

In order to regulate the use of X-rays and prevent such incidents, government guidelines have been published. There are two main regulations. The first is the Ionising Radiation Regulations 1999 (IRR99) which is to protect the staff from over-exposure to radiation. The second is the Ionising Radiation (Medical Exposure) Regulations 2000 (IRR(ME)2000) which is implemented solely to protect the patient.<sup>1</sup>

It must be clarified that the patient receives a low dosage of ionising radiation from each X-ray. Subsequently a patient has an extremely low risk of developing any unwanted effects from a single X-ray. However there is no 'safe' dose as every exposure can potentially cause some amount of tissue damage. Therefore the principle of 'As low as reasonably achievable (ALARA)' should be implemented. This means that the dose is as low as possible in order to obtain a perfect X-ray and ensuring

that a repeat of the X-ray is not required.<sup>1</sup>

Staff members are at risk of over-exposure to radiation from the numerous radiographs taken in theatre over the course of many years. Therefore staff must wear protective jackets for each patient undergoing radiological investigation. Additionally, staff will wear a personal monitoring dosimeter which is processed in order to determine the value of the dose of ionising radiation the staff member has been exposed to.

The hospital appoints a Radiation Protection Adviser (RPA) who is a medical physicist who advises on staff and public safety in regards to IRR99. The RPA ensures that there are adequate contingency plans in case there is a malfunction with one of the X-ray machines.

When an X-ray is to be taken, the X-ray machines will flash a red light and an audible buzzer will signal the exposure time. Staff members without protective jackets should stand a minimum of 2 metres away from the X-ray machine, or ideally leave the room whilst the X-ray machine is in use.

All machines are serviced every 3 years to ensure that they are working safely. If there is an incidence in which a staff member receives a dose of 6mSv or greater or 30% greater than the dose limit, they should contact the dosimetry services.<sup>1</sup>

### WHO Surgical Safety Checklist

In industrialised countries the rate of perioperative death for inpatient surgery is 0.4-0.8% and the rate of major surgical complications is 3-17%. It has been reported that half of major surgical complications are avoidable. It has been shown that the implementation of practices to reduce surgical-site infections and anaesthesia-mishaps have improved the rate of complications. Additionally, it has also been reported that highly co-operative team work also reduces the rate of complications. The World Health Organisation (WHO) introduced the WHO Surgical Safety Checklist. This checklist is designed in three parts.<sup>17</sup>

The first part is the 'sign in' checklist which is checked prior to the implementation of anaesthesia. This includes confirming the correct identity of the patient and also the correct site of surgery and whether consent has been granted. Pre-operative risks are also assessed, including the risk of the patient bleeding greater than 500ml, the risk of aspiration and the risk of anaphylaxis to medication.<sup>17</sup>

The second part is called 'time out'. This part of the checklist is performed prior to the surgical incision. Similar to 'sign in' the identity of the patient, the site of the operation and the correct procedure is checked. Following this, the surgeon, the anaesthetist and the nursing staff consider the possibilities of complications from the procedure. First, the surgeon considers the length of the operation or anticipated blood loss. The



anaesthetist considers whether there are any possible safety concerns in regards to the procedure. Finally, the nursing staff determine whether there are any issues with the operating theatre machinery and that a sterile field has been created for the procedure to take place. Additionally checks are performed whether the patient has been given prophylactic antibiotic within 60 minutes of the procedure.<sup>17</sup>

The final part is the 'Sign out' phase. This part of the checklist must be performed prior to the patient leaving the operating room. The surgeon, the anaesthetist and the nurse review any concerns they had. The nursing staff count (and later document) the numbers of swabs, scalpel blades and needles used in the operation. They also establish whether there were any problems with the operating machinery. Additional checks are performed to ascertain if prophylactic antibiotics have been administered within 60 minutes of the procedure, if applicable.<sup>16,17</sup>

Numerous studies have confirmed the efficacy of the WHO surgical safety checklist and that since its implementation there has been a reduction in the incidence of avoidable major complications during surgery.<sup>16,17</sup>

### Surgical Equipment

This section will describe only the commonly used instruments in the operating theatre. Due to the many variations of instruments used between specialities, detailing all instruments is not within the remit of this chapter. The basic surgical equipment includes: scalpel handle and blades, forceps, needle holders, scissors, artery forceps, retractors and towel clips.

Scalpel blades and handles vary in size. In surgery, the most commonly used blades are sizes '10', '11', '15', '20' and '23' (Figure 19). A size '10' blade has a curved cutting edge and is used to make small surgical incisions in skin and muscle. It can also be used for more specialised types of procedures such as radial artery harvesting and inguinal hernia repair. A size '11' blade is a triangular shaped blade. It has a sharp tip ideal for making stab incisions and a flat cutting edge, ideal for chest drain insertion or opening of coronary arteries. A size '15' blade has a smaller cutting edge. It is ideal for making small and precise dissections, for example, excision of skin lesions. And finally a size '20' blade is similar in shape as a size '10'. It is used for larger incisions for general and orthopaedic procedures requiring large incisions e.g., an open laparotomy. A size '23' blade is 'leaf shaped'. It is used to make long incisions such as an upper midline incision of the abdomen.

The different blades are able to fit onto a scalpel handle (Figure 20). It is imperative that you take care whilst attaching the blade onto the handle. You should not grip the blade with your fingers but instead you should use a pair of forceps.



**Figure 19:** (From Left to Right) Number 10,11,15,20,23 scalpel blades.



**Figure 20:** Scalpel handle.

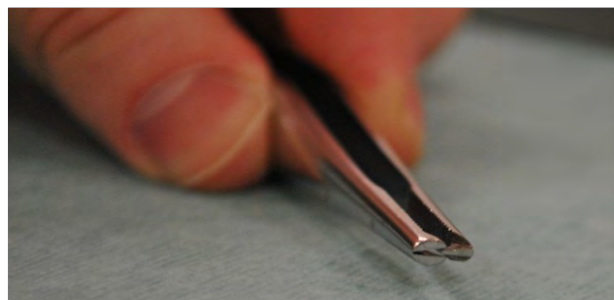
The two main types of forceps include serrated (Figure 21) and toothed dissecting forceps (Figures 22 and 23). Toothed forceps are known by this name as it has interdigitating teeth which holds tissue without it slipping (Figure 23). It is used to handle skin and dense tissue. Serrated forceps are used to handle and move delicate tissues during exploratory surgery without causing trauma. The surgeon holds forceps with his thumb on one side of the forceps and exerts pressure (in order to grip the tissue) onto the other arm of the forceps held in place by the index finger of the hand. It is also worth mentioning Babcock's forceps as in a similar nature to serrated edged forceps these also permit the handling of delicate tissue (Figure 24). It is held in a similar way to a pair of scissors or needle holders, to ensure a more



**Figure 21:** Serrated edged forceps.



**Figure 22:** Toothed forceps.



**Figure 23:** The interdigitating teeth of the toothed forceps.



**Figure 24:** Babcock's forceps.

comfortable, firm grip of the tissue.

Artery forceps (Figure 25) are used to limit blood loss in theatre. Most types have a serrated edge that allows for a firm hold onto the artery. They are used to grasp onto an artery before it is ligated using a bipolar diathermy. There are different types, varying in size and shape. This is to suit the size of an artery that is to be held in place by the forceps (Figure 26).



**Figure 25:** Artery Forceps.



**Figure 26:** Artery Forceps (From Left to Right) Halstead Mosquito Artery Forceps; Kocher Artery Forceps; Moynihan Artery Forceps; Rochester Artery Forceps; O'Shaughnessy Artery forceps.

Needle holders are used in suturing. The needle holder has 4 key parts: the jaws, joints, the clamp and handles (Figure 27). The suturing needle is held in place between the jaws. The correct way to hold needle holders is thus; the index finger is positioned below the joint, whilst the thumb and ring finger are placed within the rings of the handles. This is shown in Figure 28.



**Figure 27:** (From left to right) Debaquey's needle holder, Kilner's needle holder.



**Figure 28:** The correct position to hold needle holders.



Harold Gillies, one of the founding fathers of modern day plastic surgery, invented a needle holder which has scissor blades beneath the jaws (Figure 29). This is useful as a surgeon does not need to put down the needle holder or ask an assistant to use scissors to cut the suture thread after tying a knot.



**Figure 29:** Gillies' Needle Holder. Note the scissors blades below the jaws of the needle holder.

There are numerous types of scissors used in theatre. The main types are sharp ended and blunt ended scissors (Figures 30 and 31). In most surgical trays are the Mayo and the McIndoe scissors (Figure 31). These two types are blunted ended scissors. The Mayo scissors are used to cut sutures whilst the McIndoe scissors are used to dissect through tissue. The hardness of the scissors is important to a surgeon because scissors with harder edges stay sharp for longer and ease cutting through tissue or sutures. Different materials are used to ensure this: stainless steel or tungsten carbide. Scissors are held in a similar way to needle holders with the thumb and ring fingers passing through the rings of the scissors, the index finger supporting the shaft of the needle and the middle finger resting on one of the rings providing support.



**Figure 30:** Sharp-ended scissors.



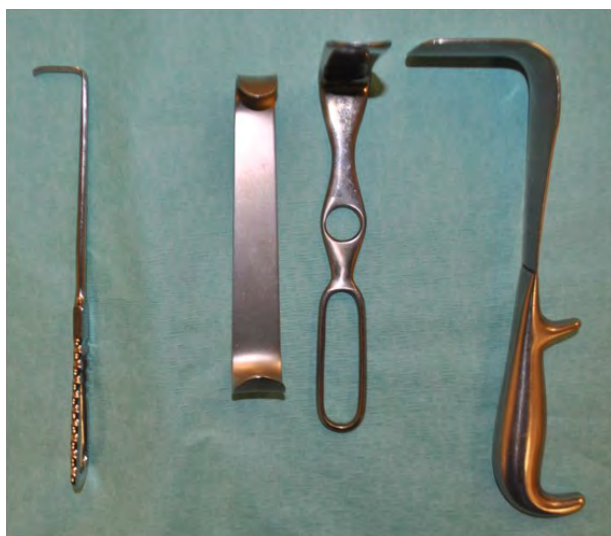
**Figure 31:** Blunt-ended Scissors. (From Left to Right) Mayo Scissors, McIndoe Scissors.

There are too many different types of retractors to describe within this section. The two main types of retractors that will be discussed are self-retaining retractors and hand held retractors. Self-retaining retractors separate both edges of the tissue being excised (Figure 32). It has a ratchet mechanism that holds the two edges of the wound in place which frees up a surgeon's hand for him/her to use other equipment. The Mollison self-retaining retractor is commonly used for small skin incisions e.g., hand surgery, whereas Mayo-Adson and Cone self-retaining retractors are used to retract larger areas of tissue in neurosurgery for laminectomy procedures.



**Figure 32:** Self-retaining Retractors. (From left to right) Mayo-Adson retractors; Cone retractors; Mollison retractors.

Hand held retractors are used to hold other tissues and organs in place, improving the field of vision for the surgeon whilst operating. Usually the assistant in the operating theatre uses the retractors whilst the lead surgeon operates. The more commonly used types are: the Langenbeck retractor, Kilner's cheek retractor used in Oral and Maxillofacial surgery, Landon's and Doyen's retractor are both used in Obstetrics and Gynaecology, and skin hooks used mainly in plastic surgery (Figures 33 and 34). It is imperative that when you hold skin hooks that you do so with the utmost care in order to prevent an injury to yourself or a colleague. These instruments can lacerate skin with only a small amount of force.



**Figure 33:** Hand held retractors (From left to right) Langenbeck retractor; Kilner's cheek retractor; Doyen's retractor.



**Figure 34:** Skin Hooks. (From Left to Right) Kilner's Double skin hook; Gillie's skin hook.

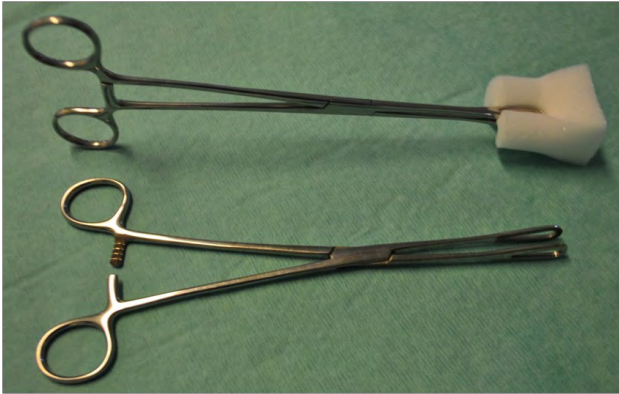


**Figure 35:** (From left to right). Chisel and Mallet.



**Figure 36:** Towel Clips. (From left to Right) Schaerdal towel clip; Backhaus towel clip; Mayo's towel Clip.





**Figure 37:** Rampley's sponge holding forceps.

### Conclusion

In conclusion, there are numerous, important basic concepts about the operating theatre a student or a junior doctor must be aware of. Knowledge about diathermy and surgical instruments will allow the reader to identify these items in theatre and understand why they are used. Understanding the safety protocols of radiography and the WHO checklist will allow the reader to be safe within theatre but understand about patient safety also. Finally, this article teaches the reader how to scrub up for theatre. This will hopefully allow the reader to enhance and consolidate their surgical experience.

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Best Six Articles from 2012-2013 (Article - 4)

## The Use of Geometric Morphometrics as a New Method to Analyse Glenoid Bone Loss after Shoulder Dislocation

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### Abstract

**Background** - Glenoid bone loss occurs at the anteroinferior and posteroinferior aspects of the glenoid rim in anterior and posterior instability respectively. This morphological change in the shape of the glenoid fossa predisposes to increasing instability.

**Aim** - The aim of this study was to use geometric morphometrics to quantify changes to glenoid morphology in traumatic shoulder instability.

**Methods** - 3D models of the surface of the glenoid fossa were created using CT scans from 8 patients with 5 dislocations and 3 controls. Ten landmarks, corresponding to the same anatomical sites between samples were digitized onto the surface of the glenoid fossa. Shape information was extracted from the landmark co-ordinates and analysed for variation in the geometric properties of the glenoid fossa using

geometric morphometrics.

**Results** - Results showed that the areas of most pronounced variation between the dislocation and control groups were as expected, at the anteroinferior, and posteroinferior glenoid regions.

**Conclusions** - This indicated that geometric morphometrics allows variation in the geometric properties of the glenoid fossa after dislocation to be accurately analysed at a good level of detail in three dimensions.

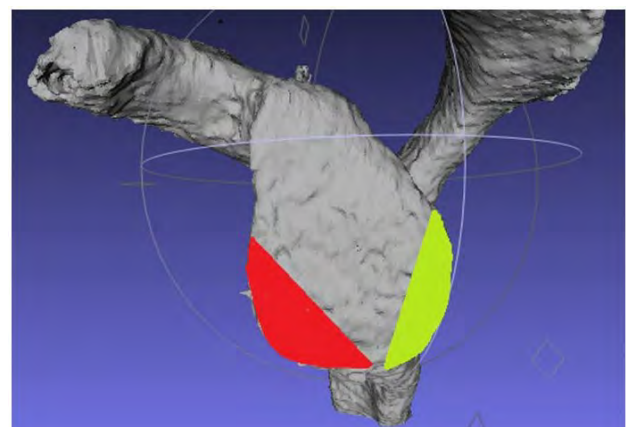
**Clinical Relevance** - Compared to conventional techniques using single glenoid measurements from 2 dimensional images, morphometrics represents an exciting new avenue for analysing the morphological changes to the glenohumeral joint involved in shoulder pathology.

### Introduction

Bony Bankart lesions are common and described in up to 71% of individuals following anterior shoulder dislocation.<sup>6</sup> The extent of bone loss increases with number of dislocations.<sup>21</sup> In posterior shoulder dislocation, the opposite occurs with bone loss from the posteroinferior aspect of the glenoid rim as shown in Figure 1.<sup>10,20</sup> The extent of bony bankart lesions is widely dependent on the method of injury with high impact injury in contact sports hypothesized to result in most extensive bone loss.<sup>4,23</sup> The decrease in articular surface area and loss of uniform concavity of the glenoid fossa acts to de-stabilize the glenohumeral joint and increase the risk of re-dislocation.<sup>22</sup>

Clinically the extent of bone loss is important for planning the appropriate surgical treatments to re-stabilise the shoulder joint in an individual who has experienced multiple re-dislocations.<sup>1,11</sup> In these patients, Computed Tomography (CT) is the imaging modality of choice in the quantification of glenoid bone loss with a high sensitivity of 93%.<sup>8,17</sup> Accurate CT interpretation by a radiologist involves viewing 2D slices of the glenohumeral joint

which can also be used to form a 3D reconstruction of the joint. Quantification of glenoid bone loss is largely



**Figure 1:** A 3D model of the glenoid fossa from the control group indicating the most common areas of bone loss after glenohumeral dislocation.

**Red** - Shows the Anteroinferior aspect of the glenoid fossa where bony bankart lesions are common after anterior dislocation.

**Green** - Shows the Posteroinferior aspect of the glenoid fossa where reserve bony bankart lesions are common after posterior dislocation.

subjective based on the radiologists overall clinical impression and no exact criteria are used in analysis of bone loss. Several novel studies used sagittal views of the glenoid to compare which typical features of glenoid bone loss most closely relate to rate of re-dislocation.<sup>8,2</sup> Of three measurements for quantifying bone loss; cross sectional area, maximum glenoid width and maximum glenoid length, the most statistically significant was reduction in maximum glenoid width.<sup>2</sup> These measurement techniques based on single measurements taken are still relatively crude and few studies using more detailed and accurate ways to quantify glenoid bone loss are reported in the literature.

Morphometrics is a method for defining the shape of an object taking into account all features with the object with the exclusion of size, orientation and position.<sup>5,15</sup> The object or specimen, in this case a 3D CT image of the glenoid fossa is represented in a form that can analysed using morphometrics by digitising a number of landmarks over the surface of the object. These landmarks each represent the same equivalent point from the surface of the glenoid. Landmarking functions to provide unique information from each specimen but corresponding shape information across the dataset to represent the morphology of the glenoid fossa.<sup>5,15</sup> Shape information is extracted by closely aligning the landmark points using a method known as procrustes superimposition.<sup>5</sup>

This study aims to use morphometrics as a more accurate method for quantification of changes in glenoid morphology following shoulder dislocation. The primary objective of this study is to assess if geometric morphometrics can be used to quantify a significant morphological change in the glenoid fossa after glenohumeral dislocation. The secondary aim is to determine if there is a critical quantitative change in glenoid morphology corresponding to each number of glenohumeral joint re-dislocations.

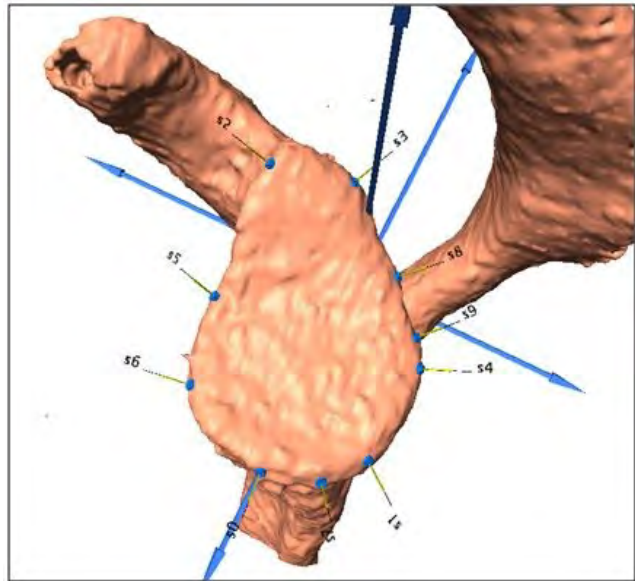
## Materials and Methods

### Dataset

This was a retrospective study using CT scans of 8 patients all with a history of shoulder pathology. For the control group, patients were required to have no previous shoulder pathology involving the glenoid fossa with no history of instability. Of the 4 patients initially selected for the control group one was excluded due to previous history of suspected instability described in the patient's notes. Patients were divided into two categories, the control group (n=3) and the dislocation group (n=5). The control group included 2 males and 1 female with an age range 21-57, mean age of 39 years, each with a CT scan of one shoulder. This gave 3 sets of CT images, two left and one right with a range of shoulder pathologies but no bony pathology to the glenoid. The dislocation group included 5 males with an age range 26-44 years with a mean age of 34 years. All patients in this group had dislocated their right shoulder,

3 anterior dislocations and 2 posterior dislocations. All patients in the dislocation group had received stabilisation surgery. Any CT scans taken after surgery, were after bankart repair of the labrum, which involves no glenoid bone replacement. Of the patients who had undergone the bone replacement technique known as the Latarjet procedure, all CT scans were taken pre-operatively before surgery altered the bony morphology of the glenoid.

### 3D model formation



**Figure 2:** A 3D model of the surface of the glenoid fossa from the control group. The location of the landmark points are indicated by the blue circles and numbered according to the description.

Anonymised CTs were obtained as a stack of 2D CT .dicom format images for each of the 8 patients. These were viewed using the freeware 3D slicer software.<sup>18</sup> Using the editor module of this software package, segmentation of each set of dicom images was achieved. Segmentation was carried out manually by using a threshold value. The threshold value for each image was individually determined by using the grayscale value from the centre of the glenoid fossa on the axial view. All voxels in the source volume in the range that had been selected by the threshold value were then labeled. Using these segmented images, the model maker module was used to create a 3D representation of the glenohumeral joint which was exported in the .stl file format.<sup>18</sup> Using the Meshlab software these files were individually imported.<sup>3</sup> The 3D model was cropped involving removal of all bones separate from the scapula, principally the humerus and acromion. Removal of the humerus allowed a clear view of the glenoid fossa. Some of the CT images were CT arthrograms, these were included due to the small number of available scans. In these cases the radioopaque dye used in the arthrogram is highlighted by image segmentation as it has a similar density and

therefore grey value to bone. The areas infiltrated by the dye were deleted to leave a clearly defined glenoid fossa and glenoid rim. These 3D surface mesh models were exported in the .ply file format. A set of 10 landmarks were digitized onto the glenoid fossa in three dimensions using Landmark version 1.3.0.<sup>25</sup> Landmarks were chosen to correspond to sites identifiable across all 9 glenoids as shown in Table 1 and displayed in Figure 2.

Landmark	Position
S 0	anterior aspect of the infraglenoid tubercle
S 1	posterior aspect of the infraglenoid tubercle
S 2	anterior aspect of the supraglenoid tubercle
S 3	posterior aspect of the supraglenoid tubercle
S 4	most posterior aspect of the posterior glenoid curvature
S 5	most medial aspect of the anterior glenoid curvature
S 6	most anterior aspect of the anterior curvature
S 7	midpoint of the infraglenoid tubercle
S 8	point of posterior curvature in line with the superior aspect of the spine of the scapula
S 9	point of posterior curvature in line with the inferior aspect of the spine of the scapula

**Table 1:** Details the position of the 10 landmarks digitized onto the glenoid fossa.

Landmark points were chosen which represented areas of the glenoid rim marked by features common to the glenoid area of the scapula across specimens. The supraglenoid and infraglenoid fossa were chosen as there is little variation in these sites between individuals. The supraglenoid tubercle represents this insertion of the long head of biceps tendon and the inferior glenoid tubercle the insertion of the long head of the triceps.<sup>9</sup> Other landmarks were chosen to give a good spread of points around the glenoid rim particularly at the posteroinferior and anteroinferior edge where bone loss

is most common following posterior and anterior dislocation respectively. The landmark points were individually digitised onto the surface mesh of each glenoid fossa to ensure accurate placement. Landmark co-ordinate values in the X,Y and Z axis were then exported in the .dta file format.

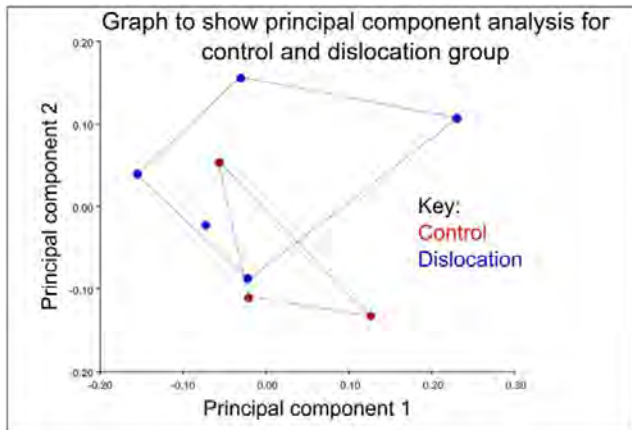
**Shape Analysis** - Geometric morphometrics was used to quantify the variation in shape of the glenoid fossa between the control and dislocation group using the MorphoJ morphometrics software.<sup>16</sup> To quantify the shape difference, co-ordinates of the landmarks digitized onto the surface of the glenoid fossa were extracted. Shape of an object is defined as the objects geometric properties with the exclusion of size, position and orientation.<sup>15</sup> For the quantification of shape variation, Procrustes superimposition of the landmark points was performed. Variation between the configurations of landmarks digitized onto the glenoid fossa after procrustes superimposition is entirely due to variation in the geometric properties of the object.<sup>5</sup> To achieve this, Procrustes superimposition excludes the contribution of size, position and orientation in three steps.<sup>14</sup> Firstly the landmarks from the glenoid fossa are scaled to a unit size.<sup>12</sup> Secondly the landmark configurations are moved to a common position and thirdly are rotated to the position of best fit so there is minimal distance between all the landmark points.<sup>12</sup> This gives the procrustes fit for the landmark configuration. Some landmarks have more variation than others. Procrustes fit acts to average this variation, so shape variation is spread out as evenly as possible between individual landmark points of the landmark configuration.<sup>13</sup> Using the procrustes fit a wireframe graph was used to show variation of the landmarks points between the control and dislocation groups. A wireframe graph simply connects the landmark points so the position and variation of the landmarks points can be visualised.

Principal component (PC) analysis was used to analyse shape variation from the landmark configurations of all the glenoid fossa used in the study. PC analysis which examines patterns of variation between data points in a multidimensional space allows the major patterns of variation to be visualised in a graphical form.<sup>16</sup>

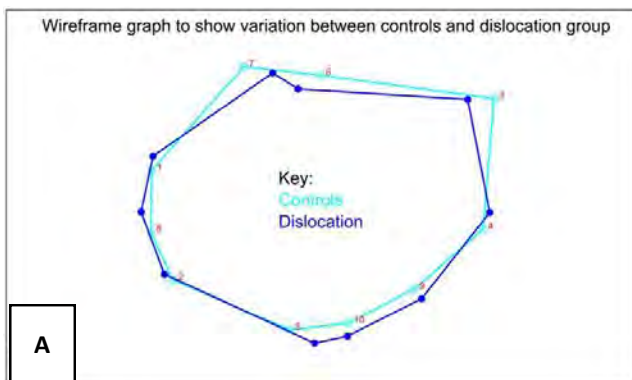
## Results

From the scatter of PC scores shown for both the dislocation group and control group in Figure 3, a number of observations can be made. The outer extremes of PC scores are connected to show the maximum variation in each group. Firstly the scatter of PC scores shows there is greater variation in the shape of the glenoid fossa seen in the dislocation group compared to the control group. Secondly it shows that there is overlap in the geometric properties of the control group compared to the dislocation group.

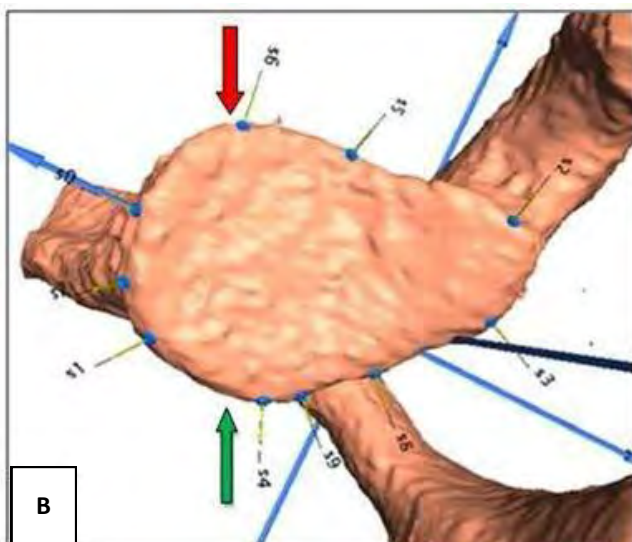




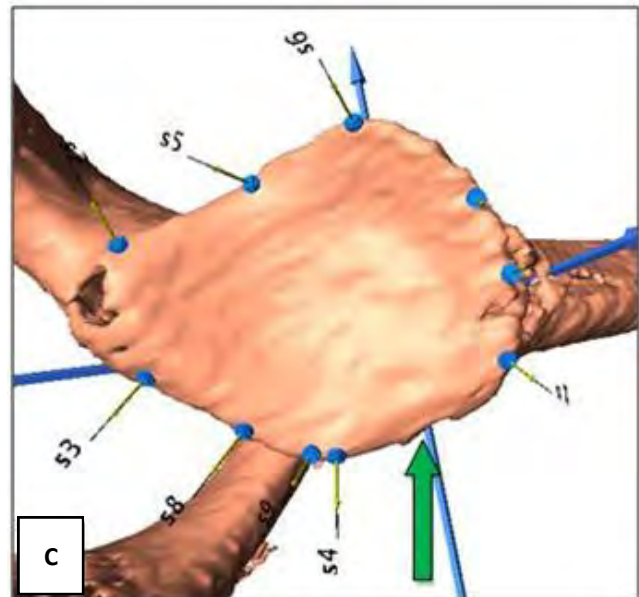
**Figure 3:** A graph to show the principal component analysis for the shape of the Glenoid Fossa. Scatter points include both the control and the dislocation group. Each point represents a plot of the Principal component score for one sample.



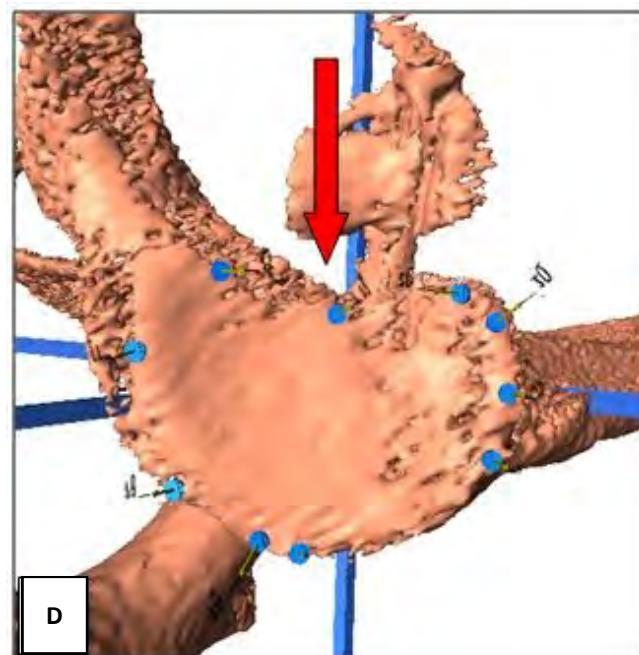
**Figure 4 (A):** A wireframe graph to show the variation of the landmark configurations representing the shape variation of the glenoid fossa between the control and dislocation groups. Orientation the same as the glenoid fossa in figure 4(B).



**Figure 4 (B):** 3D model of a left glenoid fossa from the control group to provide anatomical context and orientation for the landmark points digitized onto the glenoid surface. The green arrow pointing to the normal posterior edge and the red arrow to the normal anterior edge. Each number on the wireframe graph corresponds to the landmark number from the 3D model +1.



**Figure 4 (C):** 3D model of a right glenoid fossa with the most severe bone defect at the posteroinferior aspect of the glenoid rim following recurrent posterior dislocation. Green arrow marks the area of posterior flattening of the glenoid rim as a result of bone loss.



**Figure 4 (D):** 3D model of a right glenoid fossa with the most severe bone defect at the anterior aspect of the glenoid rim. Fractured loose bone can be seen separate from the glenoid rim as a result of recurrent anterior dislocations. Red arrow marks the area of flattening to the anterior glenoid rim to the extent that it is now concave in nature.

#### Anterior Glenoid Rim

The wireframe graph in Figure 4(A) comparing the landmarks of the control and dislocation groups

highlights a number of areas of the glenoid fossa where variation is seen. In the dislocation group there is considerable movement of point 6 (marking the most medial aspect of the anterior glenoid curvature) and point 7 (marking the most anterior part of the anterior curvature) towards each other compared to the control group. In the control group the graph shows the glenoid rim as a normal convex shape, whereas in the dislocation group, the contour of the anterior glenoid rim is concave at its midpoint. This suggests an overall morphological change in the anterior curvature of the glenoid rim. Figure 4(D) a model of a glenoid from the dislocation group with recurrent anterior instability shows a large bony deficit from the anterior glenoid rim. The normal contour of the anterior edge of the glenoid is concave in nature due to extensive bone loss. Comparing this to a normal control glenoid fossa shown in Figure 4(B) where the contour of the anterior glenoid rim is convex demonstrates the general trend seen in the wireframe graph of 4(A).

#### Posterior Glenoid Rim

In the wireframe graph points 9, 10, 5 and 2 along the posterior edge of the glenoid rim demonstrate differing trends in the contour of the posterior rim of the glenoid fossa between the control and dislocation groups. The posterosuperior aspect of the glenoid rim has a similar contour between the dislocation and control group. However at the posteroinferior aspect of the glenoid rim in the dislocation group, point 2 (marking the posterior aspect of the glenoid rim) and point 5 (marking the most posterior aspect of the posterior glenoid tubercle) are further away from each other compared to the control group. This gives the appearance of an increased flattening of the posterior-inferior glenoid rim. The morphology of the posterior glenoid rim after posterior dislocation can be directly seen by comparing Figure 4(B) (a normal glenoid) to Figure 4(C) (a glenoid from a patient with recurrent posterior dislocation). Here the green arrow of Figure 4(C) shows flattening of the posteroinferior aspect of the glenoid rim compared to the same region of Figure 4(B) where the posterior rim is convex in nature. This comparison supports the general trend of posteroinferior glenoid rim flattening in the dislocation group compared to the control group seen in the wireframe graph.

#### Discussion

Several studies have tried to find a critical level of bone loss to relate to the number of dislocations.<sup>7,8</sup> One study proposed a critical level of bone loss at 13.4% below which the average number of re-dislocations were 6.3 and above which the average number of dislocations were 10.1.<sup>8</sup> This seems a rather arbitrary figure and provides no real clinical relevance for the treatment of shoulder dislocation. The reason that these conclusions with few useful applications exist is due to a large variability in bone loss after dislocation between

individuals. The PC scatter results showed large variation in glenoid shape after dislocation with the wireframe graph showing most variation at the anterior-inferior and posterior-inferior glenoid rim. This variation is most likely due to the varying degrees of glenoid bone loss between the samples of the dislocation group. Even in individuals with the same number of dislocations bone loss varies greatly due to factors such as the force of impact of the injury and the exact mechanism of injury.<sup>19</sup> This explains why extensive variation is seen in the glenoid morphology of the dislocation group in this study and also why it is so difficult to relate the extent of bone loss to the number of re-dislocations.

A number of different techniques have been used to measure the shape of the glenoid particularly in relation to pathological glenoid morphology following dislocation. In anterior dislocation a common feature of antero-inferior glenoid bone loss is the flattening of the anterior curvature.<sup>6,8,24</sup> Studies have utilized this feature to quantify bone loss after traumatic anterior shoulder dislocation by measurements such as the length of an anterior straight line and reduced maximum glenoid width.<sup>7</sup> In one study reduced maximum width was shown to be clinically significant in relation to re-dislocation rates. However, these measurements based on 2 dimensional images only take into account a small proportion of the 3 dimensional angled surface of the glenoid fossa.<sup>2</sup> A study investigating glenoid morphology related to atraumatic posterior dislocation used CT images to measure tilting angles of the glenoid as a measure of glenoid concavity.<sup>10</sup> The glenoid was classified using these measurements as concave, flat or convex. Results showed the glenoid was the conventional concave shape in 78% of the controls with no history of instability.<sup>10</sup> However the patients in the dislocation group almost all had glenoid bony changes such as glenoid retroversion resulting in a flattened or convex glenoid surface.<sup>10</sup> Results from our study showed that using morphometric analysis to compare the control group to the dislocation group; it accurately identified the areas of glenoid bony deficit both antero-inferiorly and postero-inferiorly in the patients with anterior and posterior dislocation respectively. We therefore believe the use of geometric morphometrics represents a more complete method for analysing glenoid morphology. Using a single measure from a 2 dimensional image or measuring angles to give an overall interpretation of the morphology of the glenoid fossa provides only limited shape information. The method of landmarking and morphometric analysis takes into account a wider range of geometric components from the glenoid. Morphometrics using landmarks digitized around the glenoid therefore offers a more comprehensive three dimensional analysis of glenoid morphology. Results from this study show that using geometric morphometrics, variation of each of the landmark points can be analysed

to give information about variation in glenoid morphology at different regions of the glenoid fossa. In addition this information can be combined to examine geometric variation of the glenoid fossa as a whole when comparing morphology before and after dislocation.

There were limitations of this study. The technique is new and challenging to undertake at the moment. Also, the dataset is too small to make any statistically valid conclusions on the amount of glenoid bone loss significant and relevant to aid treatment decisions. Further exploration into the use of morphometrics to study glenoid morphological changes is required.

### Conclusions

Despite the limitations of the study a number of valuable conclusions can still be drawn from this project. The results show that geometric morphometrics has many advantages over other techniques which have been reported in the literature to analyse changes to glenoid morphology. Morphometric analysis of a three dimensional surface representation of the glenoid fossa

provides much more extensive data for analysis of glenoid geometry. This study showed areas where variation is most common at the anteroinferior and posteroinferior aspects of the glenoid fossa following anterior and posterior dislocation respectively. The techniques used in this study highlights possibilities to analyse glenohumeral morphology to a high level of geometric detail in a wide number of shoulder pathologies. In addition, morphometrics could help establish which variations in glenoid morphology occurring naturally in the population predispose to certain groups of shoulder pathology. Further research using morphometrics to quantify shoulder morphology has exciting potential as an additional tool for determining the surgical management of patients with recurrent dislocation.

### Acknowledgments

We would like to thank Dr Christian Klingenberg for his help with the geometric morphometric analysis and Dr Jonathan Harris for assisting in the interpretation of the CT scans.

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## Best Six Articles from 2012-2013 (Article - 5)

## Role of Cloud Computing in the Provision of Healthcare

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*Address for Correspondence:*Professor Sharmini Enoch: [sharminienoch@gmail.com](mailto:sharminienoch@gmail.com)**Keywords:***Medical advances, healthcare provision, cloud computing, resource-poor population, health monitoring.***Abstract**

Rapid strides in information technology coupled with enhancing interest in hybrid computing environments have resulted in the development of 'cloud computing'. This is an application that can be accessed anytime and anywhere in the world based on the 'pay-per-use' model. The healthcare industry is in a period of accelerating change that requires continued innovation. Cloud computing has got a significant potential in the healthcare system and provision of healthcare in the future. This technological advancement has led to the design of a real-time health monitoring and analysis system that is scalable and economical for people who require frequent monitoring of their health. Peoples' health data is collected and disseminated to a cloud-based information repository that facilitates analysis of the data using software services hosted in the cloud. This article reviews the existing work carried out in the healthcare system using cloud computing. It analyzes the measures, drawbacks and challenges (including security) of cloud computing in the healthcare system.

**Introduction**

Cloud computing provides high quality and low-cost information services based on the pay-per-use model. It reduces the investment on hardware, software and professional skills<sup>1</sup>. It helps user applications to access various computing resources to any specified location. This technology also allows consumers and businesses to use application without installation and access their personal files at any computer with Internet access.

In the early part of the 20th century, medical care was delivered at home, through visiting family physicians who packed the necessary medical technology into a doctor's bag. Later, advanced medical technology and specialist providers had to be centralized in hospitals to make their

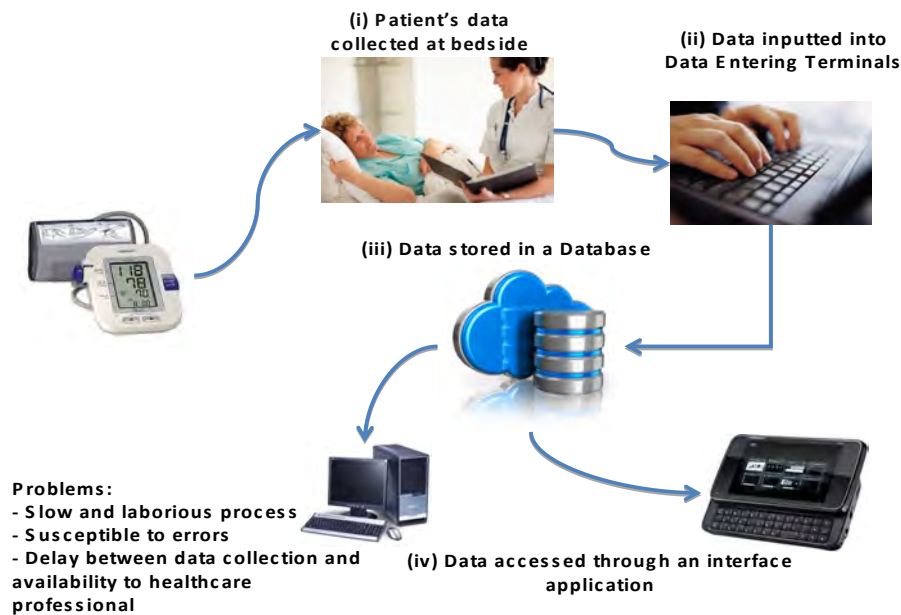
utilization effective. In the current century, the lack of sufficient hospitals in rural and resource-poor areas, the exponential complexity of lifestyle (mainly urban) and the increasing of chronic diseases make healthcare a serious issue<sup>2</sup>. Driven by quality and cost metrics, the healthcare systems have to change radically in the near future from current healthcare professional-centric systems to one of distributed network and mobile healthcare systems. In this movement, the leading part is attributed to the cloud computing technologies. Cloud healthcare, in contrast, tries to change the healthcare delivery model: from doctor-centric to patient-centric, from acute reactive to continuous preventive, and from sampling to monitoring. This approach however is to complement and not replace traditional medicine.

Rural residents have higher poverty rates, a larger percentage of elderly tend to be in poorer health, have fewer doctors and hospitals, and face more difficulty getting to health services<sup>3</sup>. Hence, one challenge of a cloud healthcare system is the provision of better healthcare services to people using limited financial and human resources. Many medical errors occur due to lack of correct and complete information necessary at the location at a particular time, resulting in incorrect diagnosis and drug interaction problems<sup>3</sup>. The required medical information can be made available at any place at any time using sophisticated devices and widely deployed wireless networks.

The design and construction of a cloud computing system for healthcare in rural areas appears very effective. It comes as a solution to help patients adjust lifestyle to their health requirements. Apart from that, through patients' behavioral recognition we can detect symptoms of diseases and predict their progression over time.

## Existing system

Figure 1 depicts how the process works based on manual notes<sup>4</sup>. The interactions are described below:

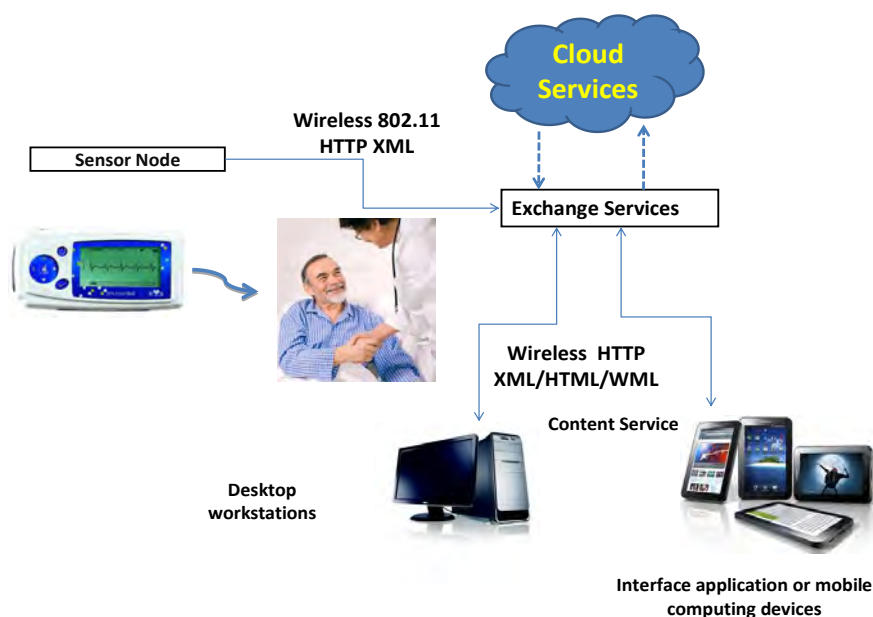


**Figure 1:** Illustration of existing system that is commonly used in current healthcare

- |  |   |
|--|---|
| <p>(i) A staff member collects patient's data at bedside, writing it down to a paper spreadsheet;</p> <p>(ii) The notes are typed in data entering terminals;</p> <p>(iii) The data is transmitted to a database server that organizes, indexes, and make it accessible through a database interface; and</p> <p>(iv) At this point, medical staff can access this</p> | <p>information through an interface application. It is clear that there is latency between data gathering and information accessibility. This is undesirable and prevents real-time monitoring of vital patients' data, restricting the clinician's monitoring capabilities. Moreover, this process is error prone, as there is a possibility of incorrect input.</p> |
|--|---|

## Cloud computing in health care

The system of manual notes is replaced by the cloud. Figure 2 depicts the proposed system structure.



**Figure 2:** Illustration of cloud computing technology in healthcare

**Patient's Data Collection in Health Care Using Cloud Computing**

A solution to automate the patient data collection process by using sensors attached to existing medical equipments that are inter-connected to exchange service has been previously explored<sup>4</sup>. This is based on the concepts of utility computing and wireless sensor networks. The information becomes available in the cloud from which it can be processed by expert systems and/or distributed to medical staff. The proof-of-concept design applies commodity computing integrated to legacy medical devices, ensuring cost effectiveness and simple integration. This paper used the cloud based services such as 'Infrastructure' as a Service, 'Platform' as a Service, 'Software' as a service and it was found to be cost-effective. The disadvantages however are the security and management with interaction of third party infrastructure service are not considered.

**Cloud Computing Security in Patient Health Care Monitoring**

Secure open cloud architecture (OpenCloudCare) for remote patient health monitoring was proposed by Mouleeswaran and colleagues<sup>5</sup>. It defines the front-end and back-end architecture that would integrate healthcare devices into the enterprise cloud. The major components required for securing the cloud infrastructure are also identified. Here the security in electronic health record (EHR) is implemented by using cloud security infrastructure. EHR stores all the data related to human activities. The human activity depicts all the actions and non actions performed by the human. Mouleeswaran and colleagues<sup>5</sup> discusses security in patient health record while the individual security components are not considered.

**Hosting ECG Data Analysis Service in Autonomic Cloud Environment**

The design aspects of an autonomic cloud environment that collects people's health data and disseminate them to a cloud-based information repository and facilitate analysis on the data using software services hosted in the cloud were discussed by Suraj Pandey and colleagues<sup>6</sup>. To evaluate the software design, a prototype system was developed that uses an experimental test bed on a specific use case, namely, the collection of electrocardiogram (ECG) data obtained at real-time from volunteers to perform basic ECG beat analysis. In this work a heuristic-based method minimizes the cost of

using cloud resources while maintaining user quality-of-service satisfaction. This could be done by cloud resource availability, and user allocations based on user priority and varying cloud resource costs. The problem which is not addressed is data security while using distributed cloud storage.

**Intelligent Manipulation of Human Activities using Cloud computing**

Intelligent manipulation of activities using Context-aware Activity Manipulation Engine (CAME) and the Human Activity Recognition Engine (HARE) has been the focus of discussion in the study by Asad Khattak and colleagues<sup>7</sup>. The human activity is recognized using video-based, wearable sensor-based and location-based activity recognition engines for context analysis. The objective of CAME is to receive real-time low level activity information from Activity Recognition engines and infer higher level activities, make situation analysis, and after intelligent processing of activities with their corresponding information take appropriate decisions. To achieve this objective, two phase filtering technique for intelligent processing of information is used and appropriate decisions based on description logic rules. The experimental results for intelligent processing of activity information showed relatively good accuracy. The security concern is not addressed in this work.

**Cloud Computing Framework for New Medical Interface Technologies**

Maya Dimitrova *et al.*<sup>8</sup> proposed to formulate a new development framework for cloud computing called User Interface as a Service (UIaaS), which is used to act as an interface between cloud and user. New multimodal interface technologies for medical instrumentation compatible with web platforms have been recently developed. The framework that explicitly aims at supporting seamless and ubiquitous health monitoring based on cloud services for healthcare are presented. The aim of this framework is the implementation of new interface technologies providing the doctors and patients with useful tools to explore conditions and perform monitoring across diagnoses – in an indirect, safe, secure and harmless way - operating as new UIaaS. The device will be integrated in a sophisticated and intelligent backend environment enabling productive end-to-end usage as a step towards modern and ubiquitous healthcare in a cloud computing framework. The security problem is not addressed in this work.

**Table 1** compares the related work carried out in health care using cloud computing along with their performance metrics and major drawback.

Related Work	Metrics	Drawback
Patient's Data Collection in Health Care Using Cloud Computing <sup>4</sup>	Time, Cost	Security
Cloud Computing Security in Patient Health Care Monitoring <sup>5</sup>	Time, Cost, Privacy	Security
Hosting ECG Data Analysis Service in Autonomic Cloud Environment <sup>6</sup>	Scalability, Cost	Security in storage
Intelligent Manipulation of Human Activities using Cloud computing <sup>7</sup>	Cost, Accuracy	Security
Cloud Computing Framework for New Medical Interface Technologies <sup>8</sup>	Cost, Time	Security

**Table 1:** Comparison of Related Work in Cloud Computing

### Conclusion and future work

Cloud computing revolutionizes all scientific fields, including healthcare. Health monitoring system monitors human health and shares this information with doctors, healthcare providers, care-takers, clinics, and pharmacies obtained from the cloud to provide low-cost and high-quality service to users. Although security can be provided in healthcare monitoring systems using the encryption method, it continues to remain as a major issue that needs to be addressed and should be the subject of future work.

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## Best Six Articles from 2012-2013 (Article - 6)

## Management of Major Trauma: A Malaysian Perspective

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**Keywords:**

*ATLS, pelvic fractures, acute abdominal trauma, limb threatening injuries, amputations*

**Introduction**

Trauma and accidental injuries remain a leading cause of morbidity and mortality worldwide. With every death, two people suffer permanent disability. In the developing world, the impact is further pronounced in view of the increasing population and the associated use of motor vehicles. The society's livelihood depends on a full functioning body as manual labour contributes greatly to the workforce in developing countries hence families faced with disability would suffer tremendously as they are often dependent on a single bread-winner. Thus, establishment of functioning trauma care systems is crucial.

In developed countries, the increased awareness of seatbelts over the recent years has resulted in a reduced number of long bone traumas<sup>1</sup>. In Malaysia road traffic accidents account for almost 80% of major trauma cases and it is the leading cause for admission to government hospitals. These trauma cases largely involve the younger population (between 15-24 years of age), 66% of which are associated with motorcyclists. This is becoming more pronounced as over speeding of motor bikes and lane splitting, more common amongst the younger age group, is on the rise. Poor awareness on importance of helmet use and motorcycle safety is also a contributing factor.

Trauma patients suffering from multiple injuries impose tremendous demands at all levels within hospitals particularly on those doctors, nurses and clinical officers caring for the patient within the first few hours of hospital admission. The first hour of admission, known as the "golden hour" for multiple trauma patients are critical in reducing permanent irreversible damage. Therefore in view of this, guidelines for major trauma care have been developed.

This article which will be accompanied by case studies summarizes important topics related to major trauma focusing on its management. The topics include:

- Management of patient according to the ATLS principles
- Management of pelvic fractures
- Management of acute abdominal trauma
- Management of limb threatening injuries
- Management of amputations to limbs or digits.

**A. Advanced Trauma Life Support (ATLS) for major trauma**Primary SurveyAirway (with cervical spine protection)

Patients with airway compromise may need acute airway management to avoid a preventable cause of hypoxia. Always maintain cervical spine immobilization by applying devices as described below in section (d).

**(a) Assess airway**

- ☐ Stabilize the patient's head by placing a hand on either side of the patient's head prior to communicating with them to protect the C-spine
- ☐ Talk to the patient to establish patency, evaluate for voice change and stridor
- ☐ Perform a general inspection looking for pooling of secretions, cyanosis, facial injuries or expanding haematomas
- ☐ Is the patient conscious or unconscious?
- ☐ Consider use of a naso or oropharyngeal airway during bag-valve mask ventilations (BVM)
- ☐ Rapid Sequence intubation if needed for airway stabilization or protection i.e., for Glasgow Coma Scale (GCS) of 9 or less
- ☐ Consider surgical airway if difficulty intubating in patients unable to maintain their own airway.

(b) Improve airway

Most common form of airway obstruction is a prolapsed tongue, thus manoeuvres below may help to clear the airway:

- Head Tilt/Chin Lift (\*Only use this method once C-spine injury has been excluded\*)

Place one of your hands on the patient's forehead and apply gentle, firm, backward pressure using the palm of your hand. Place the fingers of the other hand under the bony part of the chin. Lift the chin forward and support the jaw, helping to tilt the head back (**Figure 1**). This manoeuvre will lift the patient's tongue away from the back of the throat and provide an adequate airway. If the head tilt / chin lift is not possible, or is contraindicated (possible cervical spine injury), then the jaw thrust manoeuvre can be performed.



**Figure 1:** The head tilt/chin lift manoeuvre

- Jaw thrust

Grasp angles of the patient's lower jaw and lift with both hands, one on each side (**Figure 2**). This will displace the mandible forward and prevent the tongue obstructing

the hypopharynx. Care must be taken to prevent extension of the neck whilst performing this manoeuvre.



**Figure 2:** Jaw thrust

(c) Remove foreign bodies

The oral cavity is inspected. Any visible debris is removed manually and secretion is cleared via suction.

(d) Cervical spine immobilization

Devices such as cervical collar and head immobilizer (consisting of head blocks and straps) should be placed on patient prior to patient movement (**Figure 3**). If no collar can be made to fit patient, towel or blanket rolls may be used to support neutral head alignment. The head must be supported at all times prior to exclusion of C-spine injuries, hence prior to use of collar and immobilisers or if they are removed at any point (e.g., when log-rolling to perform a full examination), neutral alignment must be maintained manually with a hand placed on either side of the patient's head. Use rigid spinal boards during patient transfer to prevent unstable fractures causing further neurological deficits.



**Figure 3:** Cervical collar and head immobilizer in place

Top  
Tips

## Box 1

**Suspect cervical spine injury if****there is:**

- ✓ N – neurological deficit
- ✓ S – spinal tenderness
- ✓ A – altered mental status
- ✓ I – intoxication of drug/alcohol
- ✓ D – distracting injury

Top  
Tips

## Box 2

**Seven life threatening thoracic****conditions:**

- ✓ A – airway obstruction
- ✓ T – tension pneumothorax
- ✓ O – open pneumothorax
- ✓ M – massive haemothorax
- ✓ F – flail chest
- ✓ C – cardiac tamponade
- ✓ H – severe haemorrhage

**Breathing**

Place your ear near the victim's nose and mouth with your eyes looking towards their chest. Inspect for difficulty in breathing, asymmetrical chest movements, or see-saw appearance. In infants, intercostal recession may be present. Listen for breath sounds (normal, laboured or shallow) or abnormal sounds *i.e.*, complete silence (complete obstruction), cough or wheeze (bronchoconstriction). Feel for breathing, the absence of which may indicate inadequate air moving through the nose or mouth.

The respiratory rate is often the most sensitive indicator of sick patients. Monitor the respiratory rate (normally between 12 to 25) by calculating the breaths per minute (BPM) rate by counting the chest movements 15 seconds, then multiplying by four. Treat hypoventilation and identify seven life threatening thoracic conditions (see **Box 2**).

Give the patient high flow oxygen 15L via a non-breathable mask, even in patients with COPD. In acute situations, hypoxia will kill more quickly than hypercarbia. Once stabilized and the patient shows signs of CO<sub>2</sub> retention, then oxygen levels can be tailored to the individual.

Oxygen treatment can be monitored by blood gas measurements or non-invasively by pulse oximetry. Blood gas analysis provides accurate information on the pH, PaO<sub>2</sub>, and PaCO<sub>2</sub>. Oximetry provides continuous monitoring of the state of oxygenation.

**Circulation**

The aim of cardiovascular management is to ensure adequate circulation of blood volume by controlling haemorrhage and replacing lost fluid. Pallor, tachycardia, hypotension, cold, clammy peripheries and a decreased level of consciousness are signs of decreased perfusion. The capillary refill time and pulse rate can be assessed in any setting and is useful in gauging patient's overall perfusion. Any external bleeding should be controlled by applying direct pressure - not tourniquets. Occult blood loss may be from the chest, abdomen, pelvis or from the long bones.

Intravenous access (two large bore lines) should be immediately established followed by fluid resuscitation. Bloods should be sent for cross match. Bladder catheterisation (provided there are no signs of urethral damage) should also be performed to assess urine output.

Continuous bedside monitoring including cardiac monitoring and blood pressure measurements are essential to gauge patient response to ongoing treatment.

The ATLS classification of haemorrhagic shock is illustrated in **Appendix 1**<sup>2</sup>.

**Disability (Neurological Evaluation)**

A quick assessment of the patient's neurological status can be done using the AVPU scale shown in **Table 1** below:

Component	Description
<b>A - Alert</b>	a fully awake patient
<b>V - Voice</b>	patient responds when verbally addressed
<b>P - Pain</b>	patient responds to painful stimuli
<b>U - Unresponsive</b>	patient does not give any eye, voice or motor response to voice or painful stimuli.

**Table 1:** AVPU scale



A gross motor/sensory examination is performed to determine if the cranial nerve system is intact. This is not a full neurologic examination. For example, the patient is asked to wiggle his toes to assess motor response to a verbal command. A full neurologic exam is done later in the secondary survey.

Pupils are assessed for size, symmetry and reactivity.

Uncal herniation will present as a "blown pupil." A dilated pupil is seen due to unopposed sympathetic activity.

A more objective way of recording a patient's state of consciousness is by using the GCS (**Table 2**). The best possible score is 15 and the worst score is 3.

Eye Opening Response	Verbal Response	Motor Response
4 - spontaneous	5 – oriented	6 - obeys command
3 - to verbal command	4 – confused	5 - localizes to pain
2 –to pain	3 –inappropriate	4 - withdraws from pain
1 - none	2 –incomprehensible speech	3 - Abnormal (spastic) flexion, decorticate posture
	1 - none	2 - Extensor (rigid) response, decerebrate posture
		1 - none

**Table 2:** GCS scale

#### *Exposure and Environmental control*

Patient should be completely undressed to provide adequate exposure. At the same time, warm blankets should be used to prevent hypothermia.

Finally, log roll the patient using spinal immobilization technique to palpate the spine for step-offs or tenderness (**Figure 4**). To perform the "log roll", at least 5 people are required - three are to manoeuvre the body, one to position the head and lastly one to examine. Steps on performing the log roll are as follow<sup>2</sup>:



**Figure 4:** The log roll

- ❑ Apply and maintain cervical stabilization. Assess distal

function in all extremities

- ❑ Apply a cervical collar
- ❑ Rescuers at an appropriate level to the patient *i.e.*, if the patient is on the floor, then three people should kneel on one side of the patient and place hands on the far side of the patient. One person should be at the head and this person should communicate clearly with the rest of the team when to roll the patient.
- ❑ On command, rescuers roll the patient toward themselves, quickly examine the back, slide the backboard under the patient and roll the patient on to the board
- ❑ Position the patient in the middle of the board
- ❑ Secure the upper torso first
- ❑ Secure the chest, pelvis and upper legs
- ❑ Begin to secure the patient's head by using a commercial immobilization device or rolled towels
- ❑ Place tape across the patient's forehead
- ❑ Check all straps and readjust as needed. Reassess distal function in all extremities.

#### *Primary survey adjuncts*

Below are investigations that can be done during the primary survey:

- ❑ Standard Trauma X-rays: lateral cervical, AP chest and pelvis
- ❑ Focused Assessment Sonography in Trauma (FAST)  
The four views include sub-xiphoid cardiac, spleno-renal, hepato-renal and bladder views. Any free fluid detected during the FAST exam may represent peritoneal penetration

- ❑ Basic laboratory tests should be ordered simultaneously
- ❑ Further x-rays are best grouped and ordered after the secondary survey.

#### Secondary Survey

Once the primary survey is completed, head to toe evaluation of a trauma patient begins which includes a complete history, full physical examination and reassessment of all vital signs. Each region of the body is fully examined and additional X-rays as indicated by clinical suspicion are obtained.

Top  
Tip

#### Box 3

##### The hidden eight injuries

##### include:

- ✓ P – pulmonary contusion
- ✓ A – aortic disruption
- ✓ T – tracheobronchiole disruption
- ✓ M – myocardial contusion
- ✓ E – esophageal disruption
- ✓ T – traumatic diaphragmatic hernia
- ✓ S – spontaneous haemothorax
- ✓ H – haemothorax

If at any time during the secondary survey the patient deteriorates, another primary survey is carried out as a potential life threat may be present.

Summary of approach to the trauma patient as practised at the Emergency Department, Sultan Abdul Halim Hospital, Sungai Petani, Kedah, Malaysia is illustrated in **Appendix 2**.

### B. Management of pelvic fractures

The pelvis comprises of two innominate bones and the sacrum. Trauma to the pelvis results in fractures, which may be stable or unstable in nature. The former is common especially amongst the elderly after a simple fall. Unstable fractures, however results from significant kinetic forces such as a fall from height or a motor vehicle accident which often include an increased risk of associated injuries, morbidity and mortality.

Details of treatment strategies are illustrated in the algorithm<sup>3</sup> below (**Figure 5**).

Pre-hospital management of patients including appropriate immobilization, airway protection and initial circulatory support with expedient transport is vital.

#### Case Study

*A 24-year-old gentleman was brought to the Red Zone at the Emergency Department after a motor vehicle accident. Upon arrival, his GCS was 15 however he was clinically pale. His BP was 70/40mmHg and pulse was 125/min. On examination, there was scrotal haematoma with bruising over the suprapubic region.*

- ❑ What sort of injury should be suspected?
- ❑ What are the initial investigations to be performed?
- ❑ How should this patient be managed?

Top  
Tip

#### Box 4

Pelvic ring disruption may shear blood vessels such as the pelvic venous plexus or internal iliac arterial system leading to severe haemorrhage *i.e.*, up to 2-3L of blood loss which may be hidden

Upon arrival at ED, pelvic stabilization to help tamponade bleeding in patients with pelvic fractures who are haemodynamically unstable is crucial. Initial treatments include using a pneumatic anti-shock garment (PASG), wrapping a sheet around the pelvis or placing a pelvic binder<sup>4</sup>. A chest radiograph and a FAST should be done promptly to exclude other sources of haemorrhage. If the patient continues to be unstable, arterial angiography and embolization should be considered.

If possible, pelvic fractures should be classified according to the Tile and Young and Burgess Systems. These classifications describe fractures based on integrity of the posterior sacroiliac complex (Tile) or based on mechanism of injury (Young).

If the pelvic fracture type is unstable (Tile B or C; Young and Burgess APC II, APC III, LC II, LC III, VS), the patient will require operative fixation and can be treated with more definitive stabilization, such as an external fixator or a pelvic C-clamp.

The principles of pelvic fracture fixation<sup>5</sup> are:

- ❑ With complete instability of the posterior ring (*i.e.*, the posterior SI ligaments are disrupted), anterior fixation alone is inadequate

- With complete instability of the posterior ring and vertical instability, any posterior fixation should be supplemented with some form of anterior stabilization.
- With partial instability of the pelvic ring (*i.e.*, the posterior SI ligaments are intact), anterior fixation alone is adequate and full weight-bearing may be permitted.

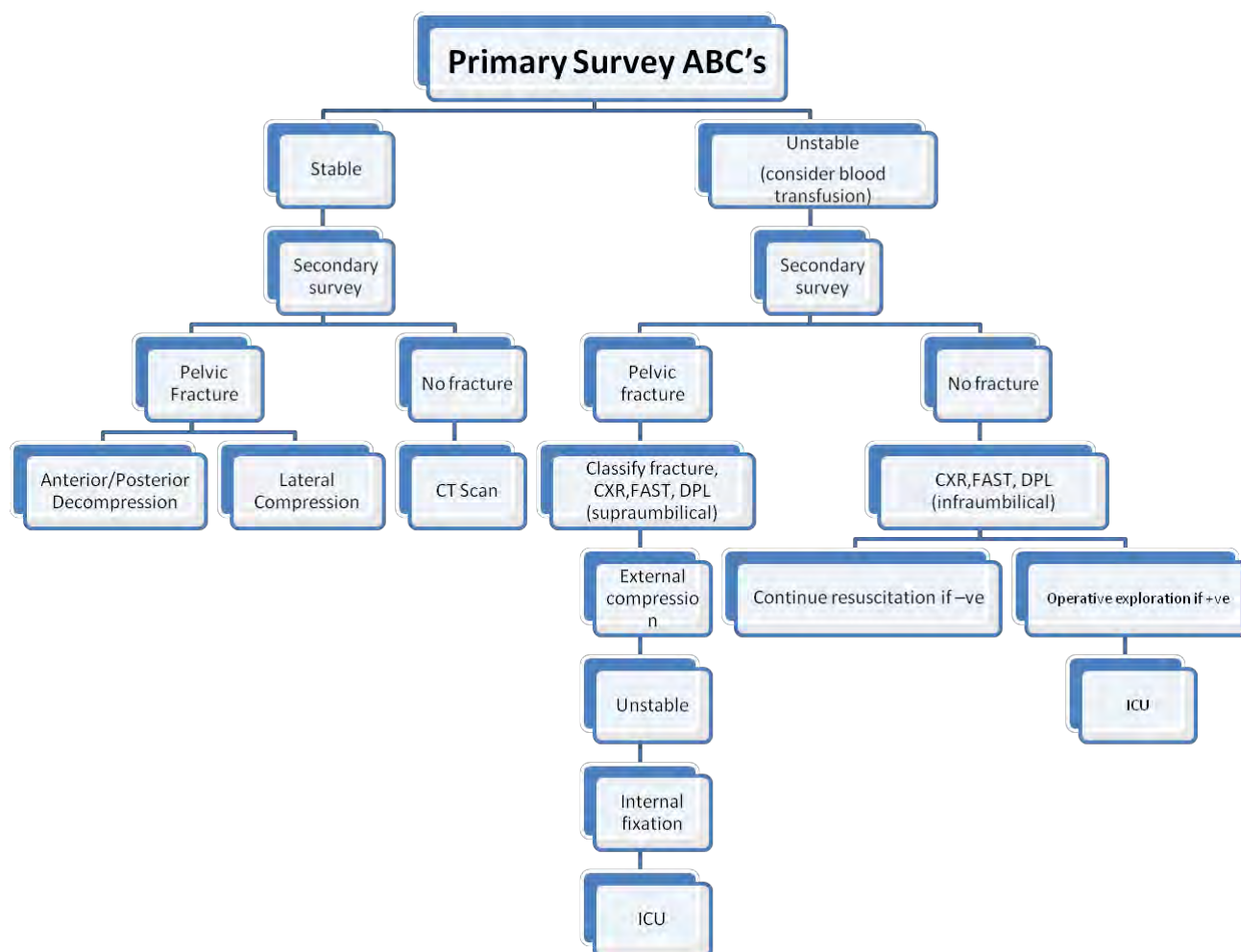


Figure 5: Pelvic fracture management algorithm

### C. Management of Acute Abdominal Trauma

#### Case Study

A 33-year-old lady was brought in by ambulance and was attended promptly by the surgical resident on call. This patient was knocked down by a motorcycle from behind while walking along the roadside. Her vital signs were stable and her GCS was full. Upon examination, there was bruising over the upper abdomen and along her left flank. Also noted, blood stained urine in the catheter bag.

- What sort of injury should be suspected?
- What are the initial investigations to be performed?
- How should this patient be managed?

Abdominal trauma can be broadly divided into penetrating *i.e.*, stab wounds, gunshot wounds or blunt injuries *i.e.*, motor vehicle accidents, falls, assaults and occupational accidents. From an anatomical perspective, abdominal trauma can be categorized into intra-peritoneal, retro-peritoneal and pelvic injuries.

Signs and symptoms include abdominal pain, tenderness, rigidity, distension, haematoma and diminished or absent bowel sounds. Early indications of abdominal trauma include nausea, vomiting, and fever. Haematuria is another salient sign. Seatbelt injuries if significant enough to cause external bruising may have related internal injuries which will also need to be excluded.



Investigations may include ultrasonography, computed tomography, exploratory laparotomy and peritoneal lavage. Treatment may be conservative but if the patient is unstable, he or she will require surgery.

Top  
Tip

#### Box 5

Look for Cullen's sign of periumbilical bruising or Grey-Turner's sign of flank bruising, both associated with retroperitoneal haemorrhage

#### Hepatic injuries

CT is the recommended diagnostic modality for evaluation of hepatic trauma.

##### A. Penetrating trauma

- ❑ Initial haemostasis  
Rapid mobilization of the injured lobe is done by bimanual compression and perihepatic packing
- ❑ Definitive haemostasis  
Deeper wounds are usually managed by hepatotomy and with selective ligation of bleeding vessels
- ❑ Damage control  
Perihepatic packing with ICU admission and resuscitation followed by return to the operating room in 24-48 hours

##### B. Blunt trauma

- ❑ Haemodynamically unstable  
Require operative exploration and control of haemorrhage
- ❑ Haemodynamically stable  
Patient is treated conservatively whereby ongoing assessment is done to monitor blood loss

#### Splenic Injuries

##### A. Penetrating trauma

- ❑ Penetrating splenic injuries are diagnosed at laparotomy. Initial haemostasis is possible through manual compression. Bleeding from small capsular lacerations can be controlled with direct pressure or topical haemostatic agents. In stable patients, splenorrhaphy can be employed<sup>6</sup>. Devitalized tissue should be debrided.

##### B. Blunt trauma

- ❑ CT remains the diagnostic modality of choice in diagnosing blunt splenic injuries. In stable patients,

close observation with continuous monitoring of vital signs and bed rest is indicated. However, if patient becomes unstable, splenectomy is performed.

#### Bowel injuries

CT abdomen is the investigation of choice in evaluating abdominal trauma.

##### A. Small bowel

- ❑ Given its large volume and anatomy, the small bowel is prone to penetrating and blunt trauma (**Figure 6**). Besides imaging, diagnosis can also be made during laparotomy. Treatment consists of primary repair or segmental resection with anastomosis<sup>7</sup>. Mesenteric defects should be closed.



**Figure 6:** Penetrating bowel injury post motor vehicle accident

##### B. Large bowel

- ❑ Colonic injuries typically occur secondary to penetrating trauma and are diagnosed at laparotomy. Single agent prophylactic antibiotics are indicated during surgery due to risk of faecal contamination. Primary repair should be considered in all colonic injuries *i.e.*, end to end anastomosis with diverting colostomy.

#### Kidney injuries

Ultrasound and intravenous pyelogram (IVP) have commonly been used in the past in investigating kidney injuries. Currently, the gold standard in diagnosing kidney injuries is with CT urography.

If the patient is stable and injury to other organ systems has been ruled out, non-surgical treatment is opted. The patient will need bed rest and continuous monitoring to ensure haematuria resolves.

For clinically unstable patients, surgical exploration and kidney repair is indicated. Evidence of kidney dysfunction should prompt arteriography of renal artery. If the injury is discovered within six hours, revascularization is performed. Nephrectomy is indicated if laparotomy is performed for associated injuries<sup>8</sup>.

There are also other less invasive techniques to treat kidney injuries such as angiographic embolization.

#### D. Management of limb threatening injuries

##### Case Study

A 45-year-old construction worker had a fall from a 10-foot height platform. Fortunately he landed on a sand pit however he hit his right leg on an edge of a metal frame. Subsequently, he was unable to ambulate and his right calf was grossly swollen. Patient claims there was no head trauma and he remained conscious throughout the event. On further examination, there was a ragged wound noted over the medial aspect of his right calf measuring 5x2 cm as well as a bony protrusion seen at the proximal tibia with minimal blood oozing from the wound.

- ☐ What type of fracture has this patient sustained?
- ☐ How should this patient be managed?
- ☐ What is the best method of fixation for this injury?

##### Vascular injury

Penetrating wound and blunt force trauma such as fractures and dislocations may cause arterial and other vascular injuries. This may lead to significant haemorrhage through the open wound and soft tissue.

##### Assessment

Injured extremities should be assessed for external bleeding, loss of previously palpable pulses and change in pulse quality. A cold, pale and pulseless extremity indicates an interruption of the arterial supply. A rapidly expanding hematoma also suggests a significant vascular injury. Doppler Ultrasound is a useful tool to check for pulses.

##### Management

Before surgery, the application of tourniquet is lifesaving. It is not advisable to apply vascular clamps in bleeding open wounds unless a superficial vessel is clearly identified. During surgery, arterial repair and sometimes arteriography is done<sup>9</sup>.

##### Crush Injury

Crush injury of the limbs can lead to crush syndrome or traumatic rhabdomyolysis (**Figure 7**). A combination of muscle ischaemia and cell death releases myoglobin which can cause acute renal failure. As a result, elevated creatine kinase levels in these patients may precipitate disseminated intravascular coagulation (DIC)<sup>10</sup>.



**Figure 7:** Crush injury caused by sugarcane grinder machine

##### Assessment

Dark amber urine that may test positive for haemoglobin is a useful indicator for rhabdomyolysis in this clinical scenario. Rhabdomyolysis can lead to hypovolemia, metabolic acidosis, hyperkalemia, hypocalcemia, renal failure and disseminated intravascular coagulopathy.

##### Management

Fluid resuscitation along with administration of sodium bicarbonate and electrolytes is done to prevent renal failure. Myoglobin induced renal failure can be prevented by intravascular fluid expansion and osmotic diuresis to maintain high tubular volume and urine flow. It is recommended to maintain urinary output at 100ml/hour until the myoglobinuria is cleared. If the limb cannot be salvaged and/or the patient is developing sepsis or severe systemic effects from the trauma, then amputation of the affected limb can be considered.

##### Compound/open fractures of the lower limb

Open fractures represent a communication between the external environment and the bone. This break in barrier makes fracture sites prone to infection thus subsequently affects healing and may cause loss of function.

The classification of open fracture as described by Gustillo-Anderson is illustrated in **Appendix 3**.

#### Assessment

Look at size of the wound, extent of soft tissue injury or any signs of neurovascular compromise.

#### Management

Wound irrigation is done with Normal Saline whereby amount of saline needed depends on severity of the fracture *i.e.*, wounds measuring > 10cm requires at least 9 litres of normal saline irrigation. Additionally, broad

spectrum IV antibiotics should be started.

Wound debridement is compulsory if contamination is noted to be severe. Definitive fixation of the bone is ideally done within 24 hours.

The best method of fixation in open fractures is external fixation or Ilizarov<sup>11</sup>.

**Figures 8-11** illustrate the preoperative and postoperative sequence of management of an open tibia/fibula fracture.



**Figure 8:** Grade IIIB open distal tibia/fibula fracture. The wound size measures > 10cm and soft tissue is severely damaged. However, there is no vascular involvement



**Figure 9:** An AP view of a distal comminuted tibia/fibula fracture with butterfly fragment



**Figure 10:** Post-operative application of biplanar external fixation at the fracture site



**Figure 11:** Lateral view of biplanar external fixation under radiological imaging



Top  
Tips

Box 6

Acute compartment syndrome usually develops after a severe injury and the clinical manifestations can be described as the 6Ps:

- ✓ Pain
- ✓ Pressure
- ✓ Paraesthesia
- ✓ Paralysis
- ✓ Pallor
- ✓ Pulselessness

### E. Management of amputation to limbs or digits

#### Case Study

A 5-year-old boy was injured after a firecracker he lit went off unexpectedly. He was rushed to the nearest hospital as his left hand was blown apart. At the Emergency Department, his father managed to bring in the detached part (left hand) in a plastic bag filled with ice within 1 hour post trauma.

- ☐ Is the detached left hand salvageable?
- ☐ What are the contraindications for replantation in amputated limbs?
- ☐ How should this patient be managed?

An amputation is a surgical or traumatic separation of a particular body part from its origin (**Figure 12**).

Amputations involving the upper limb or children are usually prioritized when selecting candidates for replantation. Clean cut injuries with minimal contamination are associated with higher rates of successful replantation.

Contraindications for replantation of amputated limbs include coexisting serious injuries or disease that preclude a prolonged operative time, multiple levels of amputation, severely crush or degloving injury, dirty mangled wound, prolonged ischaemia time and mentally unstable patients or self-inflicted wound<sup>6</sup>.

#### Handling of amputated limb part

The goal is to preserve the limb for reattachment. Therefore, delays in transportation should be avoided. The amputated part should be covered with saline moistened gauze and sealed in a clear plastic bag on a



**Figure 12:** Amputated right hand after a 'parang' assault

mixture of ice and water. The part should never be placed directly on ice or immersed in saline<sup>12</sup>.

#### Amputation repair techniques

The aim is to preserve residual limb length balanced with soft tissue as well as reconstruction to ensure good healing, non-tender and functioning residual limb. The proximal stump is cleaned and a compressive dressing is applied. Tourniquets are not used. The sequence of repair involves identification of affected structures, debriding edges for reattachment, stabilizing bone by using plates, screws or external fixation. The amputated bony edges must be well smoothed. After providing bone stability, the arteries are repaired, followed by repair of the tendon and then veins and nerves. As for the skin, a tension free flap may be attempted or alternatively, a skin graft can be done.

Top  
Tip

Box 7

The acceptable window period for replantation (ischaemia time) is 6 hours for proximal limb amputations and 12 hours for fingers.<sup>6</sup>



Rehabilitation

Limb amputation should not be viewed as a failure but as a way of enabling the patient to function at a higher level. The importance of approaching amputation with a positive, constructive frame of mind cannot be overemphasized. On-going, long term rehabilitation aids patients particularly those facing difficulties with prosthetic fitting, the residual limb, performing specific activities and psychosocial adjustment.

Conclusion

Pre-hospital treatment along with prior preparation of the resuscitation room is the key to successful trauma management. Establishment of a trauma team whereby

there is efficient coordination between emergency room physicians and trauma surgeons is vital to ensure a satisfactory final outcome. The advanced trauma life support algorithm provides a good basis in identifying life threatening conditions rapidly as well as stabilizing patients to buy time for definitive assessment. Assessment of the trauma patient must involve a full assessment of the actual and potential injuries with the appreciation that resuscitation is often on-going and the patient's condition can change dramatically at any point of time. Prompt recognition and identification of patients requiring immediate surgery is often life-saving and provides a chance for patients to make a better recovery.

**Appendices****Appendix 1: ATLS classification of haemorrhagic shock**

	Heart Rate	Blood Pressure	CNS status	Urine output	Blood Loss	Treatment
<b>Class I</b>	<100	Normal	Slightly anxious	>30ml/hr	<15%	Normal Saline
<b>Class II</b>	>100	Normal	Mildly anxious	20-30	15 - 30%	Normal Saline
<b>Class III</b>	>120	Decreased	Confused	5-15	30 - 40%	NS + Blood
<b>Class IV</b>	>140	Decreased	Lethargic	nil	>40%	NS + Blood

**Appendix 2: Approach to the Trauma Patient practised at Sultan Abdul Halim Hospital, Sungai Petani, Kedah, Malaysia**

**PRIMARY SURVEY**

		Assess and Identify	Immediate Management
A	AIRWAY + Cervical Immobilization	<b>A</b> Airway obstruction	Blood/secretion □ suction/remove debris Floppy tongue □ oropharyngeal airway Maxillo-facial injury □ attempt reduction, intubation, cricothyrotomy Mechanical blockade □ finger sweep and removal of foreign object Partially obstructed airway □ jaw thrust/chin lift
B	BREATHING	<b>T</b> Tension pneumothorax Clinical diagnosis, not radiological □ Tracheal deviation □ Respiratory distress □ Absence of breath sounds – unilateral □ Distended neck vein Cyanosis – late sign	Needle thoracocentesis Chest tube insertion
		<b>O</b> Open pneumothorax "Open sucking chest wound"	*Do not remove object * Cover defect with 'sterile occlusive dressing' Chest tube insertion Definitive surgical closure
C	CIRCULATION	<b>M</b> Massive haemothorax 1500mls immediately evacuated or 200mls/hour for 3 hours or 300mls/hour for 2 hours Paediatric – 30mls/kg/hour	Rapid volume restoration Chest tube for chest compression Thoracotomy
		<b>F</b> Flail chest When three or more adjacent ribs are fractured at two points	Adequate ventilation and oxygen Volume restoration Analgesia Chest tube if required
		<b>C</b> Cardiac tamponade Beck's triad □ Muffled heart sounds □ Distended neck veins □ Elevated JVP Narrowed pulse pressure Kussmaul's sign FAST – pericardial effusion	Pericardiocentesis Open thoracotomy
		<b>H</b> Severe Haemorrhage Eg: Total amputation	Control bleeding Fluid replacement Blood transfusion Intraosseous cannulation
D	DISABILITY	Assess conscious level (AVPU), GCS and pupil size	For definitive airway if GCS<8

\*Survey Adjuncts: Xrays - lateral cervical, chest and pelvic as well as FAST

## SECONDARY SURVEY

Assess	Identify	Management
Further History + examination	Identify "hidden eight injuries" PATMET + SH	
AMPLE history Head to Toe Examination  A – Allergy M – Medication P – Past medical illness L – Last meal E – Event	P – pulmonary contusion A – aortic disruption T – tracheobronchiole disruption M – myocardial contusion E – esophageal disruption T – traumatic diaphragmatic hernia S – spontaneous haemothorax H – haemothorax	Advanced intervention Adjuncts and tests

## Appendix 3: Gustillo-Anderson classification of open fractures

<b>Grade 1</b>	<input type="checkbox"/> Wound < 1 cm <input type="checkbox"/> clean <input type="checkbox"/> simple bone fracture with minimal comminution
<b>Grade 2</b>	<input type="checkbox"/> Wound > 1 cm <input type="checkbox"/> no extensive soft tissue damage <input type="checkbox"/> minimal crushing <input type="checkbox"/> moderate comminution and contamination
<b>Grade 3</b>	<input type="checkbox"/> Extensive skin damage with muscle and neurovascular involvement <input type="checkbox"/> High-speed crush injury <input type="checkbox"/> Segmental or highly comminuted fracture <input type="checkbox"/> Segmental diaphyseal loss <input type="checkbox"/> Wound from high velocity weapon <input type="checkbox"/> Extensive contamination of the wound bed <input type="checkbox"/> Any size open injury with farm contamination
<b>3A</b>	<input type="checkbox"/> Extensive laceration of soft tissues with bone fragments covered <input type="checkbox"/> usually high-speed traumas with severe comminution or segmental fractures
<b>3B</b>	<input type="checkbox"/> Extensive lesion of soft tissues with periosteal stripping and contamination <input type="checkbox"/> severe comminution due to high-speed traumas <input type="checkbox"/> usually requires replacement of exposed bone with a local or free flap as a cover
<b>3C</b>	<input type="checkbox"/> Exposed fracture with arterial damage that requires repair

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## Dental-derived Stem Cells and Whole Tooth Regeneration: An Overview

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**Keywords:**

*Dental Stem Cells, Tissue Engineering, Tooth Regeneration, Stem cell isolation*

**Abstract**

Recent advances in the identification and characterisation of dental stem cells and in dental tissue- engineering strategies suggest that bioengineering approaches may successfully be used to regenerate dental tissues and whole teeth. As clinically relevant methods for generation of bioengineered dental tissues and whole teeth continue to improve, interest in the application of tissue regeneration increases. This paper describes dental derived stem cells and their characterization.

**Introduction**

Replacing teeth in modern dentistry utilizes titanium implants capped with a ceramic crown. Although these implants serve the purpose, factors that interfere with osteointegration (contact between bone and implant surface without the interposition of non-bone or connective tissue) may cause surgery failure. With advances in the stem cell biology and tissue engineering, 'biological teeth'<sup>1</sup> may become an alternative for replacing missing teeth. Stem cells are the 'Master cells' of the human body, and can differentiate into many types of cells, such as heart, muscle, bone or brain cells. They then proliferate, depending on the surrounding tissue, to form the specific desired tissue or organ. Stem cells are one of the most fascinating areas of biology today. They are unique cells and regardless of their source have three general properties – capacity to divide and renew

themselves for long periods, being 'unspecified', with the ability to give rise to specialized cell types<sup>2</sup>.

Stem cells could be used to create a natural substitute for missing teeth. They would need to be programmed to adopt a dental lineage by cultivation with odontogenic induction signals, which work through epithelial mesenchymal interactions, and then developed over a scaffold matrix.

**Stem Cell Classification**

**Stem cells are classed according to their 'potency', or ability to produce other specialised cell types:**

1. **Totipotent** – these cells can differentiate into embryonic and extra-embryonic cell types. They are produced from fusion of the egg and the sperm cells and during the first few divisions of the fertilized egg.
2. **Pluripotent** – these cells can differentiate into cells derived from any of three germ layers. They are descendants of the totipotent stem cells and include some dental stem cells.
3. **Multipotent** - these can produce cells of closely related cell families e.g. hematopoietic stem cells can differentiate into red blood cells, white cells, platelets etc.
4. **Unipotent** - unlike the other stem cell types, these can produce only one cell type but are distinguished from non-stem cells by the property of self-renewal.

In dental research, there are two major categories of stem cells which are available for clinical application, embryonic and somatic stem cells. The isolation and use of human embryonic stem cells is ethically controversial. Somatic stem cells are easier to access and their uses do not bring up ethical concerns<sup>3</sup>, hence these are the most practical for use in dentistry. Mesenchymal stem cells (MSC) cells reside in post-natal organs and tissues like bone marrow, brain, liver, kidney, skin, adipose and dental pulp. These can be sourced by bone marrow biopsy (although often low yield), or by suction-assisted lipectomy. However, somatic stem cells number and function decreases with age, for example in new born it is 100%, by teens 10%, by 30 years 4%, by 50 years 2.5%. The functions decline in form of loss of lineage specificity, loss of self renewal, depletion due to senescence.

### Stem Cell Isolation

Recently, it has been found that specific populations of dental stem cells can be isolated from three dental recourses, the dental follicle, the dental pulp stem cells (DPSCs) from exfoliated deciduous teeth (SHED), and the developed periodontal ligament.

Stem cells have been successfully cultured from both dental pulp tissue and periodontal ligament by Vagra and co-workers<sup>4</sup>. They demonstrated that both cell cultures showed typical fibroblast-like morphology, with clonogenic activity, and were STRO-1 positive on immunoreactivity testing. These results mean DPSCs are capable of self-renewal and multilineage differentiation.

The commonly known sources of stem cells are umbilical cord and bone marrow. However, it is a tedious process to retrieve stem cells from bone marrow and the umbilical cord requires preserving at the time of birth if for this purpose. Dental stem cells therefore provide a

useful and simpler option for retrieval of stem cells (Figure 1).

### Stem Cell Preservation

The milk teeth of children (6 to 12 years of age) and the wisdom molars of adults are potent sources of dental stem cells. However, other teeth can be viable sources, particularly in young patients. If stem cells are to be preserved to be used in potential disease treatments, they are best taken sooner, in younger patients. Examples of disease where stem cells therapy may be future therapy include heart diseases, myocardial infarction, arthritis, Parkinson's disease, bone defects, liver diseases and multiple sclerosis. Banking stem cells can increase the chances of better life expectancy and is a mode of 'Biological Insurance' (Figure 2)

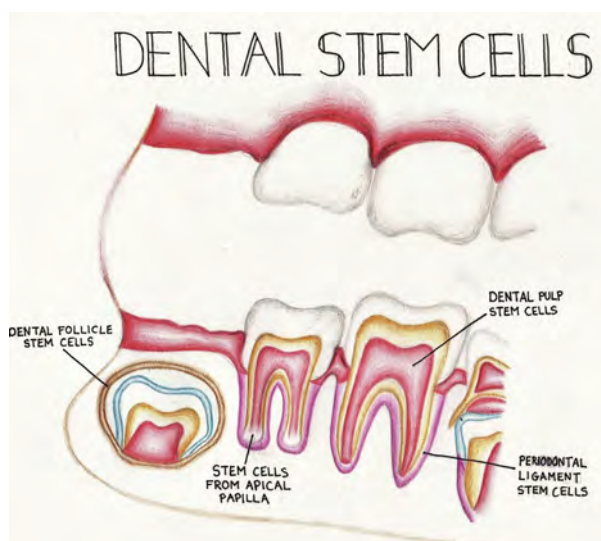


Figure 1: Location of Dental Stem Cells

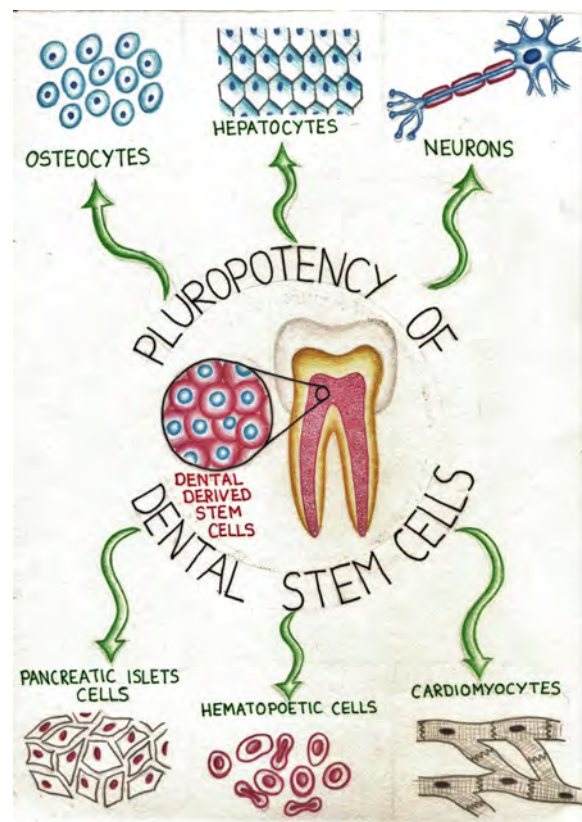


Figure 2: Pluropyotency of Dental Stem Cells

### Stem Cell Characterisation

It is important to be able to identify the odontogenic stem cells from dental tissue samples. Gronthos et al. first described a method of identification in 2000<sup>5</sup>, based on their clonogenic ability, rapid proliferation rate and capacity to form mineralized tissue both in vitro and vivo. Subsequent studies have isolated single cell colony-derived DPSC populations which demonstrate multipotentiality, forming adipocytes, neural precursors and the dentine-like tissues.

interactions that occur between neighbouring cells and include growth factor receptors, cell adhesion molecules and other cell surface markers expressed by MSCs are summarized in (Table 1).

Bone marrow stem cells and DPSCs, express similar putative surface markers, including CD4, CD106, CD146, 3G5 and Stro1. Both also express matrix proteins associated with mineral tissue formation, such as alkaline phosphatase, osteocalcin and osteopontin. However, in contrast to bone marrow stem cells, DPSCs have been shown to maintain a 30% higher proliferation rate and a higher growth potential.

Marker Type	Examples
Surface Markers	CD13,CD29,CD44,CD73, CD90,CD105,CD106, Stro-1,Stca-1
Cytokine receptors	IL-1R, IL-3R, IL-6R, IL-7R
Extracellular matrix receptors	ICAM-1, ICAM-2, VACM-1, ALCAM, endoglin, hyaluronate receptor integrins $\alpha 1, \alpha 2, \alpha 3, \alpha A, \alpha V, \beta 1, \beta 2, \beta 3, \beta 4$
Growth factor receptors	BFGF-R, PDGF-R
Other receptors	Thy-1, IFN- $\gamma$ R, TGF- $\beta$ R, TNF-R
<i>Commonly used cell surface proteins/receptors that are characteristic markers for isolation and characterization of MSC are shown. Fluorescently tagged antibodies to most of there are commercially available and can be used in a flow cytometry setting.</i>	

Table 1: Kind courtesy ofnAous Dannan. "Dental derived stem cells and whole teeth regeneration. An overview: 1 clinical Med Res" 2009, 1(2): 63-71}

### Tissue Regeneration

Stem cells are considered tools for replacing, repairing, regenerating, and rejuvenating dead, degenerating or injured tissue and cells. Lifelong treatment is possible by engrafting stem cells into tissue or organs, such as liver, bone, kidney, lungs, heart, spinal cord etc.

Once implanted, stem cells interact with the surrounding micro-environments, facilitating regeneration by secreting certain factors. An extracellular matrix is required to provide physical support, nutrient, growth factors, cell migration, proliferation and cell adhesion<sup>6</sup>. Three dimensional scaffolds are used for growing mineralized tissues. The scaffold has regulated microporosities, are hydrophylic, biocompatible and biodegradable. They are fabricated out of a co-polymer

of polylactic acid and polyglycolic acid. Although for cartilage and bone growth collagen sponges, hydroxyapatites can be used.

### Replacement Tooth Engineering

The concept of engineering a whole tooth is theoretically feasible and has exciting potential. Significant clinical challenges remain however, with issues about tooth shape and size, availability of the dental epithelium, growth and eruption of the tooth require resolution.

Research is currently in progress on developing complex scaffolds with bioengineered components to enhance

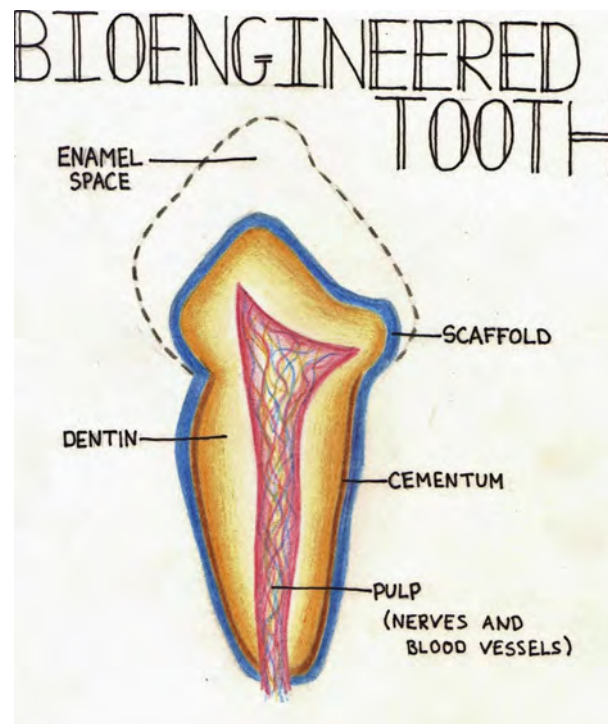


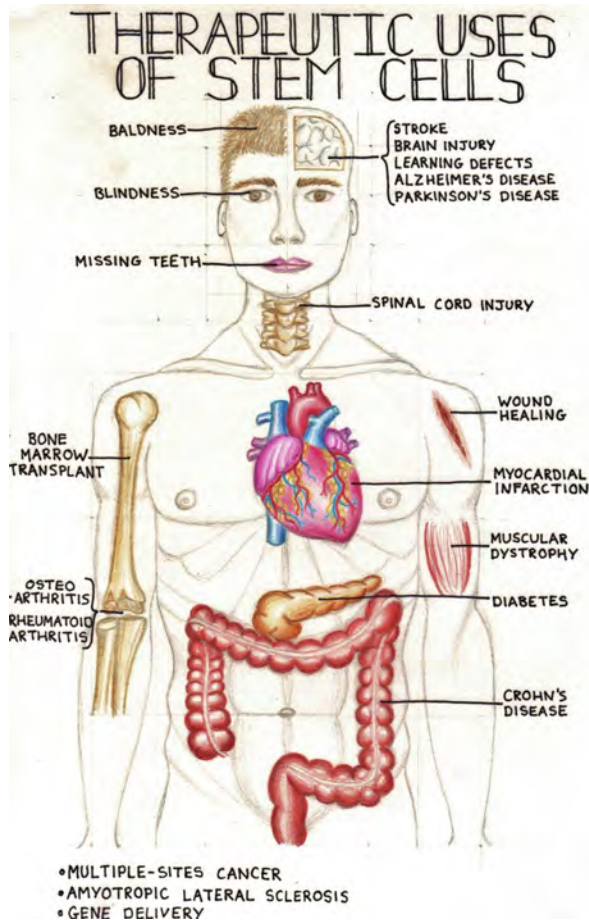
Figure 3: Potential bio-engineered tooth

stem cell and tooth regeneration (Figure 3).

The regeneration process requires identification and guidance of epithelial and mesenchymal cells interactions, to form a natural tooth. An ideal scaffold material has appropriate porosity, biocompatibility and biodegradability (usually degrading within weeks to one year). It requires the ability to support cell growth and act as a controlled gene and protein vehicle.

Two approaches to culturing stem cells are now possible now. In the first approach, stem cells are grown in vitro on a designed three-dimensional scaffold, composed of pores and intercommunicating channels. The second approach grows stem cells in vivo, in the organism itself for example as a subcutaneous transplant or in the kidney capsule. These culture sites provide nutrient and oxygen to nurture tooth-germ; a small tooth is cultivated there before it is implanted in to their anatomical sites.





**Figure 4:** Therapeutic Uses of Stem Cells

## Conclusion

In conclusion, regeneration of dental tissues provides an attractive alternative to traditional approaches for patients with missing teeth (replacement using natural tissues). The development of new approaches requires precise regulation of regenerating events to maintain tooth structure. There is an opportunity to move restorative dentistry into a new era, harnessing the biological activity of dental tissue, stem cells and tissue regeneration. Already, isolation, collection and cryopreservation of dental stem cells for banking and clinical use is now feasible and commercially possible. Stem cells are not yet fully understood but have great potential therapeutically. There needs to be careful research before routine clinical use is possible.

*Acknowledgement: We are grateful to Ms Alice Butler (Medical Student, Cardiff University, UK) for the medical illustrations included in this article.*

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## A Career in Child and Adolescent Psychiatry

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*Child and Adolescent Psychiatry, Child Psychiatry, CAMHS, Career, Training in UK*

"We are guilty of many errors and many faults, but our worst crime is abandoning the children, neglecting the fountain of life. Many of the things we need can wait. The child cannot. Right now is the time his bones are being formed, his blood is being made, and his senses are being developed. To him we cannot answer 'Tomorrow,' his name is today."

### Introduction

Child and Adolescent Psychiatry, a branch of Psychiatric medicine, involves the diagnosis and treatment of psychiatric disorders in children and young people up to 18 years old. It offers a rewarding career for doctors who like to work with children and their families. It enables one to intervene early in a child's life and address the issues which in later life may manifest as intractable problems. Though a relatively young speciality, Child and Adolescent Psychiatry has made major advances over the past two decades in clinical, academic and research areas. There is a greater understanding about the speciality amongst general public and referrals to child psychiatry services have seen a significant increase over the past few years.

### History of the speciality

Childhood was only recognised as an important phase in the psychosocial development of an individual in the late 19<sup>th</sup> century. In fact, the psychiatric taxonomy published by Emil Kraepelin in 1883 had no mention of disorders in children.<sup>1</sup> One of the earliest centres of Child Psychiatry was developed by Johannes Truper, who founded a school in Sophienhohe, Germany, in 1892. He also co-founded a journal called 'Die Kinderfehler' in 1896, which was a leading journal for research in child psychiatry at the time. In 1899, Manheimer published a monograph titled *Les Troubles Mentaux de l'Enfance* in which the term 'child psychiatry' was used for the first time. The first academic child psychiatry department in the world was founded in 1930 by Leo Kanner (1894–1981), at the Johns Hopkins Hospital, Baltimore. His seminal paper on autism in 1943 laid the foundations for recognition and

treatment of this condition, about which little was known until then<sup>2</sup> (Figure 1). The Maudsley, the famous London psychiatric hospital, contained a small children's department from its beginning in 1923<sup>3</sup>.

From the 1970s to 1980s, an expansion in the speciality came from the work of Michael Rutter. He is often described as the 'father of Child Psychiatry'.

The first comprehensive survey of children and adolescents on the prevalence of psychiatric disorders was carried out by him in the Isle of Wight in 1970, which improved the understanding of the social factors in children's mental health.<sup>4</sup>

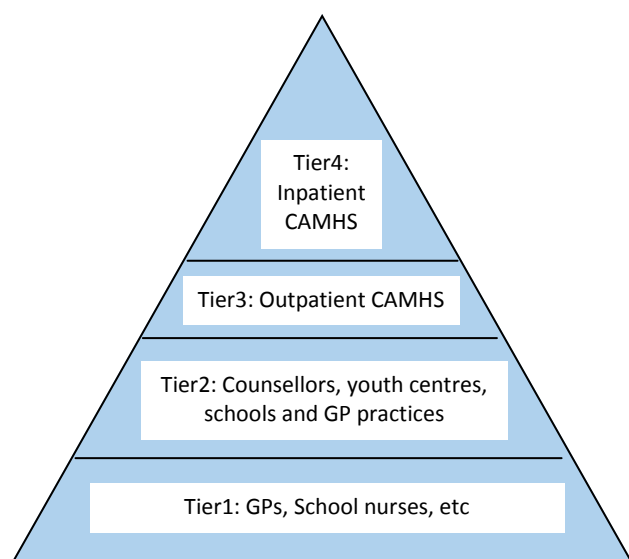
In the last two decades, there has been recognition that intervening at this early period in life is effective and ideal. The speciality has developed greatly with special interest areas such as: Inpatient, Eating disorders, Learning Disability, Forensic, Substance Misuse, Liaison and Neuro-developmental Child Psychiatry.



**Figure 1:** Leo Kanner, founder of first academic child psychiatry department

### UK Service Structure

In the UK, there is a 4-tiered service model for delivering care to children and young people with mental health problems.



**Figure 2:** UK 4-tiered service model for delivering care to children and adolescent with mental health problems

**Tier 1 and 2** – these are uni-disciplinary settings in the community, where services are delivered by GPs or mental health specialists, and include the voluntary sector.

**Tier 3 and 4** – these include Child and Adolescent Psychiatrist-delivered care.

Tier 3, popularly known as CAMHS (Child and Adolescent Mental Health Services) are multi-disciplinary teams working in a community mental health clinic or child psychiatry outpatient service, providing a specialised service for children and young people with more complex disorders. The team members include child and adolescent psychiatrists, social workers, clinical psychologists, community psychiatric nurses, child psychotherapists and occupational therapists. Tier 4 consists of tertiary level CAMHS services for children and young people with the most serious problems. They can be day units, highly specialised outpatient teams or in-patient units. They also include secure forensic adolescent units, eating disorder units and specialist Neuro-psychiatric teams.

### Content of speciality work

Psychiatrists in an Outpatient CAMHS team, sees patients referred from the community by GPs, social workers or school authorities. Consultations include the parents or carers and often have support from multiple disciplines. Psychiatrists will manage a range of problems arising in childhood and adolescence, such as:

#### Neuro-developmental Disorders:

- Attention Deficit Hyperactivity Disorder
- Autism Spectrum Disorder
- Tic disorders

#### Emotional and Behavioural Disorders:

- Disruptive behaviour
- Feeding and toileting difficulties
- Deliberate self harm
- Attachment disorders
- Separation Anxiety
- Deliberate self harm

#### Serious Mental Health Disorders:

- Mood Disorders
- Neurosis
- Eating disorders like Anorexia nervosa
- Psychosis

Treatment includes psychopharmacology, cognitive behavioural therapy, psychodynamic therapy and family therapy. CAMHS recognises the importance of family and society in a child's life and so works with other agencies like social services and schools. Admission to inpatient units is less frequent than in adult psychiatry.<sup>4</sup>

### Training in the UK

The basic qualification required is an MBBS degree or an equivalent medical qualification. After two years of Foundation training there is competitive entry into three years of Core Training (CT1-3) in Psychiatry. During this time the successful completion of the MRCPsych examinations is required before one is allowed to further progress in specialty training. On completing Core Psychiatry Training, the budding psychiatrist will require a further three years of Specialist Training (ST4-6) in Child and Adolescent Psychiatry. This leads to the award of the Certificate of Completion of Training (CCT) making one eligible to practise as a Consultant in Child and Adolescent Psychiatry.

### Rewards and challenges

Child and Adolescent Psychiatry is both a rewarding and challenging speciality. It is a rewarding experience to journey through a young individual's emotional difficulties and be able to make a difference in their lives. The clinical problems are often challenging and many are intertwined with complex familial and social issues. It also offers opportunities for research and also teaching at all levels, from medical students to colleagues from other disciplines. The specialty values family life and emotional well-being and is supportive of flexible training and career.

Child and Adolescent Psychiatry is also a growing specialty. Although there are no formal GMC recognised subspecialties, there are evolving areas of special interest within this specialty such as Learning Disabilities, Eating Disorders, Forensic Psychiatry and Infant Mental Health.

([www.medicalcareers.nhs.uk](http://www.medicalcareers.nhs.uk)) for further information and resources. Opportunities are available to learn and experience more about the specialty by applying for elective placements as a medical student or taster sessions whilst working as a foundation year doctor. Foundation year posts have become recently available in

Psychiatry which may aid a junior doctor in deciding whether Psychiatry would be a suitable career for them. From a personal perspective, I enjoy the many challenges and the privilege of influencing and hopefully improving the mental health of the children of today.

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## Ulceration of the Lower Limb: An Introduction to Medical and Surgical Intervention

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*Lower limb ulceration, venous ulcer, arterial ulcer, neuropathic ulcer, pressure ulcer*

### **Introduction**

Ulceration of the lower limb is defined as the loss of epithelial integrity of the skin in the area between the ankle and knee, and as such can have multiple aetiologies. The majority are of venous origin, however arterial and neuropathic classes represent a significant proportion of disease burden. In all cases, occurrence should be used as an index of systemic disease progression, rather than an isolated incident. While preventative measures can be taken, the incidence and subsequent socioeconomic burden and patient morbidity remain a challenge within the healthcare community. The primary aim of this article is to provide trainees with a systematic approach to lower limb ulcer identification, investigation and treatment with a view to improve vigilance and patient morbidity in the hospital setting

### **Clinical Assessment**

When a patient presents with ulceration of the lower limb in a primary or secondary care setting, a thorough assessment consists of three phases: the patient as a whole, both limbs of the patient and of the ulcer itself. An appreciation of patients' comorbidities is crucial in identifying risk factors to healing, recurrence, and fitness for surgery. Furthermore, time invested in establishing the impact on the patients' quality of life, concerns and treatment expectations is necessary for a successful outcome for both parties.

#### *Venous*

Persistent venous insufficiency allows retrograde flow from deep to superficial venous systems and thus creates an environment of chronic venous hypertension. Relevant risk factors include varicose veins (Figure 1), deep vein thrombosis, obesity, pregnancy, leg fracture or previous surgery on the lower limb.

Secondary precipitants of venous incompetence include any conditions predisposing conditions deep vein thrombosis (protein C, protein S, and anti-thrombin III deficiency), infection or thrombophlebitis<sup>1</sup>.



**Figure 1:** Prominent varicose vein along the long saphenous distribution in the leg (left) of a 52-year-old gentleman

On examination of the patient, venous ulcers are typically situated in the gaiter area of the lower limb (Figure 2) with characteristic gentle sloping edges.





**Figure 2:** Early venous ulceration in the medial gaiter region of the left leg in a 61-year-old lady

Other features that suggest venous aetiology include:

- Venous eczema – itchy, scaly, erythematous and tender
- Haemosiderin deposition – brownish discolouration caused by breakdown of haemoglobin which has seeped out of the circulation
- Pitting oedema
- Varicosities
- Lipodermatosclerosis – fibrosed and indurated dermal and subcutaneous tissue layers
- Atrophie blanche – white fibrotic areas due to repeated scarring



**Figure 3:** Non-healing chronic venous ulcer in the leg of a 48-year-old lady

Inadequately treated venous ulcer can result in an increase in the size of the ulcer as well as chronicity as seen in figure 3.

#### Arterial

An estimated 22% of chronic ulcers have an arterial origin, and within this group the unifying aetiology is that of peripheral arterial disease with sustained secondary tissue hypoxia<sup>2</sup>. Underlying atherosclerosis of medium and large vessels are the most common cause, hence pertinent cardiovascular risk factors such as hypertension, diabetes, raised lipid profiles, family history, smoking history and previous cardio- or cerebrovascular events should be elicited in the patient history. Disease severity can be assessed by claudication distance or rest pain. Thromboembolic precipitants such as vasculitis, thromboangitis and haematological disorders (sickle cell anaemia and thalassaemias) should not be neglected as they too carry increased risk of chronic ischemia<sup>1</sup>.

Examination findings suggestive of arterial disease include:

- Typical arterial ulcer which is painful, punched out edges. These are usually situated on the toes, heels, and bony prominences of the foot (figure 4).
- Surrounding skin pallor, cool to touch
- Atrophic changes including shiny skin, hair loss with wasting of the calf or thigh musculature
- Gangrene
- Reduced or absent pulses. Objective measure severity of arterial disease can be determined by the Ankle Brachial Pressure Index (ABPI)
- Positive Buerger's test in severe ischaemia



**Figure 4:** Arterial ulceration with slough in the wound bed. Note the extensive contact dermatitis and eczema mimicking cellulitis

Symptoms of acute arterial disease

- 6Ps: Pallour, Pain, Paraesthesia, Pulselessness, Paresthesia, Perishing cold

**Neuropathic**

Currently five percent of ulcers encountered will be secondary to micro- and macrovascular complications of diabetes, and as such the nature can be venous, arterial, neuropathic (see Figure 5) or a combination thereof <sup>1</sup>.



**Figure 5:** Grade 3 or 4 pressure ulcer in the heel of a patient with spina bifida

Sheering, frictional forces of gait leading to callous formation is the leading precipitating factor in the development of neuropathic ulcers. As such they are commonly sited on the pressure points of gait, such as the plantar aspect of the toes and foot under the metatarsal heads.

**Assessment of ulcers**

Leg ulcers of differing aetiologies have their own characteristics which have been alluded to in the text above, and are summarized in table 1 below.

When describing an ulcer, the characteristics including size, position, shape, borders, tissue status (sloughy or granulation) and depth at time of presentation should be documented, and if possible the use of supportive photography is recommended to monitor disease progression. Atypical morphology, sudden alteration in characteristics or failure to respond to 12 weeks of active therapy may be indicative of neoplastic change and prompt specialist referral <sup>3</sup>.

	Arterial	Venous	Neuropathic
<b>Location</b>	Distal limb over bony prominences Heel, metatarsal heads, toes	Loyal to the venous anatomy of the limb, typically over the medial malleoli and the gaiter area	Friction sites and pressure points such as peripheral edges, metatarsal heads, ankles and toes
<b>Appearance</b>	Punched-out, well demarcated edges	Ranges from discrete areas with shallow sloping borders to elevated margins encompassing the circumference of the lower limb	A callus may be associated and signify long standing frictional forces.
<b>Capillary refill time</b>	Prolonged	Reduced	Variable owing to the absence or presence of mixed arterial disease
<b>ABPI</b>	0.7 – 1.0 mild disease 0.5 – 0.7 mild to moderate 0.3 – 0.5 severe <0.3 critical ischaemia	ABPIs performed to exclude mixed aetiology	

**Table 1:** Characteristic clinical findings of venous, arterial and neuropathic ulcers to help in correct identification

**Investigations**

Investigations, especially in a specialist setting, are used to confirm the aetiology, guide management and monitor disease progression. The correct diagnoses allow the most successful intervention to be chosen, and as a consequence, hopefully reduce complications of the disease.

- Blood Tests: Full blood count (FBC), inflammatory markers (ESR and CRP) assesses infective or inflammatory states. A baseline renal function is useful when referring patients for imaging and interventional procedures. Blood glucose or HbA1c can be helpful in

identification of new onset diabetes or treatment compliance.

- Bacterial swabs: Routine swabbing of ulcers yields low sensitivity owing to colonization of ulcers with skin commensals. However, in cases where clinical suspicion of infection are present (pain, tenderness, malodour, pyrexia), swabbing of the ulcers allows clinicians to choose the most appropriate antibiotics. Wound care and debridement of necrotic tissue allows clinicians to better assess viable tissues as well as reducing bacterial infections<sup>4</sup>.

- Biopsy: As mentioned above, a low threshold for ulcer biopsy should be maintained, especially in ulcers that present in atypical area and fail to respond to three months of treatment to exclude malignant change<sup>3</sup>.
  - Radiographs: Ulceration extending into deeper structures, non-healing or signs of active infection should alert one to the possibility of deep soft and hard tissue infections, specifically osteomyelitis. The treating clinician should have a low threshold for requesting orthogonal radiographs to search for signs consistent with osteomyelitis: periosteal reactions, areas of lucency with sclerotic halos and soft tissue swelling which should prompt aggressive treatment<sup>5</sup>. Prolonged broad spectrum intravenous antibiotics covering both gram positive and negative agents, debridement of diseased bone and soft tissue and draining of a deep abscess can be limb and lifesaving.
  - Duplex ultrasonography is required especially when one seeks more invasive therapies for both venous and arterial diseases. In venous disease, duplex can detect any obstructions to flow e.g. deep vein thrombosis (where stripping of superficial venous system is contraindicated) and to detect the extent of valve incompetence. For arterial diseases, duplex ultrasonography provides visualization of narrowing, obstruction or dilatation of the arterial tree distal to the common femoral and is the investigation of choice for those presenting with limb claudication. However, views may be limited in heavily calcified vessels, and can be better interpreted in conjunction with radiological images.
  - Ankle Brachial Pressure Index (ABPI): Calculated from the higher systolic blood pressure of the leg from the dorsalis pedis or posterior tibial pulse divided by the systolic brachial blood pressure. ABPI is a useful non-invasive test, although heavily calcified vessels can produce a false negative result. Values of  $<0.8$  suggests arterial disease, and a value of  $<0.3$  is suggestive of critical ischaemia requiring urgent referral.
  - Digital subtraction angiography: This invasive procedure provides diagnostic and interventional potential. Pre and post contrast infusion imaging and subtraction of the background structures produces a detailed and superior composite image. If a short length stenosis is detected at the time of imaging, angioplasty with or without stenting can also be performed. Although described as the investigation of choice for those presenting with peripheral vascular disease, it has a substantial risk profile – including formation of pseudoaneurysm, embolization of thrombi and damaging the vessel wall.
  - Computer tomography angiography (CTA): CTA generates composite three-dimensional images which are ideal for assessing the degree of blood vessel calcification, especially when imaging the aorta for consideration of abdominal aortic aneurysm repair. In peripheral vascular disease, this form of imaging can be used for patients unable to undergo magnetic resonance imaging for example, patients with metallic implants and claustrophobic patients. However, this modality exposes the patient to high dose radiation, and requires the injection of nephrotoxic contrast which is not ideal for patients with poor baseline renal function.
  - Magnetic resonance angiography (MRA): MRA is the investigation of choice for peripheral vascular disease in conjunction with duplex ultrasonography as it is non-invasive, provides detailed imaging for contemplation of further treatment and does not require injection of contrast. It is however contraindicated in those with metallic implants, such as pacemakers or prosthesis, and may not be tolerated by patients who are claustrophobic.
- Specialist referral is indicated in patients with the following features<sup>2</sup>:
- Suspicion of malignancy
  - ABPI  $<0.8$ , or urgent referral if  $<0.5$
  - Complicated by diabetes mellitus, rheumatoid arthritis, vasculitis or suspected dermatitis
  - Atypical distribution of ulcers
  - Non-healing ulcer (failure to progress after 12 weeks of treatment)
- Conservative Management**
- The main aim of conservative management is to correct the underlying cause and regular wound care to improve healing. Any breach of the skin's epithelial integrity impairs the ability of this organ to protect the body from pathological invasion. In the ulcerated state, moist, necrotic tissue is a breeding ground for bacteria and predisposes to secondary infections. Debridement and regular cleansing with normal saline are effective measures to reduce this risk.
- A selection of dressings is available for ulcers, and the appropriate choice is driven by the ulcer condition rather than the aetiology. Dry, shallow ulcers can be covered with a simple non-adherent dressing, while exudative ulcers are better addressed with an alginate dressing<sup>6</sup>.

For the wounds complicated by necrosis are better managed with hyaluronic acid dressings<sup>7</sup>. At present, there is insufficient published evidence to establish whether the use of topical antiseptic dressings such as iodine, peroxide, silver, or manuka honey is beneficial<sup>2</sup>. Nevertheless, these dressings are often seen in clinical practice.

#### *Venous*

The mainstay of venous ulcer healing, in the absence of arterial disease (ABPI >0.8) or neuropathy, is the use of graded compression stockings and these should be offered at the highest pressure in keeping with patient concordance<sup>8</sup>. Practitioners should be vigilant of skin changes in the first 24-48 hours following application. Typically there are three classes defined by the ankle pressure; class three describes an ankle pressure of 25-35mmHg that reduces to the order of 17mmHg with proximal progression. One can expect 66% and 89% of venous ulcers to be healed within 12 weeks and 24 weeks of treatment respectively, hence a low threshold for ulcer biopsy (to exclude malignancy) is required in cases where this is not achieved<sup>8</sup>.

Unfortunately a third of ulcers can persist for up to a year and in these cases, there is emerging evidence for the use of pharmacological therapy. Pentoxifylline has demonstrated healing enhancement by a further 21% in compression resistant ulcers, and 23% in those initially unsuitable for compression therapy, by a mechanism of microvascularization<sup>2</sup>.

#### *Arterial*

Addressing the underlying mechanism of disease is essential in these cases and is best achieved by using best medical therapy (BMT). This is a multimodal approach to reduction of the patient co-morbidities consisting of:

- Smoking cessation
- Supervised exercise focused on calf-muscles to develop collateral circulation and improve haemodynamics
- Weight control
- Lipid lowering therapy
- Anti-platelet therapy
- Improved glycaemic and hypertensive control

Analgesia in the management of chronic ischaemic pain is useful, however, persistent rest pain for over two weeks will require urgent vascular referral as definitive management may be warranted for treatment of critical ischaemia.

#### *Neuropathic*

The main aim of neuropathic ulcer treatment is to

prevent repeated friction in ulcer-prone areas, and to prevent formation of new ulcers. Good glycaemic control for diabetics will help prevent further progression of peripheral neuropathy. Referral to the orthotic department may help in providing specialized shoes to reduce pressure on the ulcer.

#### **Surgical Intervention**

Although surgical intervention of venous ulcers aims at secondary prevention and arterial a definitive treatment, both circumstances are united in addressing the underlying pathology.

#### *Venous*

Patients with varicose veins who have residual function within the superficial and perforating systems are eligible for operative intervention. This can involve laser ablation, foam sclerotherapy or the traditional open varicose vein surgery dependent on patient factors and surgeon's preference. The ESCHAR trial demonstrated that recurrence risk of ulcers after varicose vein intervention can be reduced by up to 90%<sup>9</sup>.

In ulcers which are slow to heal, skin grafting may be an option. In the presence of lipodermatosclerosis or dystrophic calcification shave excision with split thickness skin grafting offers promising results<sup>10</sup>. Patients with significant co-morbidities or wishing to avoid general anaesthesia can be offered pinch skin grafting where small <0.5cm islands of healthy donor skin are harvested from the patient and embedded in the base of the ulcer wound.

#### *Arterial*

The three broad strategies for improving arterial flow are angioplasty, endarterectomy and bypass, while amputation is reserved for cases where restoration of flow is unachievable.

Angioplasty is indicated when short occlusions or stenosis are present in the iliac or superficial femoral arteries. Stent placement allows compression of the plaque against the vessel wall, thus increasing lumen patency and flow restoration. Endarterectomy is the treatment of choice for smaller vessel disease<sup>11,12</sup>, where the vessel is clamped, an incision performed and the atherosclerotic plaque is dissected carefully from the vessel wall, and the vessel is repaired. Perhaps the most invasive surgical option is that of bypass surgery and as such is reserved for those patients unsuitable for angioplasty and endarterectomy. Extent of disease, anatomical position and patient factors and comorbidities determine the finer details of bypass revascularization.





**Figure 6:** Bilateral vasculitic ulceration in the leg of a 49-year-old lady with rheumatoid arthritis

It has to be borne in mind that in addition to the aforementioned aetiologies, leg ulceration may result from atypical causes such as connective tissue diseases (such as rheumatoid arthritis and systemic lupus erythematosus) that result in vasculitic ulcers as illustrated in figure 6.

### Conclusions

Chronic leg ulceration is recognized as debilitating and disfiguring complication of systemic disease and as such contributes highly to patient morbidity and reduced quality of life. There are multiple medical and surgical treatment options but the key to successful management lies in identifying the aetiology and addressing the cause, hence a thorough history and clinical examination is imperative.

Pure venous ulcers are treated with graduated compression bandaging in the first instance (where patient compliance may be an issue). For those with associated varicose veins, surgical options can be explored. Arterial ulcers need prompt vascular referral as the presence of an ulcer indicates critical limb ischemia, and may warrant urgent surgical intervention. For the remaining 15% of chronic ulcers of a mixed arterial and venous pathology or those with neuropathic ulcers, a multidisciplinary approach is often required. However, in all cases, one must not forget to involve the patient in decision making, encourage lifestyle modifications and risk factor management.

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## An Introduction to a Career in Psychiatry

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### Introducing Psychiatry

*"As psychiatrists we straddle a unique blend of science and humanity. Bridging the social, medical and neurosciences, we strive to improve the mental health of individuals, families and societies, and provide strong leadership throughout the care pathway."*

Sue Bailey, President of the Royal College of Psychiatrists

Psychiatry is indeed a holistic speciality that incorporates the biological, psychological and social aspects of a patient, and more often than not, gives the psychiatrist the opportunity to delve into the patients' past and study the workings their minds. Patients may present similarly, but no two patients have the same life stories, making psychiatry a branch of medicine that offers a higher level of autonomy to make decisions.

Many of us may already have some sort of experience with mental health problems; either first hand or as a third party. We may have a partner, family member or friend suffering from depression, or who has had to deal with the effects of bereavement, marital problems, drugs or alcohol addiction, or take responsibility for an elderly suffering from memory loss, children with learning difficulties or adolescents with painful emotional problems. These are issues, which could affect any one from different walks of life. These are the myriad problems psychiatrists come across daily, making a day in the life of a psychiatrist varied, rewarding and never dull.

### Life as a Psychiatrist

As a psychiatrist, your typical working day will begin at 9am and finish at 5pm. During the time as a trainee, you can be expected to take part in ward rounds, liaising with different healthcare professionals, doing home visits, carrying out risk assessments and emergency work including using the Mental Health Act to section people. You could be treating numerous mental health disorders including schizophrenia, mania, depression, learning disabilities, alcoholism or drug addiction, eating

disorders, phobias (such as fear of heights or open space), post-traumatic stress disorder, anxiety and personality disorders. You could also be helping patients and their families to cope with marital or family problems, bereavement, memory impairment such as Alzheimer's Disease, the mental health problems of children and teenagers and make criminal proceedings and Court appearances.

As a vast speciality, psychiatry offers an enormous range of subspecialties e.g. general psychiatry, child and adolescent, forensic, old age, psychotherapy, psychiatry of learning disability, liaison psychiatry, addiction psychiatry and rehabilitation psychiatry. Moreover, it is varied in that you can work in a number of settings such as hospitals, the community, schools, special units, residential homes and even prisons. If you work as part of a hospital, then you may be required to work on call. On calls tend to be quiet and from senior trainee onwards can be done from home.

The speciality requires excellent listening skills, empathy and attention to detail. Sometimes it can be difficult to make a diagnosis so a psychiatrist must be able to deal with ambiguity and uncertainty. It can be an intellectually stimulating and rewarding work combining the rigours of medicine and the creativity of psychotherapy. An interest in research is beneficial, as psychiatrists are required to stay up to date with treatments and managements of different conditions. In Psychiatry, all trainees are guaranteed supervision for one hour a week, and many are given one day a week for research or preparing for the examinations.

### Facts and Figures

#### • Competition ratios:

In 2012, the Level 1 competition ratio for CT1 and ST1 training is 1.4 : 1, where there were 609 applications for 439 posts. The competition ratio for ST3/ST4 posts according to different subspecialties is as below.

Specialty	Applicants	Posts	Ratio
Child & Adolescent Psychiatry	82	69	1.2
Forensic Psychiatry	60	37	1.6
General & Old Age Psychiatry	27	26	1.0
General Psychiatry	242	144	1.7
Learning Disability	38	40	1.0
Old Age Psychiatry	59	70	0.8
Psychotherapy	15	18	0.8

• **Salary:**

The salary for a consultant psychiatrist in the NHS ranges from £70000-90000. This can be substantially higher if you choose to work in the private sector.

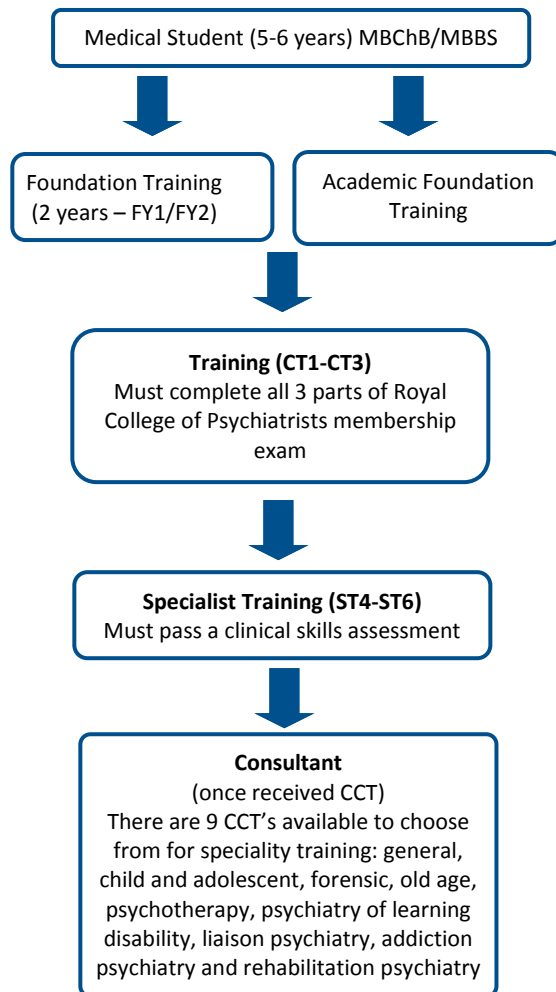
• **Prevalence of mental health problems:**

1 in 4 people in the UK will have a mental health problem at some point in their lives. For those coming to Casualty or GP, this figure is even higher.

**The Future**

Research in psychiatry is one of the fastest growing of all specialities. Generally, the amount of money invested into psychiatry has risen steadily. This may be in part due to the fact that there are an increasing number of psychiatric conditions being associated with cognitive deficits. This may lead to an increased demand and responsibility for psychiatrists in the future, and subsequently more training posts available.

**Psychiatry Training Pathway**



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## Post Operative Surgical Care

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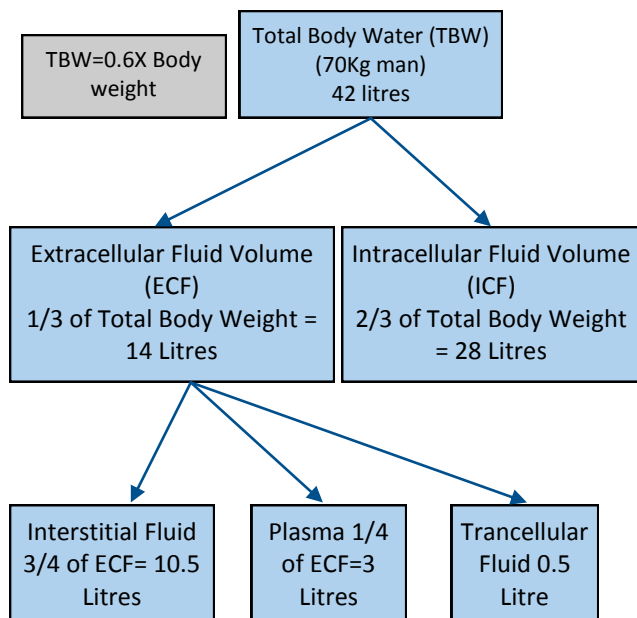
Post operative surgical care, post-operative complications

**Introduction**

There are a number of key issues that need to be considered in the post-operative period to ensure the safe recovery of the patient after surgery. These need to be managed remembering the patient's co-morbidities, actual surgery and progress.

**1. Fluid Balance**

Fluid balance is integral in caring for the surgical patient. Normal fluid distribution within the body is shown below:



**Figure 1:** Diagram showing the major fluid compartments. *Anaesthesia UK, 2012. Relationship between the volumes of major fluid compartments [image online] Available at: <http://www.frca.co.uk/article.aspx?articleid=289> [Accessed 10 April 2013].*

The most important compartment is the plasma, as this is the circulating medium which carries cells, nutrients and oxygen around the body, to the tissues. Interstitial fluid is

found between tissues, and transcellular fluid is that between cells.

Surgery disrupts the normal balance of fluid and electrolytes. Fluid balance charts should be kept to accurately document fluid volumes going in and out of the patient. When considering whether there is need for supplemental fluids, consider maintenance and replacement fluids.

**Maintenance fluid** – in a 24 hour period a 70-kg patient needs to take in 2500 ml of water, 100mmol of Sodium and 40mmol of Potassium. If a post-operative patient is not able to take fluids orally, maintenance fluid can be given as 2000ml 5% Dextrose with 40mmol Potassium and 500ml of 0.9% Saline solution.

**Replacement fluid** – this is calculated by adding pre-existing fluid loss, ongoing losses and insensible losses. Ongoing losses in post-operative patients can be measurable as vomit, urine or bowel content, and from nasogastric tube, stomas, fistulas, drains and/or catheters. Insensible or immeasurable losses include losses through sweating and breathing.

Unwell surgical patients can be fluid depleted or overloaded when they have their surgery. Correction of these fluid imbalances may continue into the post-operative period and if not done slowly, may precipitate heart failure and/ or oedema.

**2. Nutrition**

Adequate nutrition is paramount for recovery in post-operative patients. Nutrition can be provided via either the enteral or parenteral route.

Enteral nutrition uses the gastrointestinal (GI) tract and is used preferentially if possible. This can be through oral supplements, nasogastric/ nasojejunal tubes or gastrostomy/ jejunostomy tubes.



Parenteral nutrition bypasses the GI tract. This is given directly into the blood stream, either into a peripheral or central vein. It is reserved for those who cannot use their GI tract, such as patients with Crohn's disease or short gut syndrome.

### 3. Analgesia

There are three main groups of analgesia available, non-

opioids, non-steroidal anti-inflammatory drugs, and opioids. Recommendation for their use is shown in the World Health Organisation (WHO) pain ladder (see Figure 2). This was originally designed for treating pain in cancer patients, but is now widely used for all patients in pain. It describes the step-wise combination of analgesics to ensure adequate pain relief.

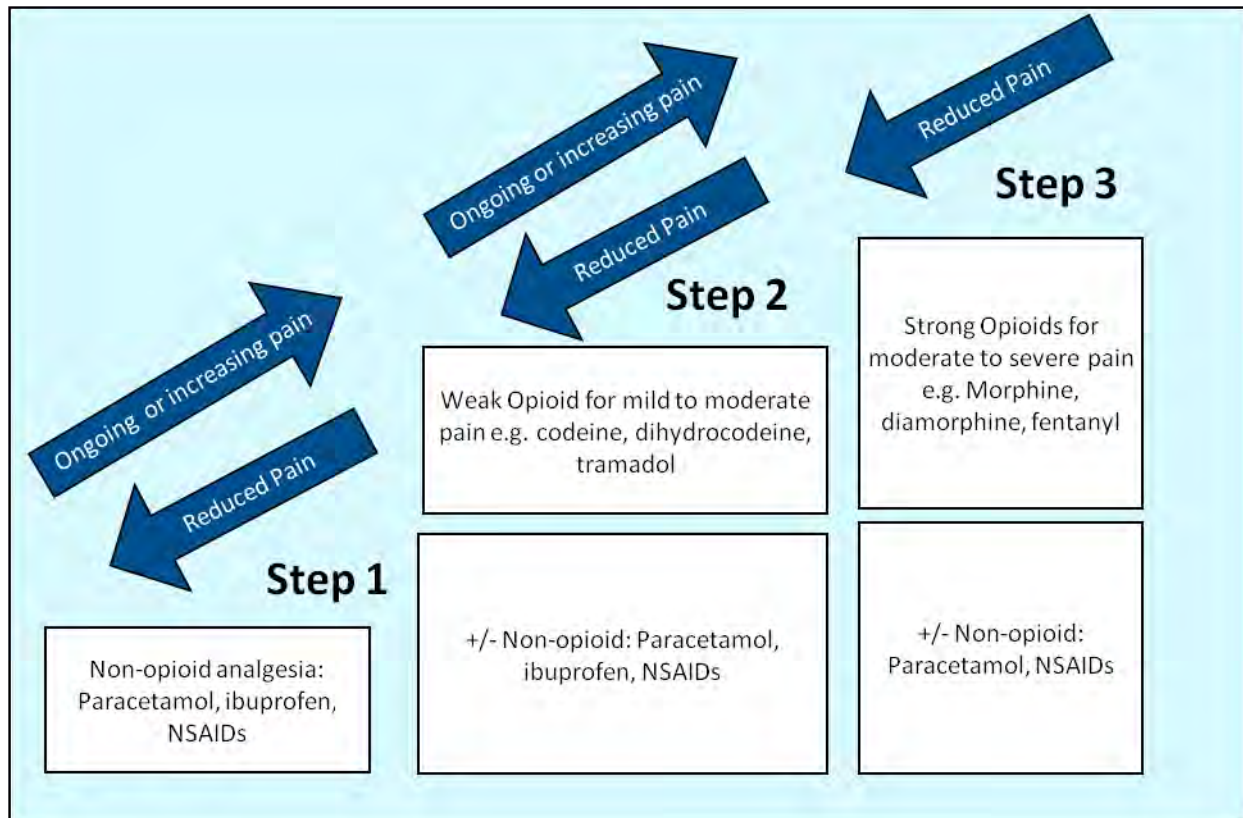


Figure 2: World Health Organisation pain ladder

Non-opioids (e.g. paracetamol) can be given orally, intravenously or subcutaneously. They are best given regularly to achieve maximum effect and combine well with other stronger analgesia.

Non-steroidal anti-inflammatory drugs (NSAIDs) are also often used in combination with other analgesia. They have to be used carefully in patients who have asthma, peptic ulcer disease or are at increased risk of bleeding.

Opioids are the strongest class of drugs and are widely used after surgery. They can be either weak or strong opioids. Weak opioids include codeine and dihydrocodeine.

They have many adverse reactions, the most serious being respiratory depression. Opioids can be delivered by

a multitude of methods. Apart from oral, and intravenous boluses, some frequently used post-surgical methods of administration include:

- Patient-controlled analgesia (PCA) pump - patient can self-administer a pre-set dose of morphine by pressing the button on the pump as they feel the need. The pump only delivers morphine if a certain amount of time has passed to avoid overdose.
- Epidural – this delivers analgesia around the spinal nerve roots. There is less risk of respiratory depression but as the drugs block both pain and sympathetic supply to the lower half of the body, there is profound vasodilatation which can cause problems with hypotension.

**Post-operative Complications**

Complications can affect any patient undergoing surgery. They can be classified into **early** (0-24hrs), **intermediate** (24-48hrs) and **late** (2-5 days).

*Early and intermediate complications include:*

**Respiratory**

Atelectasis is the collapse of small airways caused by inadequate ventilation. This leads to a build-up of bronchial secretions. These secretions can block off airways and eventually cause Pneumonia, if left untreated.

Risk factors for respiratory complications are smoking, chronic airways disease (asthma or COPD) and post-operative pain, which hampers deep breathing and coughing. Adequate analgesia and regular chest physiotherapy are needed throughout recovery. Investigations for these complications are prompted by shortness of breath, productive cough, low oxygen saturations and pyrexia. These investigations include arterial blood gases and a chest x-ray.

**Cardiovascular**

Haemorrhage can be arterial or venous.

- Primary haemorrhage is bleeding which starts in surgery and continues post-operatively.
- Refractory Haemorrhage is an early post-operative complication (4-6 hrs after surgery) and is due to continuation of primary haemorrhage, removal of primary clots due to coughing or an increase in primary blood pressure, slippage or loosening of sutures, staples, etc.
- Secondary Haemorrhage is a late complication (>5 days post-op) and is usually due to infection.

Shock is inadequate circulation causing poor tissue perfusion and hypoxia. The hallmark clinical features are hypotension and low urine output. There are numerous causes of shock including hypovolaemic (dehydration, haemorrhagic), cardiogenic (heart failure) and distributive (septic, anaphylactic, neurogenic).

Hypovolaemic shock is suggested by cold and clammy peripheries, tachycardia and low central venous pressure (CVP). Septic shock can look similar but patients typically have warm peripheries. Cardiogenic shock is usually secondary to acute myocardial ischemia, arrhythmias or heart failure. It is suggested by signs of fluid overload - raised CVP, basal lung crepitations and a gallop rhythm.

**Confusion**

This more often occurs post-operatively in elderly

patients and can be due to unfamiliar surroundings, pre-existing dementia or changes in their medication regime. Patients who are susceptible should be monitored carefully. In new confusion, there is a need to rule out complications such as:

- Infection
- Effects of sedatives or anaesthetic agents – particularly anti-cholinergics or drugs with these side effects, opioids, benzodiazepines and anticonvulsants.
- Metabolic changes e.g. dehydration, acid-base disorders, hypo-or hyperglycaemia
- Hypoxia
- Substance (such as alcohol) withdrawal

**Renal Failure**

Renal failure is divided into three categories, pre-renal, renal and post-renal. Dialysis may be needed depending if the renal injury is severe.

Pre-renal failure is caused by insufficient blood supply to the kidneys. If left untreated pre-renal failure can progress to renal failure.

Renal failure has numerous causes. These include prolonged pre-renal failure, medications, hepato-renal syndrome, incompatible blood transfusion, and myoglobinuria (due to crush injury of soft tissue).

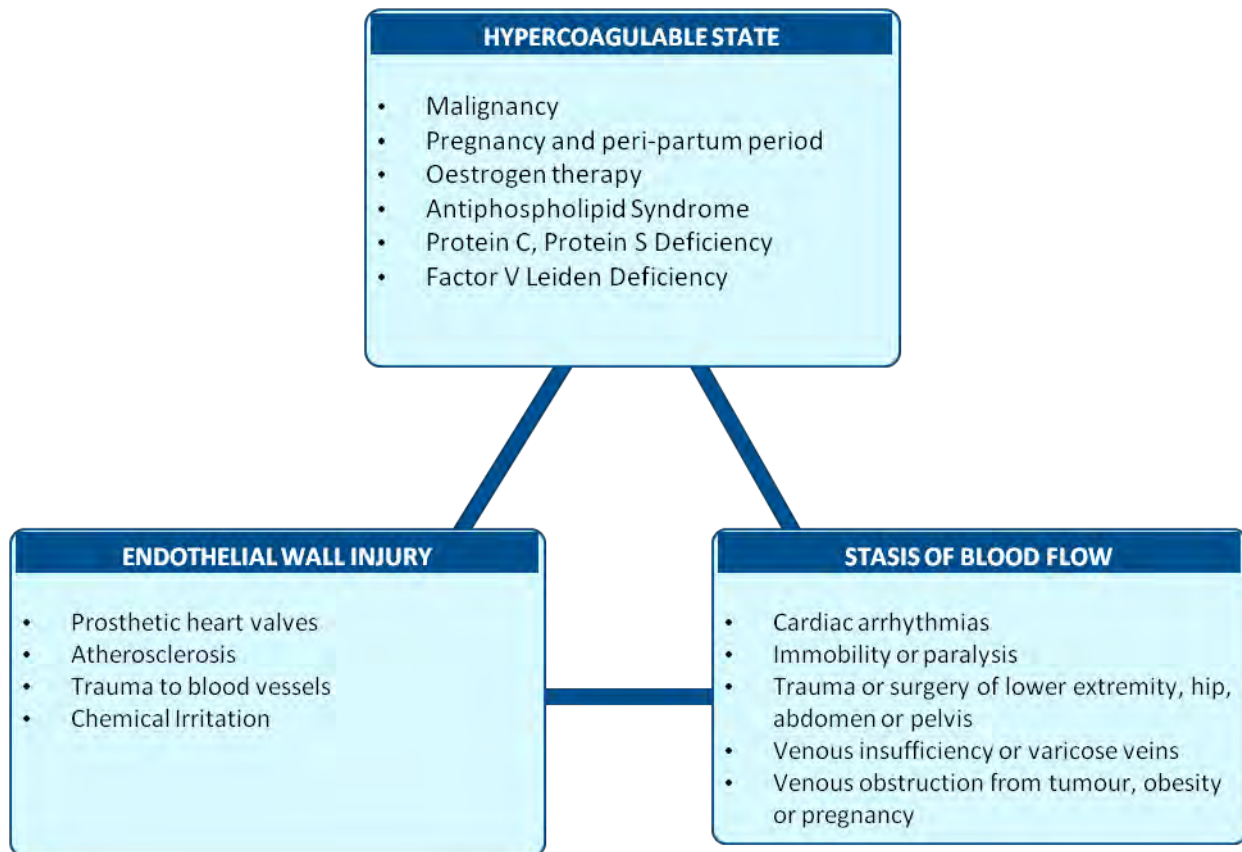
Post-renal failure is caused by a urinary outflow obstruction such as an enlarged prostate, catheter blockage or damage to the ureters.

*Late (3 – 5 days) Complications include:*

**Thromboembolism**

Deep vein thrombi (DVT) or pulmonary emboli (PE) can occur during surgery or post-operatively. Factors that contribute to the formation of thrombi include hypercoagulability, venous stasis and endothelial damage, and is known as Virchow's Triad (see figure 3).

In healthy, active people, the calf muscle pump prevents venous stasis, and regular hydration prevents a hypercoagulable state, hence there is low risk of developing deep vein thrombosis. However, intra-operatively and in the initial post-operative period where mobility is impaired, deep vein thrombosis has a higher risk of forming. Furthermore, the thrombi in the lower limb can then detach and embolise to the pulmonary circulation. Hence after surgery, patients are often given low molecular weight heparin and compression stockings to reduce this risk whilst mobility is reduced and they recover.



*Figure 3: Virchow's triad – factors which contribute to thrombi formation*

Hypercoaguability can occur due to dehydration or problems with clotting. Stasis can occur in theatre due to positioning particularly in long operations, and post-operatively if not mobile. Endothelial damage occurs due to surgery and inflammatory responses.

General patient risk factors include age, obesity, varicose veins, pregnancy, oral contraceptive pill, smoking, previous history of deep vein thrombosis or pulmonary embolism and malignant disease.

A DVT classically presents as a tender, swollen calf and requires Doppler ultrasonography to confirm the diagnosis. If there is a large PE, it can cause cardiac arrest and even death. If the clot is moderate symptoms include pleuritic chest pain, cyanosis, haemoptysis and progressive dyspnoea. The gold standard for diagnosis is to perform a computed tomography pulmonary angiography (CTPA), although in some instances, a ventilation-perfusion (V/Q) scan may suffice.

#### **Wound Complications**

Wound infection usually presents around the fifth post-operative day. Signs of infection include erythema, tenderness, warmth, oedema and foul smelling discharge. Patients thought to be at risk may receive antibiotic prophylaxis.

Risk of wound infection can be related to the cleanliness of the surgery being performed. "Clean" surgery carries the lowest risk of wound infection e.g. thyroidectomy, hernia repair. "Potentially contaminated" surgeries include elective gastrointestinal surgeries. "Contaminated" and "dirty" surgeries carry the greatest risk of wound infection as these have definite faecal contamination. Surgical technique can also influence risk of wound infections. Good technique such as careful debridement and washout, good haemostasis, no tissue ischaemia and minimal tissue trauma have been shown to reduce these risks.

Patient factors that increase wound infection include obesity, diabetes mellitus, immunocompromised patient for example if they are on glucocorticoid therapy or are malnourished. Infection risk is also increased if there is haematoma formation as collected blood is an excellent breeding ground for bacterial growth.

Superficial wound infections can be managed conservatively with regular wound care +/- antibiotics. Deeper infections or wounds involving prosthesis (i.e. synthetic graft or implant) may require surgical exploration, removal of prosthesis and healing by secondary intention.

Wound dehiscence is when healing fails and the wound falls apart. This usually occurs around 7-10 days post-operatively. Surgical risk factors include poor surgical technique, e.g. too much tension on sutures, or patient poor wound healing or infection. Treatment depends on depth of dehiscence but may involve re-suturing under anaesthesia.

Other infectious complications can occur anytime so it is important to monitor patients' infection markers (WBC, CRP, temperature, etc.) to ensure there are no system signs of infection. Line infections occur from peripheral cannulae, central lines, and catheters and may include MRSA pathogens.

**Urinary Tract Infections (UTI)** are predisposed to by

instrumentation of the urinary tract and indwelling urinary catheters.

#### Specific Surgical Complications

Different operations have unique approaches and anatomy, as so there are specific complications that may occur. It is important to be aware of the operation details including the common and serious complications for the consent process. Generally speaking, any surgery done as an emergency has more associated risks. Open operations will have more pain afterward and greater risk of wound infection, ileus and respiratory complications. Laparoscopic operations have specific complication including bowel / blood vessel injuries when inserting the trocars, injuries associated with limited field of view and conversion to open operations.

#### General Surgery (Upper and lower GI):

Operation	Description	Complications
Appendectomy	Removal of the appendix	<ul style="list-style-type: none"> <li>Intra-abdominal abscess (including sub-phrenic, pelvic)</li> <li>Ileus – if open as handle bowel</li> </ul>
Cholecystectomy	Remove the gallbladder	<ul style="list-style-type: none"> <li>Bile leak</li> <li>Damage to biliary system</li> <li>Retained stones in biliary ducts</li> </ul>
Inguinal/ femoral hernia repair	Repair of defect in the abdominal wall	<ul style="list-style-type: none"> <li>Recurrence</li> <li>Bleeding</li> <li>Infection</li> <li>Chronic groin pain and numbness</li> <li>Ischaemic orchitis</li> </ul>
Hartmann's procedure <sup>5</sup>	Removal of sigmoid bowel, end colostomy and mucus fistula	<ul style="list-style-type: none"> <li>Ileus</li> <li>Small bowel obstruction</li> <li>Stoma complications (parastomal hernias, prolapse, skin excoriations)</li> </ul>
Abdominal-perineal resection <sup>7</sup>	Removal of rectum and anus, end colostomy	<ul style="list-style-type: none"> <li>Sexual dysfunction</li> <li>Stoma complications (see above)</li> <li>Ileus, small bowel obstruction</li> </ul>
Anterior Resection	Removal of upper rectum, join colon to anus	<ul style="list-style-type: none"> <li>Anastamotic leak</li> <li>Sexual dysfunction</li> <li>Ileus, small bowel obstruction</li> </ul>
Flexible sigmoidoscopy or colonoscopy	To investigate bleeding or pain from the colon	<ul style="list-style-type: none"> <li>Perforation of viscus</li> <li>Bleeding</li> <li>Colicky abdominal pains, bloating and excess flatus</li> </ul>
Splenectomy	Removal of spleen	<ul style="list-style-type: none"> <li>Bleeding</li> <li>Intra-abdominal abscess</li> <li>Bloods abnormalities</li> <li>Predisposition to infections – will require vaccines and lifelong antibiotic prophylaxis</li> </ul>

**Table 1:** Common surgical operation by speciality, and the common/ important/ serious complications



**Vascular:**

Surgery	Description	Complications
Open AAA Repair	Repair of an aortic aneurysm with graft replacement	<u>Early:</u> <ul style="list-style-type: none"> <li>• Renal failure</li> <li>• Impotence</li> <li>• Anastomotic leak</li> <li>• Peripheral emboli ("trash foot")</li> </ul> <u>Late:</u> <ul style="list-style-type: none"> <li>• Graft infection or thrombosis,</li> <li>• Aorto-enteric fistula</li> <li>• Pseudoaneurysm</li> </ul>
AAA Repair - endovascular	Repair using an endoluminal graft under image guidance	<ul style="list-style-type: none"> <li>• Endoleak</li> <li>• Device failure</li> </ul>
Femoral-popliteal bypass graft	Bypass of femoral artery stenosis	<ul style="list-style-type: none"> <li>• Re-stenosis</li> <li>• Thromboembolic events</li> <li>• Failure resulting in limb loss</li> </ul>
Carotid Endarterectomy	Correcting carotid artery stenosis	<ul style="list-style-type: none"> <li>• Nerve injuries (esp. hypoglossal, marginal mandibular, recurrent laryngeal)</li> <li>• Intra-operative CVA</li> <li>• Re-stenosis</li> </ul>

**Orthopaedics:**

Fracture healing has a number of potential complications. These include malunion, non-union and infection. As many of these operations involve opening up a sterile cavity, and/or inserting prosthesis, they are carefully planned and the theatre environment is kept as sterile as possible.

Operation	Description	Complications
Total hip replacement	Replacement of hip joint with prosthesis	Loosening Periarticular calcification Adverse reaction to cement
Total knee replacement	Replacement of knee joint	Patellar dislocation
Fixation of neck of femur fracture	Restore stability and alignment of neck of femur	<u>AO screws - non-union</u> <u>Dynamic Hip Screw (DHS):</u> displacement of proximal fragment, malrotation <u>Dynamic Compression Plate (DCP):</u> malalignment
Fixation of ankle fracture	Restore stability and alignment of ankle complex	Compartment syndrome Distal ischaemia Poor skin healing
Fixation of Colles' fracture	Restore stability and alignment of distal radius (+/- ulnar)	<u>Early:</u> <ul style="list-style-type: none"> <li>• Compartment syndrome</li> <li>• Tendon (Extensor pollicis longus, EPL) rupture</li> <li>• Acute carpal tunnel syndrome</li> <li>• Peripheral oedema</li> </ul> <u>Late:</u> <ul style="list-style-type: none"> <li>• Radial shortening</li> <li>• Complex regional pain syndrome</li> </ul>
Shoulder relocation	Correction of dislocation	Rotator cuff or capsular tear Damage to axillary or brachial plexi Recurrence
Carpal tunnel decompression	Release of Median nerve compressed in carpal tunnel	Injury to median nerve or vascular arch Recurrence

Urology<sup>13</sup>:

Surgery	Description	Complications
Nephrectomy	Removal of kidney, can be open/ laparoscopic	<ul style="list-style-type: none"> <li>• Haemorrhage, haematoma</li> <li>• Injury to surrounding structures</li> </ul>
Rigid cystoscopy and transurethral resection	Endoscopic inspection and sampling of urethra and bladder	<ul style="list-style-type: none"> <li>• Bladder perforation</li> <li>• Infection – UTI, orchitis</li> <li>• Acute urinary retention</li> <li>• Urethral stricture</li> </ul>
Scrotal exploration	To determine if a testes is strangulated	<ul style="list-style-type: none"> <li>• Infertility</li> <li>• Bleeding</li> <li>• Infection</li> </ul>

## Conclusion

Postoperatively, patients need close monitoring to identify common early complications of surgery such as infection or haemorrhage. These can be adequately managed and have a better prognosis if caught early. Intermediate and late complications such as DVT or PE must also be examined for. Wound complications are also a common postoperative complication that can be prevented by aseptic surgical technique and careful monitoring of the wound site.

Every surgery is not without risk. If these risks are managed adequately and patients optimised before surgery, then complications are usually minimal. Patients recover uneventfully and are discharged in a timely manner. It is the management of pre and postoperative risks that determines the rate of complication. Sound management leads to a reduction in complication rate and happy patients.

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## Introducing a Career in Pathology

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**Keywords:**

*Pathology, Career, Training Pathways, Histopathology, Haematology, Immunology*

**Introducing Pathology**

Pathology is an integral speciality within medicine with great emphasis placed on the analysis and detection of disease processes. Pathologists thereby have a huge influence on the diagnosis and shaping the patient management in staging disease and advising treatment targets. It has greatly advanced since humans first began examining bodies centuries ago to the use of diverse imaging and laboratory techniques available today. Knowledge and curiosity are the foundations of this specialty as pathologists seek to explain how and why people fall ill.

Such is the importance of pathology that there are several sub-specialties to diversify into; it is a training pathway with many opportunities. The path to specialising into one of these branches depends on the sub-specialty. Haematology and Immunology require core medical training for two years whereas the others are run-through training (you enter specialist training straight after foundation years). Histopathology is the largest specialty but others include Chemical Pathology, Microbiology and Virology.

**Life as a Pathologist**

The bulk of a pathologists work on a daily basis will involve interpreting results of investigations related to their sub-specialty. Furthermore, a pathologist will go on ward rounds and journal clubs as well as advise other consultants as to what investigations to perform. This can either be via telephone, or in person, as well as visiting specific patients (in the case of Haematology, Chemical Pathology and Microbiology). There is much interaction with other specialties as many pathologists frequently attend multidisciplinary (MDT) meetings in order to discuss cases. For example, at an MDT for lung cancer, the input from the pathologist is essential to determine

the type and stage the tumour which directly affects the treatment aims and prognosis.

There are many opportunities to pursue other interests in pathology. There is a strong emphasis on teaching biochemistry at a post graduate level in the clinical setting, and it is easy to get involved in research projects. The level of teaching depends on the hospital association. District general hospitals will mainly teach graduates. Undergraduate teaching is usually only found at teaching hospitals. Also, there are opportunities to increase patient contact by further sub-specialising. For example, a pathologist could pursue diabetes and then run a diabetes clinic once a week (this mostly applies to chemical pathology).

A typical day in the life of a pathologist varies on a daily basis. This in itself provides excitement as well as the challenge of deciding which investigation is most appropriate or determining what disease process is occurring. Some pathologists can work remotely at weekends which can aid a better work-life balance. This is still considered to be elective and will be in addition to a full working week. There is less paperwork (due to less patient contact) which means more time spent performing clinical tasks. For Histopathology, this mostly involves interpreting histology slides.

Paperwork mainly consists of accreditations and writing responses to referral letters. Furthermore, the on-call requirements of a pathologist are small compared to other specialties. This will usually involve a rota such as working on-call once every three weeks. Even so, these on-call sessions will often involve only two to three calls per week and will usually consist of reviewing analytical data.

A career in pathology does not lend itself to private practice very well. The only way to become involved in private practice is through the clinics run as an interest within the main specialties. These can be in any subject where pathology plays a major role in diagnosis or management e.g. dermatology. A pathologist may also advise private laboratories, but does not have direct involvement with the private sector. This branch of medicine is almost completely contained within the NHS and it is rare for a pathologist to work completely in the private sector.

Pathology is also a specialty which is unique to countries within the British Commonwealth, and so international opportunities are available only in these countries. Other countries, for example America, do not recognise some pathology disciplines as a medical specialty. Instead, scientists perform many of the duties of a pathologist without direct patient interaction.

This specialty will suit someone who enjoys the 'detective' side of medicine, thriving in trying to understand the cause of different diseases. This career might not provide as much patient contact as some of the other branch of medicine but the amount of variation is superior to most specialties. Pathology offers an interesting profession with enough flexibility to allow for a work-life balance

#### Facts and Figures

Pathology isn't as competitive as some of the other specialties but nevertheless, studying another degree is beneficial particularly if it involves laboratory work. The national ratios for some of the sub-specialties are shown below:

	2010	2011	2012
<b>Histopathology</b>	Not available	1.1	1.5
<b>Haematology</b>	Not available	3.1	3.9

*Figure 1: National Competitive Ratios within U.K. <sup>2</sup>*

The training pathways differ for each sub-specialty, most of which involve run-through training whereby you commit to specialty training after completion of foundation years. The exceptions to this are Haematology and Immunology which require two years of core medicine before entering specialty training. Histopathology requires completion of four stages over a minimum of five years. Throughout these stages, knowledge of the pathological traits and analytical techniques are introduced then built upon. Clinically, cut-up of specimens such as mastectomy and prostatectomy are learnt under supervision before becoming competent independently in the latter stages of training. Both parts of the FRC Path examination must be completed by ST2 and ST4 respectively as well workplace-based assessments and both parts of the ARCP.

#### The Future

The future of pathology could have huge implications for other specialties. There are increasing amounts of research dedicated to diagnosing patients with certain conditions at the bedside, or through other methods. There are also ideas to utilise the human genome in pathology with the aim to provide individualised care. This could completely alter the way medical treatment functions in the future, but this level of care is several years away at least.

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## Abstracts from The International Academic and Research Conference 17<sup>th</sup> August 2013, University Place, University of Manchester

### Prize Winning Abstracts

*The following three abstracts have been selected as the best in their respective category. They were chosen from the 470 abstracts that were submitted for consideration in the 3<sup>rd</sup> International Academic and Research Conference 2013.*

#### ***Doctors Academy Prize for Best Abstract in the Clinical and Laboratory-Based Research Category***

##### **ECD and DCD Renal Allografts in the West of Scotland: Their Place in the Kidney Allocation Process**

Hesse KWX\*

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**Background:** A rising disparity between demand and availability means organs from donations after circulatory death (DCD) are increasingly used. The purpose of this study was to report outcomes of DCD renal allografts from a single centre.

**Methods:** The study was a retrospective analysis of prospectively gathered data from a single centre for renal transplants performed between 2001 and 2010 inclusive. Patients were placed into four strata: DBD:SCD, DBD:ECD, DCD:SCD, DCD:ECD. Kaplan-Meier survival analysis was undertaken on the primary long-term outcomes: 5-year graft survival and patient survival. Differences in CIT, WIT, and donor and recipient characteristics were also compared, using appropriate statistical tests.  $p < 0.05$  was defined as significant.

**Results:** 729 renal transplants were performed. There was a significant difference in graft survival between groups ( $p = 0.005$ ) with ECD organs doing worse than SCD organs. Recipients of ECD organs were generally older ( $p < 0.05$ ) and longer on dialysis ( $p < 0.05$ ). For patient survival, there was a difference that did not achieve significance ( $p = 0.065$ ). DCD:SCD organs had better outcomes than DBD:SCD organs. The CIT was significantly shorter in DCD:SCD organs, compared to DBD:SCD organs ( $p < 0.001$ ).

**Conclusions:** ECD organs do worse than SCD organs, yet a refined allocation process that reduces CIT assault and considers recipient age and the chronicity of the patient's renal disease can improve their results. DCD allografts are at least comparable to DBD kidneys, probably due to a shorter CIT, and this should encourage their integration into the national allocation scheme, with guidelines specific to them. Our study's main limitation is a small DCD, particularly DCD:ECD, group.

*Doctors Academy Prize for Best Abstract in the  
Clinical Audit and Service Evaluation Category***Obesity and prescription of combined oral contraception in the general practice: findings from a closed audit loop**

Prapa M\*; Mudawi R; Lovett SM  
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**Background:** Combined oral contraception (COC) pill is the most commonly used contraception in the UK. Females on COC with an increased body mass index (BMI) are at a higher risk of myocardial infarction (MI) and venous thromboembolism (VTE). A lack of routine BMI recording has been noticed in our practice leading to inadequate COC counselling.

**Methods:** This audit was conducted at a single General Practice Surgery managing approximately 10,000 patients, in East Yorkshire, UK. As per the UK Medical Eligibility Criteria (UKMEC), we set a standard of an annual follow-up in 100% of women on the COC with a BMI of 30-34kg/m<sup>2</sup>; 0% of women with a BMI>35kg/m<sup>2</sup> should be on the COC pill.

**Results:** Initial data was collected over March 2011-2012. Out of 307 women on COC, 28 (9.12%) had a BMI of 30-34kg/m<sup>2</sup> with a careful follow-up in 26 (92.86%). Six (1.95%) women with a BMI>35kg/m<sup>2</sup> were prescribed the COC. Proposed changes included departmental teaching on COC prescription and addition of BMI to the "COC template" on our clinical data system. Repeat data collection 6 months following change implementation revealed an improvement in careful follow-up of 23 (96%) females on COC with a BMI of 30-34kg/m<sup>2</sup>. However, out of 295 women on the pill, 5 (1.7%) had a BMI>35kg/m<sup>2</sup>.

**Conclusion:** Education of all staff involved in COC prescribing is essential. The "COC template" on our clinical system was the most effective prompt for regular BMI assessment. Calculation of BMI should be a core part of COC prescription.

*Doctors Academy Prize for Best Abstract in the  
Clinical and Patient-Related Work Category***An unusual presentation of pulmonary-renal syndrome: Learning points for prompt diagnosis and management**

Daum P\*; Gill D  
 Charing Cross Hospital, London, UK; Hammersmith Hospital, London, UK

**Background:** Pulmonary-renal syndrome is defined as the combination of diffuse alveolar haemorrhage and glomerulonephritis. Patients may present with severe respiratory and/or renal failure; with a mortality of 25-50%, their outcome is based on early diagnosis and aggressive management.

**Presentation:** A 61-year-old lady presented to the Emergency Department with a 5-week history of malaise, nausea and epigastric pain followed by an acute episode of reported haematemesis and anuria. She was alert and orientated but tachycardic and hypotensive; the remainder of her examination was unremarkable.

**Investigation:** An arterial blood gas demonstrated a partially compensated metabolic acidosis and haemoglobin of 8.9g/dL; her initial chest X-ray was normal. First managed as an acute upper GI bleed, blood tests later revealed acute renal failure with creatinine 2713µmol/L and urea 90.6mmol/L; urinalysis was markedly positive for both blood and protein and subsequent testing for p-anticytoplasmic antibodies was positive.

**Management:** Following the diagnosis of pulmonary-renal syndrome, this lady was managed in the intensive care unit with methylprednisolone, ultrafiltration and plasma exchange. Over forty-eight hours she developed frank haemoptysis and type-1 respiratory failure with a chest X-ray demonstrating bilateral airspace shadowing consistent with pulmonary haemorrhage. Following further treatment with cyclophosphamide and then rituximab, she eventually made a good recovery and remains independent of dialysis.

**Discussion and Learning Points:** Pulmonary-renal syndrome is a life-threatening condition with an acute onset and fulminant course if left untreated. Despite variable presentations, early diagnosis through timely investigation and the immediate initiation of appropriate management is crucial.

## Abstracts from the 'Winner of Winners' Competition

*The first prize winners of the oral and poster presentations from various UK national student conferences were selected to present their work to the entire 5th International Medical Summer School 2013 that comprised of 220 delegates. In addition, the winner of the oral presentation from the Indian National Medical Students Association Annual Meeting 2013, Kolkata, India, was also offered the chance to present in this competition. From this, the best presenter was selected to give a short talk at the 3rd International Academic and Research Conference 2013.*

### ***Winner of Winners – Abstract 1 (From Hull-York Surgical Society Conference)***

#### **An Introduction to hand allograft**

Aslet MED\*

Hull York Medical School, Yorkshire, UK

The loss of one or both hands can be detrimental to an individual's quality of life. Losing a hand does not simply result in loss of function, but loss of ability to express one's personality, to gesticulate, and to take part in cultural behaviours such as wearing a wedding ring. Although there are alternatives to transplant such as use of prosthesis and reimplantation of the damaged hand, rarely are they able to match the natural look and functional possibilities of a transplanted hand. To a small number of carefully selected patients, hand transplant can restore a missing hand (or hands), and regain a similar look, and potentially similar function to a normal hand. Past failures have been learnt from and so far, promising results are being seen. Extrinsic function has been found to return within days, and intrinsic after 9-15 months. Importantly, protective sensory function returns within 12 months. However, the procedure is not without its risks. A life time of immunosuppressive therapy may cause organ damage and increase cancer risk, episodes of acute rejection are almost certain, and there is no guarantee as to the longevity of the hand. Therefore alternative treatments must not be overlooked before opting for hand transplant.

### ***Winner of Winners – Abstract 2 (From National Medical Student Paediatric Conference)***

#### **Non-attendance at paediatric outpatient appointments in Brighton; a quality improvement project**

Biggart R\*; Hallows MR

Royal Alexandra Children's Hospital, Brighton, UK

**Background:** There are a considerable number of non-attendances at paediatric outpatient appointments in Brighton despite appointment letters and SMS reminders sent a week before.

**Aim:** To determine the reasons why families do not attend their appointments with a view to change the service provided to achieve better patient outcomes and maximise NHS financial resources.

**Method:** Over a 2 month period the families of the children who did not attend (DNA) were called and were asked a series of standardised questions.

**Results:** Between the 19<sup>th</sup> November- 14<sup>th</sup> December 2012 there were 107 DNAs whilst between 14<sup>th</sup> January- 15<sup>th</sup> February 2013 there were 170. The main reasons for not attending, according to those who were contacted across the 2 months, are listed from most to least significant: forgetfulness (42.4%), the hospital not informing families of the appointment (20.2%), the hospital not recording that parents had rescheduled (15.1%), that parents were too busy to take their child (11.1%), that the child was too unwell to attend (6.1%) and finally because the parents felt the appointment was unnecessary (5.1%). Nearly 47% of families did not answer when called, but correct contact information was an issue as 17.7% of the DNAs had an incorrect number recorded or no number recorded.

***Winner of Winners – Abstract 3***  
***(From Barts & The London National Undergraduate Surgical Conference)***

**Spring-mediated cranioplasty for Mercedes-Benz Syndrome**

Phillip CC \*

*Brighton & Sussex Medical School, Brighton, UK*

Craniosynostosis is a rare condition in which the fibrous sutures of the infant skull are prematurely ossified preventing normal skull growth. The cranium is forced to grow in a direction parallel to the affected sutures, resulting in abnormal skull shape. Ineffective compensation can lead to increased intracranial pressure and its sequelae (impaired vision, sleep, feeding and mental development).

This case describes a six-month old infant with bi-lambdoid and sagittal synostosis; known, due to its pattern, as 'Mercedes-Benz' syndrome. Restriction in cranial growth caused compensatory expansion leading to marked scaphocephaly, a hypoplastic posterior cranium and an occipital concavity. Effective treatment for this specific type of craniosynostosis is described, using a combined plastic and neurosurgical approach. The intraoperative techniques employed included surgical suture excision and spring-mediated cranioplasty in order to achieve cranial vault reconstruction with good cosmesis. It demonstrates the importance of early intervention to prevent potential complications of craniosynostosis, with excellent post-operative prognosis.

***Winner of Winners – Abstract 4***  
***(From National Undergraduate & Foundation Surgery Conference)***

**Readability assessment of online patient directed material related to Colonoscopy**

Hamilton L\*; Zia K

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**Background:** With the move towards a greater emphasis on patient-centred care it is only right that patient education materials reflect the national reading age. In 2003, an estimated 12.5 million online health-related searches were conducted globally each day. Patients are able to access a plethora of information online but in order to make an informed choice, they should be able to understand and interpret the information directed to them.

**Objective:** To assess the readability of online patient directed material regarding colonoscopy, to ascertain whether the material met the UK's average reading level.

**Method:** A systematic search was performed using the phrase 'Colonoscopy procedure' on three internet search engines: Google, Yahoo, Bing. The readability of 50 websites were assessed using the following readability indices: Gunning Frequency of Gobbledygook Index, the Flesch Reading Ease Score and Simple Measure of Gobbledygook.

**Results:** The quality of online information regarding colonoscopy is highly variable. The following results demonstrate that the majority of online information regarding colonoscopy would require a patient to have at least secondary school knowledge to understand the prose.

**Conclusion:** Healthcare professionals, should endeavour to recommend websites, which give a basic overview of what a colonoscopy entails. Websites should use a standard readability tool to ascertain the readability of the material and revise the text to meet national readability recommendations. Failure to do so may result in a patient being unable to express their concerns or make an informed decision.



***Winner of Winners – Abstract 5***  
***(From Barts & The London National Undergraduate Surgical Conference)***

**Examining the Effects of in situ Metal-on-Metal Hip Implants on Bone Resorption in Patients**

Ryan HS<sup>1\*</sup>; Helen H<sup>1</sup>; Rachel W<sup>2</sup>; Alastair S<sup>2</sup>; Stephen J<sup>1</sup>; Alun J<sup>1</sup>

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**Introduction:** Patients with cobalt-chromium alloy Metal-on-Metal (MoM) hip implants produce nanoscopic metal debris ions which are released into surrounding tissues. This can cause inflammatory tissue reactions, such as osteolysis, resulting in implant failure requiring revision surgery. Early detection of tissue damage is key to successful revision surgery. The objective of this study was to histologically observe samples of hip bone taken during revision surgery. The presence of bone resorbing osteoclasts was examined and related to clinical parameters.

**Methods:** Six peri-prosthetic bone samples were randomly selected from patients undergoing MoM hip revision surgery at Cardiff and Vale Orthopaedic Centre. The samples were decalcified, wax embedded and 5µm sections prepared. Sections were stained with Hematoxylin and Eosin and analysed for the number of osteoclasts. Pre-revision MRI reports and plasma metal ion concentrations were obtained. The study had ethical (REC for Wales) and health board approval.

**Results:** Two of the six cases had pre-revision plasma metal ion concentrations greater than recommended (4 ppb). Four of the six cases, including three cases with normal metal ion concentrations, had obvious peri-prosthetic osteoclastic activity. Interestingly, the case with the lowest plasma metal ion levels demonstrated the greatest quantity of osteoclasts whilst the case with the highest metal ion levels had the least.

**Conclusion:** The findings of this pilot study suggest that plasma metal ions levels are not a good indicator of adverse bone reaction to MoM implants. This adds further evidence to the proposition that a more reliable indicator of local tissue reaction to MoM implants needs to be developed.

***Winner of Winners – Abstract 6***  
***(From St. Andrews National Surgical Conference)***

**Improving outcomes for paediatric supracondylar fractures: Completing the cycle**

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**Background:** The gold standard of treatment for displaced supracondylar paediatric fractures is by closed reduction (CR) and percutaneous pinning. However, open reduction (OR) is required if CR fails. There is great controversy regarding the timing of treatment within the literature. A previous audit within Tayside demonstrated OR rates of 31%. Out of hours surgery was found to significantly increase the OR rate. As a result, a series of educational measures were undertaken and if no neurovascular compromise was found on presentation, treatment was delayed until the next available routine trauma list.

**Aim:** To complete the audit cycle after promoting the issue within the trust.

**Method:** Retrospective study from 2004-2010 for the original audit (A) and 2011-12 for the re-audit (RA).

**Results:** 115 patients in the A group and 48 in the RA group were identified. The OR rate was 36/115 (31%) in the A which was significantly reduced to 4/48 (8%) in the RA (p=0.001). 25/115 in A displayed neurovascular compromise compared to 7/48 (15%) in the RA group. In those with no neurovascular deficit, fewer operations were undertaken out-of-hours (from 17% to 7%) often meaning that surgery was undertaken over 6 hours after presentation (from 55% to 82%). There were no increases in adverse outcomes.

**Conclusion:** Significant improvements in management of supracondylar fractures can be achieved by the audit process. If no neurovascular deficit is found, delaying operative intervention until daylight hours has a lower OR rate and has no increase in complication rates.

***Winner of Winners – Abstract 7***  
***(From National Surgical Conference for Foundation and Student Doctors)***

**Learning Laparoscopy: A DIY Job?**

Rapaport B\*

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Laparoscopic surgery has over the last two decades become a mainstay of conventional practice. Surgeons have rapidly had to learn new skills to stay abreast of such technical advances. Simulators have historically provided a safe environment in which to acquire and improve surgical skill. Various homemade simulators, being vastly more economical than commercial counterparts, have previously been reported. Such equipment promises to aid acquisition of key visual-spatial skills. Personal users, in particular medical students with poor access to expensive training equipment, stand to benefit from these cheaper alternatives.

The aim of this project was to critically review previously described homemade laparoscopic simulators, to construct an improved simulator and to evaluate it as a viable option for surgical education.

Using publically available materials and tools, a laparoscopic simulator was constructed, drawing on the best elements from a number of previously described simulators. Novel additions include the use of a highly mobile high definition camera introduced from an angle that more closely simulates laparoscopic surgery in addition to a separate light element that allows easy manipulation of lighting conditions during tasks.

This project demonstrates a simple and scalable design that offers high quality simulation, at an approximate cost of £60 excluding tools.

All standard laparoscopic training exercises tested on the homemade simulator preformed well, providing a sufficiently challenging visual-spatial task with an overall experience comparable to commercially available simulators.

***Winner of Winners – Abstract 8***  
***(From 2<sup>nd</sup> Aberdeen Surgical Undergraduate Conference)***

**Correlation of MRI findings with histopathology following radical prostatectomy; an audit**

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**Background:** The aim of this audit was to assess the accuracy of MRI findings in prostate cancer and determine its limitations as a staging investigation. Treatment is guided by differentiating between organ confined disease and extracapsular extension, and determination of both tumour volume and grade. NICE recommends imaging to only be used in men for whom radical treatment is intended, this is preferred for those of assigned intermediate and high risk category.

**Methods:** Data obtained from a prospectively maintained database of all patients presenting to one consultant surgeon in Ninewells Hospital and Perth Royal Infirmary between 2004 to 2012 with a diagnosis of prostate cancer, who underwent pre-operative MRI scanning. 103 patients presented during this time, patients were excluded if they did not meet the criteria. MRI reports and pathological reports were obtained and cross referenced in order to ascertain the accuracy of the pre-operative MRI report.

**Results:** 103 patients, 34 excluded, n=69

MRI predicted 63/69 cases as T2 when only 37 cases were T2. In T3 disease; MRI predicted 2/28 cases. MRI failed to detect all T4 (n=3).

Cancer detected 68/69 cases, sensitivity =99%. Staging 35/69 cases correctly, specificity=50%. Of the 34 incorrectly staged, 94% were down staged.

**Conclusion:** It can be said from the findings that MRI does display a degree of sensitivity in detecting the presence of disease. However in terms of the specificity, from this study MRI has not been shown to detect stage of disease accurately, and underestimated the severity of disease.

*Winner of Winners – Abstract 9  
(From International Head and Neck Conference)*

**Beware of the dog: oculofacial reconstruction following paediatric dog bite injury**

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**Background:** Paediatric dog bite injuries are a serious medical and public health issue posing functional, aesthetic and psychosocial consequences. There are 6,450 hospital admissions secondary to dog bite injuries annually in Britain alone. We describe a severe case of paediatric dog bite injury, its management and prevention strategies.

**Methods:** A 9-year-old boy presented with full thickness upper and lower right eyelid margin tears with involvement of upper lacrimal canal, puncture of upper eyelid, full ptosis of right eye and five lacerations of the face following attack by neighbour's dog. The dog was a fully-grown domesticated Labrador Retriever. The patient was first assessed by a house surgeon on call who administered rabies prophylactic vaccine and thoroughly cleaned and sutured the facial wounds. The patient was then referred for oculoplastic evaluation and underwent reconstructive surgery.

**Results:** The surgical outcome was good with returning function of the eyelids and an acceptable aesthetic appearance of the eyelids and face. The patient's ptosis fully recovered within four weeks, preventing need for a second surgical procedure.

**Conclusions:** This case study highlights the necessary steps required for assessment and successful management of eyelid and facial trauma secondary to dog bite. Moreover, paediatric dog attacks are a preventable public health issue. Prevention strategies for paediatric dog bite injuries should include public education and training of dogs and their owners.

*Winner of Winners – Abstract 10  
(From 2<sup>nd</sup> Aberdeen Surgical Undergraduate Conference)*

**To localise and detect incipient damage to the ophthalmic and maxillary branches of the trigeminal nerve during tumour surgery**

Emma S

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**Objective:** To localise and detect incipient damage to the ophthalmic and maxillary branches of the trigeminal nerve during tumour surgery

**Methods:** Observational study of patients with skull base, retro-orbital or cavernous sinus tumours warranting dissection towards the cavernous sinus at a University Hospital. Stimuli applied as normal during approach to the cavernous sinus to localise CN III, IV and VI. Recordings were also obtained from the facial muscles to localize VII. The trigeminofacial reflex was sought simply by observing a longer time base routinely.

**Results:** Clear facial EMG responses seen reproducibly, when stimuli applied to the region of V1, V2 and V3. Response latency was increased compared to direct VII stimuli seen in some cases. Responses gave early warning of approach to these sensory trigeminal branches.

**Conclusion:** We submit this as a new technique, which may improve the chances of preserving trigeminal sensory branches during surgery in this region.

***Winner of Winners – Abstract 11***  
***(From National Undergraduate & Foundation Surgery Conference)***

**BAG-1L overexpression promotes a tumour-like phenotype in a three-dimensional model of mammary morphogenesis**

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**Introduction:** BAG-1 is an anti-apoptotic protein comprising three isoforms, BAG-1S, BAG-1M and BAG-1L, all of which are frequently overexpressed in breast cancer. BAG-1L localises in the nucleus and increases transcriptional activity of oestrogen receptors (ER). Nuclear immunoreactivity has been associated with an improved survival in patients with ER+ breast cancer. Overexpression of all BAG-1 isoforms together in three-dimensional (3D) cultures of MCF10A mammary cells gives rise to acini (mammary ducts) that are phenotypically similar to ductal carcinoma *in situ* (DCIS). Here, we investigate the effect of stable overexpression of BAG-1L alone in MCF10A acinar morphogenesis.

**Methods:** MCF10A mammary cell lines were transfected with BAG-1L or control vectors and cultured as a monolayer or in 3D to form acini. Protein expression was examined by immunoblotting. Acinar morphogenesis was examined by light and confocal microscopy.

**Results:** Overexpression of BAG-1L attenuates luminal apoptosis, resulting in an increased proportion of acini with filled lumens compared to control ( $p < 0.0001$ ) - a phenotype observed in DCIS. These acini also exhibit disorganised, atypical gross morphology, and form more atypical structures than do control cultures ( $P < 0.0001$ ). Immunoblot analysis shows a loss of E-cadherin expression in the MCF10As expressing BAG-1L at high levels, a feature commonly observed in invasive lobular breast cancer.

**Conclusion:** Overexpression of BAG-1L in acini results in the formation of structures resembling a tumorigenic phenotype, and reinforces a role of BAG-1L as a contributor to the malignant process in the breast. Experiments investigating the effect of treatment with BAG-1-specific inhibitors in this model are currently underway.



***Winner of Winners – Abstract 12  
(From International Head and Neck Conference)***

**An Audit on Surgical Intercostal Drain Removal Technique and the Development of Residual Space**

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**Aims:** Residual air space is a complication following discontinuation of intercostal drains. The aims of our audit were to quantify the relapse rates of pneumothoraces post surgical intercostal drain removal, and investigate potential risk factors for relapses against local guidelines. A re-audit was conducted following our recommendations, to evaluate its outcome.

**Methods:** Prospective data was collected for all surgical intercostal drains removed during a month period for both audits. Chest x-rays performed before and after drain removal were reviewed for increased residual air space. We excluded patients with ongoing intercostal drains in-situ, post-pneumonectomy, and intercostal drainage for haemo/chylothoraces and pleural effusions.

**Results:** A total of 44 patients were included. The initial relapse rate of pneumothoraces post intercostal drain removal was 28% despite 100% compliance to the local guidelines, with which intercostal drains were removed on held-inspiration. The re-audit, after recommending chest drain removal on held-expiration, relapse rate dropped to 4.3% ( $p=0.0497$ ). No patients required drain re-insertion. The following risk factors were found not to affect outcome: type of surgery, extra suture requirement post-drain removal, timing of drain removal, grade of staff involved and patient demographics.

**Conclusions:** There is no consensus on whether surgical intercostal drains should be removed on held-inspiration or held-expiration. Our relapse rate of residual air space post intercostal drain removal has significantly reduced from 28% to 4.3% after changing our method of intercostal drain removal from held-inspiration to held-expiration. Further re-audits will be carried out ensuring standards are maintained.

***Winner of Winners – Abstract 13  
(From International Head and Neck Conference)***

**The Reporting Quality of Randomised Controlled Trials in Ophthalmic Surgery**

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**Background:** Randomised controlled trials (RCT) are regarded as the gold standard for evaluating the effectiveness of therapeutic interventions. RCTs in ophthalmic surgery pose particular challenges in study design and implementation. Therefore accurate, transparent and complete reporting is especially important for readers. The CONSORT statement guides the reporting of RCTs.

**Purpose:** To provide the first known assessment of the compliance of RCTs in ophthalmic surgery to the CONSORT extension for trials involving Non-Pharmacological Intervention (CONSORT NPT). We also compared compliance against surrogate markers of paper quality.

**Methods:** The Medline database was searched for RCTs in ophthalmic surgery from 1/1/2011 to 31/12/2011. Results were searched independently by two authors and relevant papers selected. The RCTs were independently scored against the 23-item CONSORT NPT checklist. Discrepancies were resolved by consensus. Surrogate markers of paper quality were compared against the CONSORT score using the Spearman rank correlation coefficient.

**Results:** 186 papers were retrieved from Medline. 65 papers, involving 5803 patients, met the inclusion criteria. The mean CONSORT score was 8.9 (39%) out of 23 items (range 3.0-14.7, SD 2.49). The least reported items related to title and abstract (1.6%), reporting intervention adherence (3.1%) and interpretation of results (4.7%). There was no significant difference between CONSORT score and journal impact factor ( $R=0.14$ ,  $p=0.29$ ), or number of authors ( $R=0.14$ ,  $p=0.93$ ).

**Conclusion:** The reporting of RCTs in ophthalmic surgery is suboptimal. There is a need to improve reporting quality by working with authors, journals, editors as well as guideline-developers.

***Winner of Winners – Abstract 14  
(From National Medical Student Conference (KARMIC), Kolkata, India)***

**Role of Immunophenotyping in the diagnosis of acute leukemias of ambiguous lineage – a new entity described by WHO 2008.**

Khare S\*; Kotwal J

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**Introduction:** Biphenotypic Ambiguous Leukemia represents < 5% cases of Acute Leukemia. Knowledge about BAL is *limited* in terms of clinical and biological presentation and with regard to outcome. More importantly, prognosis is poor compared with de novo AL. This study aims to analyze immunophenotypic profile of Acute Leukemias of ambiguous lineage and to study the prevalence in Indian scenario.

**Materials and methods:** Flow cytometric immunophenotyping (FCI) was performed on fresh bone marrow or blood specimens. Single-cell suspensions were incubated with combinations of monoclonal antibodies in four-color immunofluorescence. The antibodies were conjugated to fluorescein isothiocyanate (FITC), phycoerythrin (PE), peridinin chlorophyll protein complex (PerCP) and allophycocyanin (APC). Antibodies used in the analysis recognized stem cell and panleukocyte antigens including CD45. Samples were analyzed using 4 color flow cytometry and the blast cell populations were identified by CD45 versus side scatter properties using standard staining and analytical methods.

**Results:** Out of 30 cases of Acute Leukemia in 4 months we report 04 cases diagnosed as AML or ALL based on FAB (13.3%). However, on FCI these were diagnosed as BAL, Bilineage AL & ALL with aberrant myeloid expression.

**Conclusion:** Unlike commonly seen acute leukemia classified as B or T lymphoid or myeloid lineage, BAL is a type of acute leukemia with uncommon biological and clinical features. Limited studies are available for Indian population in this regard and hence at least, patients who are not responding well should be screened for ambiguous lineage using comprehensive FCI and molecular studies.

## Oral Presentations

*Clinical and Laboratory-Based Research Category***Does virtual reality simulation (VRS) training at home improve trainee confidence and self-reported ability?**<sup>1</sup>Barnes J; <sup>2</sup>Burns J\*; Nesbitt C; Horgan A<sup>1</sup>Royal Victoria Infirmary, Newcastle, UK; <sup>2</sup>Freeman Hospital, Newcastle, UK

**Introduction:** Surgical training is evolving. Tighter working times, more technically demanding techniques and increasing patient expectations can inhibit trainees gaining procedural experience. Virtual reality simulation (VRS) allows trainees to practice surgical technique outside of the operating theatre; helping them develop their skills and understanding and ensuring they get the most of time spent in theatre. However, the complexity and expensiveness of most VRS units can limit trainees opportunities to use them. This study investigated whether using SimEndo®, a portable VRS system for out of hospital use, could be a simpler alternative to conventional simulators.

**Methods:** Ten trainees were given a questionnaire which, using visual analogue scales, assessed their self-reported laparoscopic surgery competencies. They were asked about instrument and camera skills, tissue-handling, manual-dexterity, visuo-spatial awareness, depth awareness and overall confidence/ability. They were then given the SimEndo® unit to practice with in their own time before they were asked to reassess their confidence and self-reported ability in the different areas.

**Results:** Trainees spent an average of 196 minutes practicing (range 130-330) and reported a mean increase in overall confidence/ability of 93.9% (p=0.006). Improvements were reported in all domains, all bar one (camera skills) were statistically significant (p<0.05).

**Conclusion:** This study shows that portable VRS training improves trainees' surgical skills without requiring them to attend specialist centres. Further study, with objective assessment parameters is required to assess whether this method of learning may be a viable alternative to conventional simulation training.

**The use of adrenaline and long-term survival in cardiopulmonary resuscitation (CPR) following cardiac arrest**

Miller CW\*; Nolan J

University of Southampton; Southampton; UK

**Background:** Adrenaline continues as primary pharmacotherapy following cardiac arrest as instructed by international Advanced Life Support (ALS) guidelines. Adrenaline increases peripheral vascular resistance, through alpha-1-adrenoreceptor mediated vasoconstriction, whilst cardiac output is improved via adrenaline's beta-1-adrenoreceptor activity. This works to increase both coronary, and cerebral, perfusion pressure, with the anticipation of return of spontaneous circulation (ROSC) whilst preventing hypoxic brain injury.

**Methodology:** Using Medline 1947-2012 (OVID interface), the search strategy was as follows: {[CPR.mp. OR cardiopulmonary resuscitation.mp. OR internal cardiac massage.mp. OR chest compressions.mp.] AND [adrenaline.mp. OR epinephrine.mp.] AND [survival.mp. OR mortality.mp.]} LIMIT to [human]}. 242 papers were found, however, 236 were irrelevant or of insufficient quality for inclusion.

**Discussion:** Trials examining the efficacy of adrenaline following cardiac arrest are logistically, and ethically, challenging, however, data from both observational studies and randomised controlled trials (RCTs) suggest administration may be associated with reduced long-term survival. The evidence is strong for ROSC and survival to hospital admission, but associated with worse long-term survival and neurological outcome. Evidence from a retrospective analysis of an RCT examining 848 cardiac arrests demonstrated reduced survival at 1 year [12% vs. 6%, no adrenaline vs. adrenaline, OR 0.5, p=0.004], and more favourable neurological outcome in those not receiving adrenaline [11% vs. 5%, no adrenaline vs. adrenaline, OR 0.4, p=0.001].

**Conclusion:** The use of adrenaline during CPR appears contrary to the available evidence. Guidelines would be directed, and aided, by a well-designed, multicentre placebo-controlled RCT to determine the efficacy of adrenaline in CPR.

**Epilepsy Doses of Valproate Combined With the Anti-Helminthic, Niclosamide, Synergistically Kill Myeloma Cells: a Potent New Anti-Myeloma Drug Combination.**

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**Background:** Multiple myeloma (MM) is an incurable plasma cell neoplasm characterized by multiple relapses. Using drug redeployment strategies, we have shown that the addition of sodium valproate (anti-epileptic/histone deacetylase inhibitor (HDI)) which had no activity alone, to niclosamide (anti-helminthic which targets the mitochondrial respiratory chain) at clinically achievable concentrations potentially reduced viability of MM cell lines. The aim of this project was to understand the anti-myeloma mechanism of action of valproate and niclosamide (VaN).

**Methods:** Cellular oxidative stress levels and apoptosis were measured using flow cytometry. Activity/levels of antioxidant proteins were quantified using biochemical studies. Relative changes in the levels of acetylated proteins (acetylome) were measured by immunoprecipitation and mass spectrometry.

**Results:** Niclosamide induced mitochondrial superoxide production by MM cell lines; decreased cell viability and increased apoptosis, which were potentiated by valproate. Glutathione depletion in cells treated with VaN was observed. Antioxidant (N-acetylcysteine) partially rescued cells from niclosamide- /VaN-induced death. Activity of mitochondrial SOD2 was reduced in VaN-treated cells; whilst activity of cytosolic SODs1/3 remained unchanged. Preliminary acetylome analysis data demonstrated that VaN synergistically enhances histone acetylation.

**Conclusions:** We have identified a potent anti-MM drug combination of valproate and niclosamide. Our data indicates that VaN activity is mediated through induction of oxidative stress. Analysis of the acetylome indicates that valproate, at low non-toxic doses, can be used effectively as an HDI when combined with niclosamide. Importantly, the concentrations of both niclosamide and valproate used are safe and affordable which will accelerate progression of VaN therapy to phase I/II clinical trials.



### An Anatomical and Functional Classification of Aneurysmal Arteriovenous Fistulae in Tayside Haemodialysis Patients – a Pilot Study

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Haemodialysis (HD) via an autologous arteriovenous (AV) fistula is the most frequently used treatment for end-stage renal failure. Fistula dilation is a complication but there is no accepted definition of what constitutes an aneurysm. Our aims were to describe aneurysmal fistulae anatomically and functionally.

Sixty patients (60 fistulae) underwent Duplex ultrasound scanning to measure the diameter and *volume index* (volume divided by fistula length) of their fistula venous limb. Urea Reduction Ratio was recorded to assess HD function. No data was available to inform a power calculation.

*Maximum fistula diameter* and *volume index* correlated significantly with *time since creation* ( $P < 0.001$ ,  $r = 0.749$ ). There was no correlation between *maximum diameter* or *volume index* and HD function or risk of bleeding ( $P > 0.05$ ). The 75<sup>th</sup> percentile was at a *maximum diameter* of 2.0cm and a *volume index* of 130mm<sup>2</sup>. The 95<sup>th</sup> percentile was at a *maximum diameter* of 3.3cm and a *volume index* of 564mm<sup>2</sup>.

Apart from cosmetic issues, decreased HD function and bleeding issues are the main clinical concerns with aneurysmal fistulae. If the lack of correlation between these concerns and *maximum diameter* or *volume index* is confirmed in future work, the concept of an aneurysmal fistula must be challenged as a clinically relevant entity. Some studies define aneurysm as 2.0cm dilation (75<sup>th</sup> percentile); however our results suggest that a larger diameter such as 3.3cm (95<sup>th</sup> percentile) or accounting for symptoms related to dilation may be a more appropriate definition. These data will be used to inform a power calculation for future work.

### Phase III Trial for the Efficacy of VSL#3 in the treatment of IBS-Constipation and Slow Transit Constipation

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Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder, with no obvious structural or biochemical basis. The use of probiotics in IBS appears to be safe and beneficial. The aim of this study was to assess the efficacy of the probiotic VSL#3 in patients with IBS-Constipation (IBS-C) and slow transit constipation (STC).

This is a Phase III, open label, single-centre and single dose study. Patients aged between 18-60 years, with a diagnosis of IBS-C and STC were included. Patients received one sachet (4.4g) of open label VSL#3, twice a day, for 12 weeks. Patients completed a two-week stool diary recording bowel frequency and consistency, The Patient Assessment of Constipation Symptoms Questionnaire (PAC-SYM) and IBS Symptom Severity Scale (IBS-SSS), at baseline and at 12 weeks.

In total, seventy-two patients were studied (34 STC, 38 IBS-C). The mean age was 29 (age range 18-63), 61 (85%) were female, with a mean duration of symptoms of 10.3 years. There was a significant increase in both patient groups, in terms of mean weekly bowel frequency ( $p < 0.00001$ ) and mean stool consistency ( $p < 0.01$ ). IBS-C demonstrated a reduction in the average number of days without abdominal pain ( $p < 0.0001$ ), which was not found in STC.

VSL#3 improved stool frequency in both STC and IBS-C patients; it also improved pain in IBS-C patients. These data form the basis for a power calculation for a formal randomised study of VSL in STC and IBS-C.

### Insulin-like growth factors with cognition and dementia risk: the Caerphilly Prospective Study

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**Background:** The increasing incidence of cognitive impairment and dementia in an aging population poses a significant burden on healthcare and economic resources. Consequently, identifying modifiable physiological factors which may influence the onset of cognitive decline are becoming increasingly important. Previous studies have suggested an association between levels of insulin-like growth factors and cognitive function. We hypothesised that low IGF-I, IGF-II and IGF molar ratio would be associated with cognitive decline and risk of dementia.

**Methods:** We examined prospective associations between IGF-I, IGF-II and IGFBP-3 and cognitive function in the Caerphilly Prospective Study (CaPS) (n = 745 men) from samples obtained around 1986, with assessment in around 2003 for clinical diagnosis of cognitive impairment but no dementia (CIND) or dementia.

**Results:** IGF-II was associated with a reduced odds ratio for CIND (0.76, 95% CI 0.60, 0.96) which hardly altered after further adjustment for confounders. A one standard deviation increase in IGFBP-3 amongst participants without dementia or CIND was associated with greater decline in cognition (p=0.002) equivalent to 2.4 years difference in age. All the associations between IGF-I and our outcomes were consistent with chance.

**Conclusion:** We found that both IGF-II and IGFBP-3 may have a role in influencing both normal age-related cognitive decline as well as clinical pathology associated with CIND, but we failed to replicate previous associations with IGF-I. Assuming these findings are replicated, they may provide new insights into potential biological mechanisms that underlie age-related cognitive changes as well as pathophysiological pathways leading to dementia.

### Does undergraduate suture training make the cut? A national student survey

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**Background:** Suturing is a practical skill expected to be attained by all medical students on graduation, according to the General Medical Council's (GMC) Tomorrow's Doctors (2009).

There are no GMC recommendations for the minimal amount of undergraduate suture training or level of competence.

This study examines the state of undergraduate suture training by surveying a sample of medical students across the UK.

**Methods:** We produced an online survey, which was sent to five medical schools for distribution via secretarial bulletins after completion of undergraduate suture training.

This survey included questions relating to career intention, hours of curricular suture training, hours of additional paid training, confidence in performing various suture techniques and knowledge of their indications. We also asked about proficiency in injecting local anaesthetic and overall opinion of medical school suture training adequacy.

#### Results

In total, we received 332 responses from five medical schools after their scheduled curricular suture training.

283 (85.2%) reported completion of curricular suture training.

299 (90.1%) reported that they felt they did not have adequate suture training in medical school.

86 (25.9%) had paid for additional suture training.

**Conclusions:** Our study suggested that this area requires attention by the medical schools and clarification by the GMC. We recommend more opportunities for students to develop suture skills and specific recommendations for expected competency by the GMC.

**CD163 Scavenging of Extracellular Haemoglobin post Subarachnoid Haemorrhage**

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Subsequent to subarachnoid haemorrhage (SAH), extracellular haemoglobin is a fundamental constituent in the pathogenesis of delayed cerebral ischemia. This is the consequence of cerebral vasospasm. Systemically haemoglobin is metabolized by the CD163-haptoglobin scavenging system. This is the first study to investigate the scavenging system in human brains post SAH. Post-mortem brains of those that died after SAH (n=6) and those that died with no neurological pathology (n=5) were immunohistochemically stained against: CD163 (perivascular macrophage), CD68 (microglial lysozyme), ADAM 17 (CD163 inhibitor) and hypoxia inducible factors. Perls' staining was performed to assess the presence of haemoglobin. Anatomical division of the tissue into regions with and without blood provided internal controls. The meninges and grey matter underwent separate quantitative analysis using Image J. The CD163 system was significantly down-regulated in the meninges of the SAH cases in presence of blood (P=0.028). CD68 revealed a trend towards an increase in the meninges of the SAH cases with blood. Perls' staining demonstrated a trend for increased Hb scavenging in regions with blood although insignificant (P=0.169). ADAM 17 was found in both cases and controls, no difference was observed between levels in the meninges (p=0.908) or grey matter (P=0.911). Increased CD163 endocytosis was clearly demonstrated, although on its own it is insufficient. A therapeutic intervention is required to amplify this response. Future work should explore activity of other scavenging systems including CD91 to determine if there is any compensatory increase to remove haemoglobin

**Is disease progression related to CAG repeat length in Huntington's disease?**

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**Background:** Huntington's disease (HD) is classed as a trinucleotide repeat expansion disorder of the CAG codon. Previous research has found a link between CAG repeat length and the age of disease onset. However; the link between CAG length and the rate of disease progression is less clear. Functional assessment and independence scores have been found to be accurate markers of disease progression.

**Method:** Data was obtained from two sources. The preliminary method obtained relevant UHDRS scores, age of onset and CAG repeat length through patient notes. No ethical approval was required for this data mining. The second source of data was provided by the European HD Network with ethical approval. This contained the relevant information which had been previously extracted from 1,835 patients from 17 different countries.

**Results:** 86 patients matched the inclusion criteria in the data obtained from patient notes, 1,598 were included from the EHDN database. Analysis of the two datasets found that CAG length accounted for between 63% to 66% of variation in the age of onset. An analysis of the relationship between CAG length and disease progression was carried out whilst correcting for the effect of disease duration. In the patient note data, no correlation was found. An analysis of the EHDN data showed a highly significant (p<0.001) but weak negative correlation (-0.113).

**Discussion:** CAG repeat length is a strong indicator of age of onset and graphical representations of the findings may be used as a tool for estimating age of onset. This may be of benefit to some patients. The findings also show that there are other factors which affect age of onset. Further research is needed to investigate the effect of other genetic factors besides CAG repeat length.

### The role of the Eps8 binding partners Sos1 and Abi1 in Pancreatic Cancer

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Pancreatic cancer (PC) is characterised by marked local invasion, which requires actin cytoskeletal remodelling. EGF receptor pathway substrate 8 (Eps8) is an actin-binding protein with multiple binding partners including Sos1, Abi1, and certain  $\beta$  integrin subunits.  $\alpha\beta6$  integrin is overexpressed in approximately 70% of PC and enhances invasion. This study examines the role of Sos1 and Abi1 in  $\alpha\beta6$ -dependent PC invasion.

We used immunohistochemistry to examine expression of Eps8, Sos1 and Abi1 in normal pancreas and PC *in vivo*. A retrospective patient database was generated of those treated surgically for PC (2000-2008) and used to identify 39 short ( $\leq 2$  years) and 20 long ( $\geq 4$  years) survivors. Resection tissue was then stained for Eps8/Sos1/Abi1/ $\alpha\beta6$ . We identified three PC cell lines that showed  $\alpha\beta6$ -dependent motility *in vitro*, and performed Transwell® assays to study the functional roles of Sos1 and Abi1.

Eps8, Sos1 and Abi1 were upregulated in PC compared with normal tissue. Expression of these proteins in long and short survivors is currently being examined. Eps8, Sos1, Abi1 and  $\alpha\beta6$  expression was confirmed in all three PC cell lines tested. Knockdown of Eps8, Sos1 or Abi1 significantly suppressed  $\alpha\beta6$ -dependent migration and invasion.

Eps8, Sos1 and Abi1 are upregulated in PC and appear to be critical to  $\alpha\beta6$ -dependent PC motility. Interestingly, Sos1 expression was previously shown to fall in response to gemcitabine, the current gold standard chemotherapeutic agent for the treatment of PC. Sos1 therefore requires further investigation as a potential molecular target in the treatment of PC.

### Endovascular Repair of Ruptured Abdominal Aortic Aneurysms: A Real World View

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**Background:** The mortality rate following a ruptured abdominal aortic aneurysm (AAA) can be as high as 88%. Surgical repair is the only option. Endovascular Repair (EVAR) is considered to be superior compared to Open Repair (OR) for elective cases however its benefits in ruptured AAAs require further evidence. This study therefore aims to compare the two procedures and furthermore aims to investigate the effects of risk factors as outcome predictors post repair.

**Methods:** A retrospective study of a partially prospective database was carried out at Queen's Medical Centre. Patients who underwent either EVAR or OR for a ruptured AAA between the years of 2001 and 2010 were selected using an inclusion-exclusion criteria. The primary outcome of mortality (30 day and overall mortality) was investigated for EVAR and OR and the risk factors.

**Results:** 265 patients constituted the sample of this study (EVAR=113, OR=152). The 30 day ( $p=0.053$ ) mortality rate was 38.9% for EVAR and 40.8% for OR. Increasing age displayed a general increase in 30 day mortality for both EVAR ( $p=0.042$ ) and OR ( $p=0.043$ ). Presence of lung disease increased the risk of 30 day mortality by nearly 3 times ( $p=0.003$ ) and smoking history ( $p=0.01$ ) increased the risk of overall mortality.

**Conclusion:** EVAR did not show an advantage over OR and the 30 day mortality was comparable in both groups. Some risk factors as potential outcome predictors were identified, which may allow the surgical team to recognise high risk individuals and deal with them appropriately to reduce the risk of mortality.



**Upregulation of NF- $\kappa$ B by short cyld protects mice against *Listeria monocytogenes* infection via pro-inflammatory cytokines**

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The NF- $\kappa$ B pathway plays an essential role in the immune system by modulating the production of pro-inflammatory and anti-inflammatory mediators, so called cytokines. With our experiments we aimed to find out why an upregulation of the NF- $\kappa$ B pathway in innate immune cells leads to protection of mice against *Listeria monocytogenes* infection.

For our experiments we used knockout mice with an upregulation of NF- $\kappa$ B in dendritic cells, which are cells of the innate immune system. The enhanced activation is mediated by short cyld, a naturally occurring splice variant of the tumor suppressor gene cyld. Following *Listeria* infection we compared these mice to their wildtype littermates with regard to survival and bacterial loads in their spleens. In flow cytometry experiments we analysed cytokine production by dendritic cells and other leucocyte subsets. We verified the protective function of specific pro-inflammatory cytokines against *Listeria* infection by performing in vivo depletion experiments.

After infection knockout mice had prolonged survival rates as well as lower bacterial numbers in their spleens. Flow cytometry experiments revealed a higher production of the pro-inflammatory cytokines IL-12 by dendritic cells and IFN- $\gamma$  in T-cells of knockout mice.

Our research shows that enhanced activation of the NF- $\kappa$ B pathway in dendritic cells leads to protection against *Listeria* infection via elevated levels of IL-12, which in turn lead to higher production of IFN- $\gamma$  by T-cells. After depletion of IL-12 knockout mice lose their IL-12 and IFN- $\gamma$  mediated protection and become just as susceptible to *Listeria* infection as their wildtype littermates.

**Optimisation of PCR Primers for Semi-Quantitative PCR looking for Effects of Fatty Acids and Endocannabinoids on Redox Gene Expression**

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Omega-3 fatty acids and their endocannabinoid derivatives have been shown to have anti-cancer effects in breast and prostate cancer cells. It is also known that alteration of the expression of redox enzymes plays a role in formation of these cancers, and we aimed to determine whether redox enzyme gene expressions are affected by treatment with omega-3 fatty acids and their derivatives. The specific aim of this project was to optimize conditions for semi-quantitative RT-PCR to identify the effects on the expression of redox gene expression when treating cancer cells with omega-3 fatty acids and their endocannabinoid derivatives.

PCR primers for Thiredoxin Receptor (TRXR), Catalase 1 (CAT) and Glutathione Peroxidase 1 (GPX1) were optimized for semi-quantitative RT-PCR. This involved optimising the PCR conditions including temperature, Magnesium concentration and correct cycle numbers to detect differences in gene expression, using 18S internal control genes for standardization. Prostate cancer cell lines (PC3) were treated with omega-3 fatty acids and their endocannabinoid derivatives, and then RNA was extracted using Trizol. RNA was then converted to cDNA using Superscript II reverse transcriptase prior to being amplified by PCR. Densitometry was used to determine differences in gene expression.

Results have shown that TRXR1 and CAT, in particular are significantly reduced after treatment, more so, with the endocannabinoid derivatives.

In conclusion, treating the cancer cells with fatty acids and endocannabinoids reduces the expression of key redox genes, which may be a result of allowing oxidative damage to build up in the cancer cells and causing them to undergo apoptosis.

**Nutrient sensing in the human gut: Investigation of the co-localization rate between CaSR, T1R1 and GPR43 receptors with satiety peptides in the human antrum, terminal ileum and ascending colon**

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**Background:** Increasing evidence from animal studies show that apical nutrient sensing receptors, expressed in gut enteroendocrine cells, play a key role in the release of satiety peptides. Early human studies indicate a similar expression pattern of these receptors and role in peptide release. In this study the anatomical relationship between amino acid sensing (CaSR), carbohydrate sensing (T1R1), and short chain fatty acid sensing (GPR43) receptors and appetite regulating peptides GLP-1, PYY, 5-HT was investigated in the human gut.

**Methods:** Healthy full thickness human gut sections were incubated with primary and fluorescent secondary antibodies and they were viewed under the fluoroscopic microscope to investigate co-localization of the CaSR, T1R1 and GPR43 with the GLP1, PYY and 5HT.

**Results:** The co-localization rate between CaSR and PYY, GLP1 and 5HT was 0%, <1% and 43% in the antrum, 20%, 12% and 82% in the ileum and 26%, 14% and 91% in the colon, respectively. Co-localization of T1R1 and GLP1 was observed only in the antrum and the colon. GPR43 was not expressed.

**Conclusion:** The results suggest a CaSR mediated PYY, GLP1 and 5HT release in the human gut, which could be further expanded to the development of new anti-obesity strategies

**Cardiovascular, Renal and Metabolic Outcomes of Obese Living Kidney Donors**

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Increased demand for renal transplant has led to acceptance of marginal donors, such as individuals with obesity. Long-term safety of renal donation in this group has not been established. This study assessed renal, metabolic and cardiovascular outcomes following nephrectomy in obese living kidney donors.

A retrospective cohort study of living kidney donors undergoing nephrectomy at the UHW from 18<sup>th</sup> October 2004 and 18<sup>th</sup> October 2010. Donors were grouped according to BMI (at time of donation) as normal weight (NWD), overweight (OWD) or obese (OD), according to WHO categories. Outcomes were determined upto 2 years post donation. Donors who were followed up at other centres were excluded.

183 (n=121) donor nephrectomies were performed. The estimated glomerular filtration rate (eGFR) showed significant reduction from baseline at 2 years in all three BMI groups (NWD = -27.0%, OWD = -27.9%, OD = -31.7%) but no significant differences between groups. Systolic blood pressure and diastolic blood pressure were significantly higher at baseline ( $p = 0.015$ ,  $p = 0.01$ ) and at 1 year among OD than NWD ( $p = 0.047$ ,  $p = 0.006$ ), independent of confounders. There was no difference in blood glucose between all groups at baseline ( $p = 0.134$ ) or at 2 years ( $p = 0.432$ ).

Obesity is not associated with worse renal function in the medium term. Questions remain over the cardiovascular risk profile of obese donors, and whether or not donation increases this risk independently of the effects of obesity. Caution is still required when accepting obese individuals for donation.

**Using a microfluidic device to investigate the role of the furry gene in *Dictyostelium discoideum***

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**Background:** The Furry (FRY) gene is an evolutionary conserved gene that is present in yeast, *Drosophila*, amoeba and humans. In *Drosophila* the FRY gene has shown to have a role in maintaining polarized cell extensions and in the development of sensory neurons. Although the function of FRY in amoeba and humans still remains unknown, it is possible that it may have a similar role in amoeba as it does in *Drosophila*. The aim of this study was the investigation of *Dictyostelium discoideum*, and to find the potential role of the FRY gene in cell migration.

**Experimental design:** FRY was knocked out of wild type cells and rescued by reintroducing the FRY gene into the knockout strain. These strains were examined and compared against a wild type cell. A microfluidic device was used to provide a controlled environment for rapid single cell analysis of a cell migrating using a confocal microscope. The images retrieved specified the phenotype of the cell and were used to calculate cell velocity.

**Results:** FRY was not shown to affect the average cell velocity but a tail like phenotype extending from the back of the cell was produced in the FRY knockout strain.

**Conclusion:** These findings could localize the FRY gene at the back of the cell and suggest that FRY is involved in regulating the integrity of the rear cytoskeleton. The cell migration mechanics of amoeba are similar to human neutrophils and further research could elicit the role of FRY in human cells.

**A case-series evaluating the risk of distal DVTs: should we treat?**

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Deep vein thrombosis (DVT) most commonly occurs in the lower limb, and can lead to pulmonary embolism (PE). New NICE guidance recommends that all patients with high probability of DVT have proximal leg compression ultrasonography and D-dimer assay with repeat scan 1 week later in patients with negative scan but positive D-dimer. The Royal Cornwall Hospital (RCH) currently does full-leg scans and treats distal DVTs with 6 weeks warfarin.

This is a retrospective case-series of 348 patients diagnosed with DVTs via the RCH DVT-clinic during a 12-month period (up to 30 September 2012). Information was collected about patients re-presenting within 3 months of initial diagnosis to evaluate PE event-rate among these. Fisher exact test was used to analyse clinical significance of difference in PE rates between patients with proximal and distal DVTs. Statistical significance:  $p < 0.05$ .

In RCH, 36.8% of patients presenting to the DVT-clinic have distal DVTs. 0.9% of all patients in this study developed a PE within 3 months of initial presentation. While a higher proportion of patients with distal DVTs (2.3%) than proximal DVTs (0.5%) developed PEs this difference was not statistically significant ( $p = 0.14$ ).

If the new NICE guidelines are followed DVTs would be missed in a considerable portion of patients. This study found no significant difference in PE event-rates between patients with proximal and distal DVTs. However, since all patients were treated no conclusions can be drawn on this and further research is necessary to assess the true extension and PE-rate of distal DVTs in untreated patients.

### An audit of the NHS Lothian Early Rheumatoid Arthritis (ERA) Clinic: from a real life perspective

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<sup>1</sup>University of Edinburgh, Edinburgh, Scotland; <sup>2</sup>Western General Hospital, Edinburgh, Scotland

**Background:** It is clear from a number of studies that early and aggressive treatment of rheumatoid arthritis leads to sustained clinical benefit [1,2,3,4]. However, this data has been acquired in the setting of clinical studies allowing intensive review of patients. In our ERA clinic, we introduced a new treatment protocol that included a 12-week course of high dose tapering prednisolone therapy. Patients were also commenced on methotrexate and a step up combination therapy over the subsequent 12 months according to any disease activity. They were reviewed every 2 months until discharged. We aimed to audit the clinical outcome of patients diagnosed with rheumatoid arthritis for <2 years referred to the ERA clinic in Lothian.

**Methods:** A retrospective audit of medical records was conducted on 130 patients, of which 30 were not suitable for inclusion. Primary outcome measures were mean fall in disease activity score, proportion of patients with a good response (following EULAR response criteria) and working status at 1 year after treatment.

**Results:** We noted a highly significant drop ( $p < 0.0001$ ) in mean DAS28 score at first 3 months (5.4 to 3.9) with an on-going gradual reduction for the subsequent 9 months. Mean DAS28 score at 12 months was 2.6 with 92.9% patients achieving low disease activity. There were no reported serious adverse events. 6% of patients gave up working after 12 months of treatment.

**Conclusion:** An ERA protocol that includes a short tapering course of high dose prednisolone results in a rapid and sustained reduction of disease activity with no excess morbidity.

### Development of a protocol for maximising the field of view of ultra-wide-field images in premature infants with retinopathy of prematurity

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**Background:** Ultra-wide-field (UWF) imaging enables visualisation of the posterior pole as well as the peripheral retinal vasculature. Our purpose was to develop a protocol that would maximise the field of view of UWF images obtained in premature infants with ROP.

**Method:** A schematic premature model eye was constructed containing a grid with 10-degree inclinations in multiple meridians engraved on its posterior surface. UWF images of the grid were obtained with the model eye held at a variable number of distances away from the device. The horizontal field of view (HFOV) and vertical field of view (VFOV) of the images were analysed. A 4mm and 7mm pupil diameter were used for each imaging distance. All images were acquired using the Optos Panoramic 200MA device. A protocol based on optimal imaging distance and necessity of pupil dilatation was then developed. The protocol was applied to a group of 30 premature infants with ROP.

**Results:** The maximal HFOV and VFOV of images were acquired at a distance of 2.5cm in front of the imaging device. The HFOV and VFOV were shown to be statistically higher when images were acquired through a 7mm pupil diameter in comparison to a 4mm pupil diameter ( $P$  value  $< 0.001$ ). A protocol of holding premature infants at 2.5cm in front of the imaging device with pupil dilatation was able to successfully acquire ultra-wide-field images with in 30 ROP infants.

**Conclusion:** A successful protocol was developed that enabled clinical application of ultra-wide-field imaging to premature infants with ROP.



**A study examining rates of medical staff recognition of pressure ulceration in hospital inpatients**

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*The Royal Bournemouth Hospital, Dorset, UK*

**Background:** The incidence of pressure ulceration among UK hospital inpatients has been estimated at 10.2–10.3%. These patients are at increased risk of developing osteomyelitis and subsequent sepsis. This study sought to test whether medical staff recognition rates of hospital inpatients with pressure ulceration were low and to consider underlying causes and potential solutions.

**Methods:** Interviews were conducted with nursing staff on multiple wards in July 2012 to obtain a definitive list of patients with pressure ulcers, with their corresponding location and grade. Junior members of medical teams with responsibility for the same group of patients were independently interviewed and asked to identify all patients who they knew to have pressure ulcers. The number correctly identified by the medical teams was compared with the total number of known pressure ulcers to produce a recognition rate. Patients with clinical evidence of sepsis were highlighted.

**Results:** Twenty-seven patients on five wards were identified by nursing staff as having pressure ulceration areas. Nine patients were stated to have multiple pressure ulceration areas, giving a total of 38 pressure ulcers. Medical teams correctly identified eight of 27 (29.6%) of these patients. The correct site and grade was identified in four of 38 (10.5%) and two of 38 (5.3%) cases, respectively. Of these patients 14/27 (51.8%) had evidence of infection. In this subgroup five of 14 (35.7%) were correctly identified as having pressure ulceration areas.

**Conclusions:** The lack of medical awareness could lead to delayed recognition of deep-seated infection or osteomyelitis. Reasons for this are likely to be multifactorial and require a combination of cultural change, improved education and improved information sharing.

**Are patients receiving neoadjuvant therapy for rectal cancer appropriately?**

Smith R  
*Newcastle University, Newcastle upon Tyne, UK*

**Background:** Preoperative chemo/radiotherapy has been a recent addition to the management of rectal cancer. The management decision in Northumbria Healthcare NHS Foundation Trust is made following a discussion at the MDT. With the introduction of specific guidelines by NICE in 2011 this has become an important area for a new audit to be undertaken.

**Aims:** To establish whether rectal cancer patients are receiving the correct preoperative treatment based on their MRI scans and elicit areas to improve care.

**Method:** Trust registration was obtained. Analyse MRI reports and neoadjuvant therapies of all 40 newly diagnosed rectal cancer patients in 2012 in the Northumbria Healthcare Trust. Correlate with the NICE guidance to establish compliance rate of management according to the notes.

**Results**

Outcome	Number	Compliance
Excluded from study	7	N/A
Missing MRI form	3	(9.1%)
Correctly Managed	22	66.7%
Incorrectly Managed	8	24.2%

**Conclusion:** Whilst the compliance rate was high, there were areas that can be improved.

1. MRI report forms should have NICE criteria laid out that have to be filled in.
2. When decisions about therapy contradict the guidelines, the reasoning has to be recorded in the notes.
3. Further education on guidelines and management in the trust.

Pooling data with the Low Rectal Cancer National Development Programme (LOREC), started in October 2012, will allow comparisons against the compliance rate of other centres outside Northumbria. It will be important to re-audit next year to establish the impact that this audit and LOREC have made.

**Permeability of poly (glycerol-adipate) nanoparticles across an in vitro model of the blood-brain barrier**

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**Introduction:** The blood-brain barrier (BBB) exhibits selective permeability to regulate influx of molecules into intracranial regions. Most drugs are incapable of crossing the BBB and are rendered clinically ineffective due to their inability to reach their target site of action. Poly (glycerol-adipate) (PGA) nanoparticles (NPs) are versatile carriers, which can incorporate drugs within their structure to enable transport across the BBB, offering a novel solution to the problem of effective drug delivery into the brain.

**Methods:** This study investigated the permeability of polysorbate 80 coated PGA NPs tagged with the fluorescent marker Rhodamine B Isothiocyanate across an *in vitro*, three-compartment immortalised human brain endothelial cell (hCMEC/D3) monolayer model of the BBB after 1, 2 and 4 hours.

To establish the selective permeability of the model, 4, 40 and 70 kDa Dextran was used.

**Results:** Relative to unseeded controls (no barrier), flow of Dextran between compartments was cumulatively reduced 57%, 56% and 32% (4, 40 and 70 kDa respectively) across time periods investigated, attesting the barrier's functional efficacy. No such difference in permeability was observed for PGA NPs, with a reduction of only 2%, 13% and 6% at 1, 2 and 4 hours respectively post administration.

**Discussion:** This pilot study demonstrated the ability of PGA NPs to cross the BBB *in vitro* and advances the possibility of their future clinical use in treating neurological disorders. Further experiments are warranted to extend this study.

'I would like to acknowledge and thank Dr Terry Parker, my supervisor, for his support & assistance & Delyan Ivanov for the provision of nanoparticles'

**Maternal high fat diet during pregnancy and lactation alters mitochondrial electron transport chain activity and gene expression in adult mouse offspring heart**

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Obesogenic diets during pregnancy increase cardiovascular disease susceptibility in the offspring later in life. The mitochondria are involved in the pathogenesis and development of various types of heart disease. We examined mitochondrial electron transport chain activity and expression of genes with key roles in mitochondrial metabolism in heart tissues of offspring from obese mothers fed a high fat (HF) diet. Female mice were fed either a HF diet or standard chow diet 4-6 weeks prior to and during gestation and lactation. Weaned offspring were fed the HF or C diet, generating the dam-offspring groups: C/C, C/HF, HF/C, HF/HF. The left ventricle of offspring was processed for mitochondrial Complex I and II enzyme activity and for qPCR of the mitochondrial *Sirt3*, *UCP2*, *UCP3*, *ANT1*, *ANT2*, *PGC1 $\alpha$*  and *NRF1*. Complex I and II activity was reduced by 1.5 fold ( $p < 0.001$ ) in the HF/HF. *Sirt3* mRNA level was 2.6-fold lower ( $p < 0.01$ ) in offspring hearts from HF-fed dams (HF/C and HF/HF groups). *UCP2* and *UCP3* mRNA levels were 2.3 and 4-fold higher (both at  $p < 0.0001$ ), in HF/HF. *ANT1* and *ANT2* transcript levels were reduced by more than 1.3-fold ( $p < 0.01$ ) in HF/HF. *PGC1 $\alpha$*  mRNA levels were 1.4-fold lower ( $p < 0.01$ ) while *NRF1* mRNA levels were 3-fold higher ( $p < 0.0001$ ) in HF/HF. The results suggest maternal high fat diet during pregnancy and lactation alters mitochondrial ETC activities and expression of genes involved in mitochondrial function and biogenesis. This priming effect in early life increases offspring risk to cardiac pathologies in later life.

**Maternal Vitamin D Deficiency in Tower Hamlets PCT**

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**Background:** A wealth of data highlights the high prevalence of vitamin D deficiency in the UK, and association with adverse health outcomes. National guidance supports vitamin D supplementation during pregnancy. Our locally deprived and ethnically-diverse population has a high burden of adverse pregnancy outcomes. We sought to identify prevalence of vitamin D deficiency, with which to develop an evidence base to guide effective local policy and reduce adverse pregnancy outcomes.

**Method:** We performed vitamin D (25(OH) D) screening in an unbiased group of 500 women prior to the availability of supplements at their antenatal booking.

**Results:** Of 500 women screened (means: age 26, BMI 29; 60.34% Asian/Asian-British). Serum 25 (OH) D data was positively skewed with significant variation in concentrations between October and January. 85.72% of the whole sample were vitamin D insufficient (<75 nmol/L) and 74.45% deficient (<50nmol/L), the ethnic group most affected were the Asian/Asian-British (median serum 25 (OH) D 28.00 nmol/L (IQR: 14-40.75), 81.45% had severe deficiency). Significant variation was found between ethnic group serum 25(OH)D concentrations. 16 week GTT showed a significant inverse relationship between log 25 (OH) D and fasting blood glucose levels ( $P<0.001$ ,  $r^2=0.26$ , slope=  $-2.097 \pm 0.469$ , 95% CI: 1.156- 3.038). No significant difference was found in 25 (OH)D between GDM and no GDM groups.

**Conclusion:** We have identified prevalent vitamin D deficiency in all ethnicities in our local pregnant population, which has warranted the introduction of guidelines and supplementation at a population level rather than at a risk group level.

**Effect of Maternal Protein Diet On Neural Stem Cells In The E14.5 Mouse Embryo**

Smith P\*; Fleming T; Willaime-Morawek S

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A maternal low protein diet (LPD) has shown to have negative effects on the development of the fetal brain leading to structural and behavioural abnormalities. We aimed to investigate the mechanisms behind this and hypothesised that a maternal LPD would have a negative effect on neurogenesis in the fetal brain.

We took the brains of E14.5 mouse embryos from mothers fed different diets during gestation, and isolated the fetal neural stem cells (NSC). We looked at three different diets; a low protein diet, a low protein switch diet (LPSD; LPD until 3.5 days of gestation, control diet after) and a control diet. We implemented neurosphere culture and immunocytochemistry techniques to compare the effect of diet on the properties of the NSCs.

Our data indicates a significant decrease in primary neurosphere formation with the LPD compared to the control and LPSD and this is maintained into the second generation with the smaller but not the larger sized primary neurospheres. Immunocytochemistry showed an increase in the number of NSCs present and no change in the amount of proliferation and differentiation in the LPD group compared to the control. Interestingly in the LPSD group we found an increase in differentiation and a decrease in proliferation and NSC number suggesting an inability to compensate and maintain normal development.

Overall our work is beginning to reveal a profound effect of the maternal protein diet on neurogenesis in the fetus and is also indicating the importance of the timing and duration of the restriction.

### *Clinical Audit and Service Evaluation Category*

#### **Daycase TURP: An Initial Experience**

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**Introduction:** Transurethral resection of the prostate (TURP) is an inpatient procedure in the UK. There are several countries where it has been routinely performed as a daycase procedure. Furthermore, it is included in the NHS best practice tariffs, and has now been introduced on appropriate patients in our department.

**Methods:** Patients included had prostates 60g or less, no social issues, and the ability to look after a catheter. Patients were placed on finasteride, tranexamic acid used intraoperatively for larger resections, and short acting prilocaine spinal anaesthesia used.

Prospective data on the first 20 patients was collected. Information on demographics, indication for surgery, preoperative IPSS, inpatient stay, pathology and functional outcomes were obtained.

**Results:** The mean age was 67 years. 18 patients went home on the same day, 2 admitted overnight; one for anaesthetic reason, one for social reasons. Mean size of resection was 16.3g. There were no complications and no re-admissions. The mean improvement in IPSS score and bother score were 19 and 4 respectively.

**Conclusion:** Daycase TURP is a safe and effective procedure associated with a low complication rate and low re-admission rate. It should be considered in all patients undergoing TURP and extended to other appropriate endoscopic procedures

#### **Traditional versus modern wound dressings in the care of lower limb arthroplasty patients – do they make a difference?**

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**Background:** Wound care is an important part of lower limb arthroplasty. Blistering can lead to infection, increased postoperative pain, poor mobilisation and subsequently delayed discharge.

We audited current wound care following lower limb arthroplasty, introduced modern dressings, and re-evaluated using a prospective, comparative audit.

**Methods:** Two prospective audits were performed over a 6-month period. The initial audit included the traditional wound dressings of Opsite (Smith & Nephew Ltd.) and Mepore (Mölnycke Ltd.) Re-audit involved implementation of the modern dressing Aquacel (Convatec Ltd.).

Clinical success was determined by the wear time, number of in-patient dressing changes and blister rates. Statistical analysis using analysis of variances (ANOVA) with post hoc tests and two-tailed unpaired t-tests were performed when appropriate.

**Summary of results:** Seventy patients underwent lower limb arthroplasty with either total hip (n=41) or total knee (n=29) replacement. The initial audit included forty patients with traditional dressings (Mepore n=18, Opsite, n=22). Implementation of the modern dressing (Aquacel) included thirty patients. The modern dressing required fewer dressing changes during the in-patient stay (1.3) compared with the traditional dressings (2.3)  $p < 0.001$ . The mean wear time was significantly greater with the modern dressing (4.2 days), versus traditional dressings (2.3 days)  $p < 0.001$ . Blister rates were non-existent with the modern dressing and fifteen percent (n=6) with the traditional dressings.

**Conclusion:** Traditional wound dressings are associated with earlier, more frequent dressing changes in the post-operative period and blister formation.

Modern dressings (Aquacel) significantly enhance the care of lower limb arthroplasty patients



**Gynaecological history (GH) and  $\beta$ -hCG: Do surgeons accurately and routinely document this information?**

Powell-Bowns M\*; Allison J; Wilson M; Muthukumarasamy G; Khalil A; Boyd A  
*Perth Royal Infirmary, NHS Tayside, UK*

**Background:** Any female patient of reproductive age (FPORA) admitted to an acute surgical receiving unit (ASRU) must be fully assessed and surgical emergencies excluded. It was felt that the ASRU at Perth Royal Infirmary (PRI) failed to accurately document a complete GH and results of  $\beta$ -hCG for some FPORA. This project aimed to quantify this observation and propose changes in practice if required.

**Method:** A proforma was designed to collect a range of patient information specific to FPORA. Data was collected retrospectively from 80 FPORA who presented to ASRU at PRI. The results were presented at a surgical departmental meeting. Aims to improve documentation of GH and  $\beta$ -hCG were proposed using a prompt in the clerk-in. Second cycle of audit was carried out: final changes to practice are awaited.

**Results:** First audit: 50 FPORA medical records were evaluated. The initial assessment showed: 30% had GH and 26% had  $\beta$ -hCG test results documented. A prompt was added to the clerk-in document, then a second audit of 30 FPORA medical records were evaluated. Assessment of the clerk-in documents showed: 86% had GH and 72%  $\beta$ -hCG results documented.

**Conclusion:** Our initial audit demonstrates that documentation of GH and  $\beta$ -hCG results in FPORA at ASRU in PRI is often incomplete. Through amending the admission clerk-in document we have achieved a significant improvement in the accurate documentation of this information. We propose to implement a permanent amendment to the clerk-in document in order to facilitate the management of our FPORA.

**Are junior doctors best prepared to prescribe insulin?**

Sukcharoen K\*; Everson M; Smith C  
*Great Western Hospital, Swindon, UK*

**Background:** Maladministration of insulin has been identified as a never-event by the Department of Health. A recent National Diabetes Inpatient audit has identified significant errors resulting from insulin prescribing. Drug charts are usually started by junior doctors when patients are first admitted into hospital. A recent Foundation Year 1 (F1) induction survey showed that after induction week, F1s still did not feel confident in prescribing insulin.

**Aims and Objectives:** Errors in insulin prescribing have resulted in harm to patients at Great Western Hospital. Last quarter, four reported cases of prescribing error, one of which caused harm to a patient. The aim of this audit is to identify common errors in prescribing, using standards set by the National Patient Safety Agency and Department of Health.

**Methods:** The audit examined the prescription charts of 40 insulin-dependant diabetic patients who were admitted between July and November 2011.

**Results:** As maladministration of insulin is a never-event. The standards set in this audit is 100%. This audit identified comparatively more insulin prescribing errors at GWH compared to another trust, in which the same audit was performed, which has an insulin prescribing section in its drug charts.

Most notable difference is the 'units written in full' where GWH achieved 75% compared to 92% in a trust where 'units' has already been provided. Not writing 'units' in full poses a risk of the prescription being misread and many trusts have reported patients receiving the wrong dose of insulin.

**Key Findings:** The audit suggests that lack of knowledge and understanding of the importance of insulin prescribing amongst junior doctors may be one of the contributing factors for error. After presenting findings to the pharmacy and medical grand round, recommendations for change include:

- Adding an insulin prescribing section into the drug chart.
- Emphasis on junior doctor education by bringing forward the F1 insulin prescribing teaching into F1 induction week.
- Improve junior doctors knowledge by making e-learning module on diabetes compulsory

Produce a credit card sized information card on different types of insulin and how they work for easy access extra information

### A Multi-Department Audit Evaluating Dose Adjustment in Renal Impairment for Patients at the Extremes of Age

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**Background:** The British National Formulary (BNF) recommends dose adjustment in renal impairment (GFR[MDRD]<60 ml/min/1.73m<sup>2</sup>) to prevent toxicity, reduced drug efficacy and other adverse events<sup>1,2,3</sup>. A 2010 geriatrics audit found an 87.6% compliance rate. Its adjoining survey highlighted poor confidence in foundation doctors in identifying the necessary drugs<sup>4</sup>. A re-audit was undertaken and compared with paediatrics (where compliance was unknown).

#### Objectives

- a) To assess prescribing compliance with the commonest-used resource
- b) To explore the potential for an educational/ reference tool to improve prescribing accuracy

**Methods:** Part I - Data for 20 geriatric inpatients (Ward 15) and 20 renal paediatric outpatients (GNCH) were collected using online and paper records. Active prescriptions were compared with the respective BNFs and pre-admission prescriptions. Part II - a multiple-choice questionnaire was issued to doctors prescribing on Ward 15 and for paediatric renal patients.

**Results:** Of the total 343 prescriptions, 331 (96.5%) complied: 226/234 (96.6%) in geriatrics and 105/109 (96.3%) in paediatrics. 10 (83.3%) non-compliant prescriptions were present pre-admission. 6 (35.3%) of 17 non-compliant pre-admission prescriptions were suspended. The survey (n=15) found again poor confidence in newly-qualified doctors. Regarding the most useful suggestion for improvement, 40% selected more training, 40% access to renal-specific guidelines and 20% prescribing reminders.

**Conclusion:** Both departments had non-compliant prescriptions at harmful doses. However, the improvement in compliance and non-recurring pattern of non-compliant drugs makes systematic error unlikely. Foundation doctors remain poorly confident for which improved training before qualification is recommended plus ward-access to The-Renal-Drug-Handbook. A re-audit including clinical reasons for non-compliance would address limitations

### A Quality and Safety Improvement with Lasting Benefits

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The timely completion of discharge summaries (DSs) provides essential information to facilitate patients' effective and safe transition from secondary to primary care [GMC, 2009].

We conducted a standards-based audit of the completion of DSs for the general surgery department at Tameside General Hospital. Areas identified as needing improvement included; the management and tracking of case notes, the availability of adequate computers facilities, the understanding about the responsibility and acceptable time-frame for completing DSs and the handover of those responsibilities at the start of each FY1/FY2 rotation. After making these changes, a re-audit showed significant improvements and identified further action points that have since been implemented and will be assessed in the next audit cycle.

Our initial audit showed that only 34% of DSs were completed within 7 days, and 38% of discharged patients had no DS. Following the system changes this improved to 69% and 19% respectively. The improvement in the 24 hour target from 23% to 27% was modest in comparison.

The system changes improved the timely completion of DSs but more work is needed to meet the CQUIN target of 95% of DSs within 24 hours. A major challenge of this project was how to continue improving the system through repeated audit cycles after the FY1 audit-lead had left the department. This was achieved by creating a new surgical FY1 role to complete one audit cycle during each 4 month rotation. We encourage other doctors to use a similar approach in order to maintain their quality improvements.

**Use of TASC II Classification to Assess Accuracy of Lower Limb Duplex Ultrasonography**

Chan LCA\*; Sibanda A; Lee-Cheong L

*The Pennine Acute Hospital NHS Trust, Greater Manchester, UK*

**Background:** Discrepancy of lower limbs angiographic findings with pre-operative duplex ultrasonography results is not uncommonly seen. This study evaluated the validity rates of lower limbs duplex ultrasonography in patients with peripheral vascular disease.

**Method:** This is a retrospective and consecutive study over a three-month period (Oct 2012 – Dec 2012) in the radiology department in a general district hospital. We audited 82 patients who attended for angioplasty within the study period. We compared both pre-operative duplex reports and angiographic images by using the Trans Atlantic Inter-Society Consensus (TASC II) classification. The time intervals between the examinations were noted. The result of the lower limb duplex ultrasonography was considered accurate if the lesion's TASC II classification grade was consistent with the angiogram findings.

**Results:** Overall, 89% of our lower limbs duplex ultrasonography reports matched with the angiographic findings. However, duplex exam performed within 3 months of the angiogram had an accuracy rate of 93%, compared to 81% with those performed more than 3 months prior to the angiogram.

**Conclusion:** Lower limb duplex ultrasonography provided accurate information for radiologists to plan for angioplasty. However, we recommended that the needs of angioplasty should be assessed, and procedure performed within 3 months of their lower limb duplex examinations.

**Chest X-Ray Review and Documentation – A Re-Audit**

Khan SH\*; Joy D

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**Background:** It is a clinical governance issue that doctors should chase the results of investigations they arrange, and act upon them, if needed.

Mostly, junior doctors admit patients on acute medical wards and A&E. It is vital for patient safety, good clinical care, and medico-legal reasons that results of investigations are documented in medical notes and important findings are not missed.

Initially, an audit of 'Documentation of Chest X-ray reviews' was conducted in 2010. It showed 66% of Chest X-ray results were documented by doctors. Subsequently, standardized clerk-in and ward round sheets with a pre-printed section for radiology results' documentation were introduced.

This re-audit assessed the effectiveness of actions implemented after the first audit, hence closing the loop.

**Method:** Retrospective review of case notes of 50 in-patients' on Gastroenterology ward, over a period of 8 weeks in 2012. We used PACS to look up radiology images and reports. A data collection proforma was used, followed by input into MS Excel for analysis.

**Results:** Improved compliance with standards was seen, 78% of Chest X-ray reviews were documented, mostly within 24 hours of the test. A decrease in formal reporting of images noted.

**Conclusions:** Junior doctors should be encouraged to chase results and handover pending investigations. Difficult images should be discussed with radiology. More departments to use standardized ward round and hand over sheets. To introduce the 'File' option on radiology software in our trust- a time saver during busy on-calls and proof that results have been noted.

### Quality improvement in medical notes

Brown B\*; Brown P

*Leeds Teaching Hospitals Trust- LGL, West Yorkshire, UK*

Medical records form an important backbone of continuation of patient care across health services and over time. The importance of accurate and legible documentation is of ever growing importance with increased litigation and staff rotation.

We assessed 30 sets of notes within the Leeds General Infirmary to quantify existing practice. This allowed us to establish areas for improvement before making an intervention and reassessing.

Using trust approved guidelines for medical records we found that entries were consistently illegible (66%), only 30% had an identifiable author with fewer having their contact details and only 10% with a date and time. In order to address the broad range of issues we developed bookmarks that highlighted areas needing improvement and were attached in medical notes at the current admission.

Reassessing the medical records after an interval of four weeks showed a dramatic improvement in the quality of record keeping. The number of illegible notes decreased by 24% and over 95% of entries were signed, with 45% having an identifiable author and contact details. Additionally feedback from team members was incredibly positive with many saying they felt an improvement in accessibility of the records due to increased ease of finding relevant sections in medical notes.

In conclusion implementation of the bookmark is a popular way to drastically improve the quality of note taking. With more time and a larger study a more significant impact may be seen warranting implementation of the bookmark in common practice.

### Emergency Management of Pelvic Fractures: An audit of practice before and after MTC status

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**Introduction:** Since April 2012 major trauma in the UK has been consolidated to larger units designated as Major Trauma Centres (MTC). Pelvic fractures are indicative of high energy injury carrying a significant risk of morbidity and mortality. All suspected pelvic fractures should be diverted to an MTC with the expectation of improving clinical identification and treatment of these patients.

Pelvic binders have been demonstrated to effectively stabilize these injuries – reducing pain, limiting intra-pelvic volume and reducing haemorrhage. This facilitates safe transfer and aids in resuscitation. Their use is recommended for all suspected pelvic injuries.

**Methods:** We audited binder use in the six months before and after MTC status at the Royal Victoria Infirmary, Newcastle-Upon-Tyne. The standards applied were that: all subsequently proven pelvic fractures should be identified as clinically suspect pre-hospital or in resus; all suspected pelvic fractures should have a binder applied; binders should be placed correctly (at the level of the greater trochanter); binders should be visible on initial radiology.

**Results:** The number of pelvic fractures admitted post-MTC increased from 16 to 34. Binder application rates were below the standard and did not improve (38% vs. 41% ( $p=1$ )). When binders were used, they were mostly correctly positioned, (80% vs 92% ( $p=0.47$ )).

**Conclusions:** The rate of pelvic binder application has remained consistently low, and below our ideal standard of care. The expectation that increasing numbers at a single specialist unit would improve clinical identification and management has not been realised. A programme of education and re-audit is being implemented.



**Lung Cancer Pathway Audit (Routine Two Week Rule vs Fast Track)**

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**Background:** Patients with suspected lung cancer (LC) are referred to St Helier's Hospital (SHH) via the Two Week Rule pathway (TWRP). They are seen within 14 days of receiving TWR referral; investigations conducted within 28 days, treatment started within 62 days of referral. We found much inefficiency with TWRP and decided to pilot a LC Fast Track pathway (FTP). Our aim was to compare the TWRP to the FTP.

**Methods:** Information regarding referral time, date of diagnosis, treatments were gathered for all patients referred to LC clinic via the TWRP and FTP between May - July 2011. We used the SHH, Royal Marsden's Hospital database, analysed it in Microsoft Excel Software. Questionnaires were sent out to all patients.

**Results:** Of the 42 patients, 9 were referred via FTP and 33 via TWRP. The following averages were calculated, referral to histological diagnosis: FTP 12.6 days, TWRP 27.6 days, referral to MDT discussion: FTP 15.6 days, TWRP 33.3 days, referral to treatment: FTP 15.6 days, TWRP 54.9 days. 66% patients received their first treatment prior to breach date. 92% of patients were satisfied with the services received.

**Conclusions:** We found that there was a significant reduction in time to diagnosis and referral to treatment with FTP. There were no negative comments from patients taking part in the FTP. The numbers were too small to measure mortality. The audit period included the early period when there were a few logistical problems. We plan to continue piloting the FTP and to re-audit in 2013.

**Antimicrobial stewardship in the fight against resistance – an audit of antimicrobial prescribing practices for surgical prophylaxis**

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The recent report by England's chief medical officer is set to put antimicrobial resistance in the international spotlight. With very few antibiotics in development, our arsenal against increasingly resistant bacteria is diminishing, raising concerns about a bleak future where untreatable infections are rife. As such, there has been a call for antimicrobial resistance to be put on the UK national risk register and for the issue to take an international stage at this year's G8 summit and by the WHO. Prudent antibiotic prophylaxis aims to reduce the incidence of surgical site infection whilst minimising collateral effects, including development of resistant bacteria. This audit examined the peri-operative prescribing practices at Royal Hampshire County Hospital, UK. Over a specified period, data was collected regarding choice, dose, timing and duration of prophylactic antibiotics administered to patients undergoing surgery. Data collected was compared to best practice as determined by the Trust's antimicrobial guidelines. Initial findings revealed only 70% of cases complied with the guidelines, precipitating surgical-microbiological collaboration and revision of the guidelines. With a focused effort on education and awareness, and installation of laminated and highlighted copies of the guidelines in all anaesthetic rooms, successive audit cycles have shown increasing improvement. The latest audit cycle reveals that 91% of cases received appropriate prophylactic antibiotics, 89% of which were fully compliant with hospital guidelines. We conclude that simple measures can greatly impact compliance with best practice. It is this kind of *local* antimicrobial stewardship that will be vital in the global fight against antimicrobial resistance.

**An Audit of the Management of Infected Venous Leg Ulcers**

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**Background:** Venous ulcers are a significant public health issue, and infection can lead to slower healing. Currently, different aspects of management are covered by several different general ulcer management guidelines. This audit evaluated the local management of patients with infected ulcers, using standards compiled from different national guidelines against which to audit. It aimed to assess the need for specific guidance on the management of infected ulcers.

**Methods:** All patients who had a venous ulcer swabbed at Beccles Medical Practice between April and October 2011 were audited (n=50). The reason for the swab, the timing of antibiotic treatment and the treatment given were recorded in a spreadsheet using information from patient notes. Data was analysed by the calculation of percentages and confidence intervals.

**Results:** The majority of swabs (88%, 95% CI 79-97%) were being taken for clinically suspected infection, as recommended by national guidance. Just 25% (95%CI 12-37%) of patients were being started on empirical antibiotics, and only 50% of these were given antibiotics recommended by national guidance. 11 patients (25%, 95%CI 12-37%) were not prescribed antibiotics at all despite clinically evident infection.

**Conclusions:** In this study, most swabs of venous ulcers were being taken appropriately, but antibiotics were being started later than recommended, and non-recommended treatment was often used. Some patients were not treated despite infection. Infected ulcers are easily treatable, and this can prevent increased morbidity. Clear and easily accessible guidelines should therefore be introduced to ensure appropriate management of infections.

**Emergency Theatre Audit - Adherence to NCEPOD national guidelines and assessing theatre utilisation**

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**Background:** Delays in patients getting timely access to theatre are detrimental to patient outcomes. Patients with septic shock if delayed >12 hours their mortality increases from 25% to >60% <sup>(1)</sup>. Overrunning elective work, workforce shortages and waiting for imaging contribute to delays. This audit aimed to establish if we were adhering to NCEPOD target 'time to theatre' guidelines and maximising theatre utilisation.

**Methods:** Data was collated from NCEPOD emergency lists and the theatre computer database. Data collected included; booking times, entry into theatre times, NCEPOD classification, patient details and operation performed. We compared the elapsed time between booking and theatre entry to NCEPOD 'target time' over 12 weeks.

**Results:** 84 days of emergency lists were included however 8 lists were untraceable. Traceable lists involved 288 patients. Average no. of cases per week 25.9. 63% (n=182 cases) complied with NCEPOD 'time to theatre' guidelines, in 30% (n=86 cases) there was inadequate data, 7% (n=21 cases) were delayed and did not comply with guidelines. The theatre was underutilised in the evening (5PM – 9PM) only 13% of cases (n=31) performed compared to 17% (n=41) out of hours (OOH - 9PM-9AM).

**Conclusions:** Unclear from evidence collected the causation of delays. Possibilities include theatre staff reallocated to overrunning elective lists, delays in imaging, 8pm handover contributing to underutilisation of evening slot. Recommended redesign of sheet, consultants to classify operations according to NCEPOD grade, include theatre staff in 'trauma style' handover, change shift patterns to include consultant led ward round 3pm and thus utilise evening theatre space and minimise operating OOH

(1) ASGBI – Emergency general surgery guidelines: May 2012

**Perineal Repair Documentation & Support – Improving Standards for Women**

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Perineal damage during labour can result in morbidity for women and litigation for hospitals. Clinical Negligence Scheme for Trusts (CNST) Maternity Risk Management Standards requires that maternity services demonstrate compliance with documentation for perineal trauma including consent for perineal repair and discussion of support following perineal trauma.

We conducted a prospective audit of antenatal and postnatal case notes for women having vaginal deliveries over a one month period. We assessed for perineal trauma, documentation of consent for repair and provision of support. Following initial results we recommended raising staff awareness of documentation. A checklist covering support after 3<sup>rd</sup> and 4<sup>th</sup> degree tears was also introduced. We re-audited after 15 months to assess effectiveness of these measures.

Initial audit of 75 vaginal deliveries found only 8 (23%) of 52 women offered perineal repair had documentation of consent. No women had documentation of provision of support following perineal trauma. Repeat audit of 76 vaginal deliveries with 49 perineal repairs found 15 (43%) had documentation of consent and 5 (12%) had documentation of support.

Interventions at our centre to date to improve documentation around perineal trauma have shown a modest improvement. However, further measures are required to reach 75% compliance for CNST level 2, and to improve support for women and decrease litigation. We recommend further staff education, redesign of the labour notes to incorporate consent and discussion of support and introduction of a patient information leaflet on perineal trauma. This is underway and we will re-audit 6 months from implementation.

**Clinical audit on the management of acute upper gastrointestinal bleed in East Kent Health Trust (EKHT)**

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**Background:** This audit was conducted to evaluate trust performance (East Kent Health Trust – EKHT) in accordance to NICE guidelines on the management of acute upper gastrointestinal bleed (AUGIB).

NICE guidelines for AUGIB:

1. Blatchford score calculated at presentation and Full Rockall score post endoscopy. Blatchford score of 0 means patient can be discharged with outpatient endoscopy. Rockall score predicts risk of mortality and rebleeding from AUGIB.
2. Non-variceal bleeding should not be treated with adrenaline monotherapy – higher risk of rebleeding. Endotherapies combined with adrenaline (mechanical clips, thermal coagulation or fibrin/thrombin) recommended.
3. Patients with variceal bleeding should be given terlipressin and prophylactic antibiotics – reduces mortality.

**Method:** We included 47 patients, who presented to EKHT with signs of AUGIB, covering six months period from 1<sup>st</sup> July 2012. Data was gathered using hospital notes, endoscopy reports and hospital discharge letters.

**Results:** Use of Blatchford Score and Rockall score in AUGIB in EKHT was 0% and 20% respectively.

53% of non-variceal bleeds were treated with adrenaline monotherapy.

All variceal bleeds were managed with terlipressin, 80% received prophylactic antibiotics.

**Conclusion:** Use of scoring systems in EKHT for AUGIB was poor. Non-variceal bleeding management not following NICE guidelines. Not all patients with variceal bleeding received both terlipressin and prophylactic antibiotics.

Implementation of change from the audit – Pocket scoring system guides have been produced for doctors in the trust to use.

Audit was presented at local gastrointestinal departmental meeting and hospital grand round to highlight changes needed to meet NICE guidelines.

Plan: Re-audit in six month to evaluate effects of changes

### Documentation of Early Warning Scores (EWS) in an Old Age Psychiatry Inpatient Setting: an Audit

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In the setting of inpatient old-age psychiatry, the risk of acute physical deterioration given patients' age, comorbidities and reduced physiological reserve is noteworthy. Recent clinical incidents highlighted late recognition of physical ill-health within this population. We assessed the use of the EWS in an old-age psychiatry hospital.

A retrospective audit of physical observation charts was performed on 28 patients across two wards between 10<sup>th</sup> – 16<sup>th</sup> September 2012. Standards were developed from Trust guidance. Microsoft Excel was used for data analysis.

A minimum of 196 observations were expected (7x28), but in total 232 observations were recorded.

1. Physical observations monitored at least once daily.

143/196 (73.0%)

2. Minimum observations documented: heart rate, respiratory rate, blood pressure, conscious level and temperature.

0/232 (0%)

Complete set of observations never documented. Blood pressure was recorded on 97.4% occasions, heart rate 96.6%, temperature 51.7%, respiratory rate 6.9% and conscious level 0.9%.

3. EWS calculated with each set of physical observations

0/232 (0%)

4. 'Time Driven Action Plan' followed if EWS  $\geq$  2

0/232 (0%)

5. If no physical observations recorded, reason why documented

28/53 (52.8%)

Our audit highlights that recording of basic observations and use of EWS is inadequate in this setting. This may lead to delay in identification of acute physical deterioration and thus increase morbidity and mortality.

Recommendations included: 1) Present data to junior and senior medical and nursing staff; 2) Raise awareness of the importance of EWS through posters and education sessions; 3) Review trust policy regarding physical observations; 4) Re-audit Spring 2013.

### Urinary Catheterisation Audit

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Trust guidance requires every catheterisation to be documented in medical notes and catheter care charts. Patient safety is maintained by noting all catheterisation attempts and reducing associated complications. Infection is a risk, especially MRSA, where catheterisation is the top cause.

Our aim was to check whether our practice was compliant. To our knowledge, no such audit has been conducted.

Four areas at the Friarage Hospital catheterise frequently: Allerton (surgical ward), post-operative surgical day unit, Accident&Emergency, and theatres. The original audit was in July. The re-audit was between August and September. Patient notes were perused to check for chart use, correct completion and an entry inserted in the medical notes.

Our objective was to achieve 100% compliance throughout. For the first audit, 30% of the cohort used the chart, 23% documented verbal consent gained, and 60% documented catheterisation in medical notes. For the re-audit, 90% used the chart, 53% documented verbal consent, and 43% documented catheterisation in medical notes.

During the implementation period between audits, awareness was raised of trust guidelines regarding the catheter care chart, its availability was checked, colleagues were encouraged to document and their input considered. Issues raised were poorly completed form sections, consent not obtained in theatre, and double documentation. Our recommendations included changing the form, and educating staff as to correct documentation.

Documentation improved since the first audit. Together with the Patient Safety team, we modified the chart. We are raising awareness about this important issue and will re-audit after the new chart is available.



**Phyllodes tumour versus fibroadenoma: Differentiation by ultrasound and core biopsy features**

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Phyllodes tumour is a rare fibroepithelial neoplasm with an unpredictable nature, requiring complete surgical excision. Clinical, radiological and pathological findings are similar to fibroadenoma, presenting a diagnostic challenge. Often women with fibroadenoma are over-treated with complete surgical excision because the possibility of phyllodes tumour cannot be ruled out. The purpose was to determine whether sonographic or histopathological core biopsy findings allow discrimination before diagnostic excision.

69 women with breast lesions defined as B3 by core biopsy were retrospectively evaluated from 2008-2012, including 49 fibroadenomas and 20 phyllodes tumours on final histology. Comparison of pre-operative sonographic and core biopsy findings was made for each group.

49/69 (71%) cases classified as B3 "cannot exclude phyllodes tumour" at core biopsy were confirmed fibroadenomas on final histology at complete excision. A lesion was statistically significantly more likely to be a fibroadenoma if it was well-defined on ultrasound and more likely to be phyllodes if internal vascularity was present. At core biopsy, evidence of nuclear atypia, sub-epithelial or peri-ductal condensation, epithelial hyperplasia, irregular or ill-defined margins and a biphasic lesion were statistically significantly more likely to be phyllodes tumours. No other differentiating sonographic or core biopsy findings were found to be statistically significant.

The above features hold statistical significance to distinguish between the two diagnoses pre-operatively. However, due to considerable overlap, many of these features were present pre-operatively for the fibroadenoma group and subsequently lead to surgical excision. The findings presented might not change the number of patients requiring complete excision.

**An audit to identify the current use of a formal risk assessment tool within the North Crisis Resolution and Home Treatment Team, Cardiff**

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In psychiatry, appropriate use of risk assessment tools (e.g. the CPA-4) is core to holistic management of mental health service users (MHSU). This audit proposed to examine current use of the CPA-4 (examining static and dynamic risk factors) in managing MHSU under the care of the North Crisis Resolution and Home Treatment Team (NCRHTT). A literature review was conducted, including national and local risk assessment guidelines.

Audit standard: 100% MHSU having recorded CPA-4's completed according to Welsh Assembly Government guidelines (on admission, discharge and at any significant event during admission).

Cohort: the most recent 50 MHSU admitted (> 5 days) and discharged between 10/08/2012–10/11/2012 under the NCRHTT.

An audit tool retrospectively assessing CPA-4 use was piloted and revised. Complete datasets were then collected for the full cohort (n=50), via PARIS, made anonymous, and analysed using SPSS v20.0.

49 MHSU (98%) had admission CPA-4's. However, only 14% underwent CPA-4 reassessment, and 0% had >1 CPA-4 reassessment, regardless of admission duration (mean 18.7(5-60) days), until discharge. 88% had discharge CPA-4's.

On further analysis, quality of CPA-4 completion was poor with 6-30% CPA-4's incomplete; historical and current risk factors, and future management were the most frequently erroneous areas.

Audit standards were not met. Improvements could be implemented by raising guideline awareness and altering PARIS software to ensure CPA-4 completion. However, there should be recognition that complex form filling does not equal good risk management. Clinical practice and results should be recognised when assessing quality of care

### Pre-admission Analgesia and Altered Mental State in Neck of Femur Fracture Patients

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**Background:** Neck of femur fracture patients mostly belong to the elderly population, a group with increased sensitivity to opiates as well as significant incidence of cognitive impairment.

**Aim:** To assess whether pre-admission opiate analgesia affects the mental state as examined by the mental state questionnaire (MSQ).

**Methodology:** Data was collected prospectively and included individual's age, type and amount of analgesia received before ward admission, presence of confounding factors such as dementia and intercurrent infection, admission MSQ and discharge MSQ.

**Results:** The average age of the patient population was 79.8years (range 58 to 97). 33% had known cognitive impairment. The mean dose of morphine received before ward arrival was 8.7mg (range 2.5mg to 20mg). Two patients did not receive any opiate analgesia. The difference between admission MSQ and discharge MSQ was found to be that of one point or less in 85% (n = 23) of patients. None of the patients were found to have had a significantly lower MSQ on admission then at discharge.

**Conclusion:** Opiate analgesia does not significantly alter mental state as measured by the MSQ. This is an important negative finding which should encourage health care professionals involved in the initial management of neck of femur fractures to deliver opiate analgesia as necessary to control pain in this common and distressing type of injury

### A Case-Series: South East Wales Lower Limb Amputations For Trauma –How Many Walk With Prosthesis In A 2.5 Year Period, and How Many Co-morbidities Do They Have?

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**Background:** Many consider the majority of patients following lower limb amputation never walk. This retrospective study looked at all South East Wales's patients who underwent lower limb amputation due to trauma, between 01/01/2010 and the 31/8/2012 who were referred to The Artificial Limbs and Appliance Centre.

**Method:** Over 500 patients were assessed during this time period by a rehabilitation team in South East Wales to assess suitability for prosthetic rehab, 300 patients were suitable for prosthetic rehab. 26 patients met the original criteria, of the 26 patients 1 was excluded due to early mortality. The level of amputation was assessed, as well as if the patient was a unilateral or bilateral amputee. Risk factors (including 34 co-morbidity variables) were collected.

**Results:** Of the 25 patients 20(80%) mobilised with a prosthesis, of the 5(20%) not mobilising with a prosthesis 1(4%) transfers from bed to chair with a prosthesis. All amputations performed were unilateral, with 19(76%) transtibial and 6(24%) transfemoral. The mobilisation rate across transtibial and transfemoral were 16(84.2%) and 4(66.7%) respectively.

Of 34 co-morbidity variables collected it was found that only 19 were present. The most common co-morbidities were: hypertension 9(36%), Osteoarthritis 5(20%), Diabetes 4(16%), and atrial fibrillation 3(12%). On average each patient had 1.6 co-morbidities.

**Conclusion:** Unsurprisingly unilateral transtibial mobilisation rates 19(84.2%) were higher than those of unilateral transfemoral mobilisation rates 4(66.7%). While this was expected, more data is needed to validate this case series. Furthermore it is shown that trauma patients have very few co-morbidities (average 1.6 per patient).

### The Safety of Administration and Prescription of Oral Purgatives Prior to Elective Colonoscopy

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**Aim:** In 2009 the NPSA produced a rapid response report highlighting the potential for harm due to the inappropriate administration of oral purgatives. Subsequently, the consensus guidelines by Connor *et al* outlined recommendations for the safe use of such agents. This study compared practice in a small district general hospital to the guidelines to identify areas for improvement.

**Methods:** A prospective study of 40 patients who underwent elective colonoscopy between October and December 2012 was performed using information from the notes and direct questioning.

**Results:** No patients with absolute or relative contraindications received purgatives. All patients received Picolax at an appropriate dose and were given instructions on oral fluid intake. However, provision of information regarding patients' regular medication was poor with only 22% of patients being given adequate counselling. Of patients taking nephrotoxic medications, 8% were given specific information regarding their omission.

**Conclusions:** Poor medication advice resulted in regular medications being unnecessarily omitted and others being taken in too close association with purgatives for proper absorption. Deterioration in renal function can occur with the continuation of nephrotoxic drugs in the presence of purgative-related dehydration. Implementation of an updated patient information leaflet, education of endoscopy staff and re-audit are underway.

### Changing Attitudes in Enhanced Recovery Protocol Applied to Radical Cystectomy

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Radical cystectomy is commonly associated with greater mortality and inpatient stay than other urologic surgeries. The current study aims to determine the impact of an enhanced recovery protocol (ERP) on length of stay (LOS) and surgical outcome in patients undergoing radical cystectomy at our institution.

A retrospective study of patients undergoing elective radical cystectomy between October 2008 and March 2013 was performed. Data were extracted using case-notes and electronic databases. Patients receiving ERP were compared with those receiving non-ERP care; the ERP group was further subdivided into patients prior to August 2012 (old-ERP group) and those after (new-ERP group) to look for recent improvements. Statistical comparisons included age, BMI, length of stay, ASA score, complications, and mortality.

Out of the preliminary 96 consecutive patients, 45 received non-ERP care and 51 patients received ERP care (30 in old-ERP group, 21 in new-ERP group). Median LOS in the ERP group was 10.0d (IQR 7.0 to 17.0), vs. 14.0d (12.0 to 17.0) in the non-ERP group ( $p<0.01$ ). Within in the ERP group, the old-ERP group had a median LOS of 10.0d (8.0-17.3), vs. 7.0d (4.0 to 14.5) in the new-ERP group ( $p<0.05$ ). There were no statistically significant differences in complication rates or 90d mortality rates between any of the groups. The cohorts were also similar in demographic background and disease staging/grading.

ERP in radical cystectomy reduced the length of hospital stay without any observed adverse effects on mortality rate or post-operative complications. Renewed efforts in greater patient education even further reduced patient stay.

### Improving the Planning for Escalation of Care for Patients commencing Non-invasive Ventilation – a completed audit cycle

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**Background:** Patients who require non-invasive ventilation (NIV) for hypercapnic respiratory failure are critically ill and decisions regarding escalation to invasive ventilation must be made at an early stage. Communication with patients, families and carers is essential for good quality care in these patients, some of whom are in the last stages of life. We aimed to assess the quality of these aspects of care in patients initiating NIV.

**Methods:** We assessed case notes of consecutive patients starting NIV against selected British Thoracic Society recommendations, including:

- A management plan in the event of NIV failure should be made on initiation.
- Decisions regarding escalation of care should be discussed with the patient, family or carers
- Decisions must be made by ST3 doctors or higher

Following this audit, an NIV care document was developed. It included guidance on initiating and monitoring NIV. This was coupled with informal teaching of staff. A re-audit was then carried out.

**Results:** 16 patients were included in the initial audit and 17 in the re-audit. There was a significant increase in the proportion of patients with plans made (31% vs 94%,  $p < 0.01$ ). Evidence of discussions with patients or relatives improved (19% vs 59%,  $p = 0.02$ ). All decisions made in both audits were taken by doctors of grade ST3 or higher.

**Conclusion:** This completed audit cycle demonstrated that the introduction of an NIV care document in combination with informal education significantly improved management plans for patients starting on NIV. It also improved documentation of discussions with patients, families and carers

### Category 1 Caesarean section audit: comparing time to delivery and outcomes when regional or general anaesthesia is used

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**Background:** In Category 1 Caesarean section (Cat1CS), the life of mother or foetus is at immediate risk and prompt delivery is required (target  $< 30$ min).[1] Less than 15% of emergency sections should be performed under GA due to higher complication rates.[2][3] We audited our Cat1CS to establish indications for surgery, our GA rate, decision to delivery interval (DDI), and reasons for delays. We investigated relationships between anaesthetic modality, DDI, and outcomes (neonatal/ maternal).

**Methods:** Review of theatre records and obstetric notes of 48 Cat1CS (chosen at random) performed in 2012 (34% Cat1CS).

#### Results:

Most Cat1CS performed for pathological CTG (60.4%).

- 38% Cat1CS under GA (target  $< 15\%$ ).
- DDI statistically significantly longer with RA than GA (28.8 vs 24.5mins. Mann Whitney: $P = 0.03$ ).
- 71% Cat1CS performed  $\leq 30$ mins (target 75%).
- Documentation regarding delays was limited. Delays in the RA group appear to have occurred between anaesthesia and delivery (possibly due to induction time). Delays in the GA group occurred decision and anaesthesia, suggesting slow theatre transfer.
- No difference in outcomes between RA and GA groups including when DDI  $> 30$ mins. (Fishers: $P = 0.38$ ).

**Conclusions:** Our GA Cat1CS rate was above target but in line with national rates.[2] Better documentation is required regarding delays. We are working to reduce transfer to theatre times. We will extend the audit to give greater power to findings and investigate instances when DDI  $> 30$ mins to identify causes of delays.



**VTE risk assessment: are we meeting the standard?**

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**Background:** During my FY1 rotation in General Surgery, I witnessed a patient develop a pulmonary embolus eight days post-Hartmann's procedure.

The patient had been prescribed an inappropriately low dose of Enoxaparin on admission and continued to receive this throughout their admission.

I decided to audit the rate of venous thrombo-embolic (VTE) risk assessment completion in our admissions to help avoid similar adverse incidents.

**Methods:** Snapshot data collection involving 30 surgical inpatients (elective and emergency) with review of kardex/inpatient notes to determine if a formal VTE risk-assessment had been performed and documented.

I compared our rate of risk-assessment with the standard expected in the NICE guidelines and subsequently presented my findings at Audit. I also implemented a 'tick-box' on each patient's ward-round file to confirm they had been risk-assessed.

I then performed a re-audit five months later using the same method to close the audit loop.

**Results:** NICE guidelines suggest: 100% of patients should be appropriately VTE risk-assessed

Original audit, Jan 2012:

30% completion rate

Re-audit, June 2012:

68% completion rate

**Conclusion:** The delivery of my audit findings and implementation of recommended changes improved rates of VTE risk-assessment by 38% on the General Surgical ward.

Whilst there was a vast improvement this still falls below the recommended target outlined in the NICE guidelines.

Ongoing study into why our rate is falling below the National Standard is taking place.

**Pulmonary Embolism Audit**

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**Background:** Current National guidelines state that for suspicion of a Pulmonary Embolism (PE), risk should be quantitatively assessed using the Wells score. A value  $>4$  (suggesting high clinical suspicion) warrants a Computerised Tomography Pulmonary Angiogram (CTPA), whereas  $\leq 4$  (low risk/clinical suspicion) a D-dimer blood test is first line management.

**Methods:** A database was collated of all the CTPAs at the QEQM Hospital from the 1<sup>st</sup> of May to the 31<sup>st</sup> of July 2012. For each patient the CTPA outcome, any applicable D-dimer values and a retrospectively calculated Wells score from the radiology request form were recorded.

**Results and Discussion:** Out of the 302 CTPAs performed, a Wells score was documented in only 5 requests. 86.8% (262/302) of scans were negative, of these 7.3% (22/302) had a negative D-dimer and hence should not have been done. 13.2% (40/302) had no d-dimer with a Wells score  $\leq 4$ , where the scan should not have been first line.

**Conclusion:** Adherence to the national clinical pathway for PEs was poor, particularly with reference to the use of scoring systems, documented in 1.7% (5/302) of cases. This is where intervention could ameliorate practice and save resources.

**Plan:** To incorporate a compulsory Wells score box as part of the radiology request form. In conjunction, a pocket Wells score guide has been made accessible to the trust. The audit will be repeated within 6 months to evaluate the effects of the changes

### Acute Upper GI Bleeding – improving documentation and encouraging safer use of blood products

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**Background:** Acute upper gastrointestinal bleeding (AUGIB) is a common reason for emergency admission. National guidelines state that all patients with suspected AUGIB should be properly assessed and risk scored.

The transfusion of blood products conveys the risk of adverse events for patients. In addition evidence suggests that over-transfusion in AUGIB can be detrimental as it reduces the hypercoagulable state.

**Methods:** We carried out a retrospective audit of patients who had a diagnosis with AUGIB analysing whether they were risk scored and managed appropriately, and the number of blood products cross matched and given to patients.

**Results:** A total of 35 patients' notes were audited. Only 14% had a pre-endoscopy Rockall Score recorded. Of those patients who had a pre-endoscopy Rockall Score of 0, only 1 (33%) was considered for early discharge.

A total of 22 patients (62%) received a blood transfusion, and of those, half of them were over-transfused.

**Conclusion:** Our audit shows that we are currently not meeting any of the national guidelines with regards to assessment and risk -scoring of patients presenting with AUGIB.

In addition, there is the excessive cross-matching of blood putting patients at risk of potential life threatening complications.

In order to improve our documentation and assessment of patients presenting with AUGIB, we have designed a proforma, which should be used to clerk all patients with suspected AUGIB. We have also provided recommendations on when patients should be cross-matched and how many units they should be transfused

### Evaluating the impact of a regular consultant ward round

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**Background:** Regular consultant ward rounds have been shown to reduce patient length of stay and improve discharge planning (1). Balancing the competing demands of outpatient activity and inpatient oncology care has been difficult in our hospital. Previously there was no timetabled inpatient oncology consultant ward. Inpatients were managed by oncology specialist trainees, with ad-hoc review by their named consultant. A regular weekly consultant ward round was introduced.

**Materials and Methods:** To evaluate this, a retrospective case note analysis was undertaken. This included all patients admitted under oncology for the two months preceding and succeeding the new ward round. A staff survey also took place. Statistical analysis used Mann-Whitney U or Chi-Squared tests.

**Results:** 85 patient episodes met the inclusion criteria. Case notes were available for 63 episodes (74%). The average length of stay significantly decreased from 11 days to 3.5 days ( $p < 0.05$ ). The time to discharge after first consultant review also significantly decreased from 6 days to 2 days ( $p < 0.05$ ). The number of consultant reviews and time to first consultant review remained unchanged ( $p =$  not significant). The percentage of patients receiving a consultant review increased, from 54.3 to 71.4%, though this was not statistically significant. However it is likely such a large increase is clinically significant. Staff satisfaction also improved following the new ward round.

**Conclusion:** This study suggests that a regular consultant ward round improves length of stay for patients, possibly through more patients having a consultant review and by expediting treatment and discharge decisions after such a review.

*Clinical and Patient-Related Work Category***A Novel Surgical Technique to Prevent Further Development of Potentially Catastrophic Blister Aneurysms**

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**Background:** Blister aneurysms of the internal carotid artery (ICA) are rare but potentially can cause catastrophic subarachnoid haemorrhages. They are often a neurosurgical dilemma as they are very difficult to treat and identify on imaging other than 3D digital subtraction angiography. Attempts to use traditional methods of coiling or clipping are often unsuccessful due to aneurismal detachment or rupture. These specific aneurysms expand relatively rapidly, lack a surgical neck and are thin walled, unlike common berry/ saccular aneurysms.

**Discussion:** The current literature consists of case reports or series describing suspected aetiology and poor outcomes after clipping or coiling. To date, only one study examines the effect of wrapping ruptured blister aneurysms with polytetrafluoroethylene (PTFE) patches. We describe the case of a 55 year old female, whom was identified as high risk of developing aneurysms due to a strong family history. We present a successful technique in which an enhanced carotid patch is wrapped and secured by sigeta clip around a non-ruptured supra-clinoidal internal carotid aneurysm and discuss its potential importance in preventing the development and rupture of blister aneurysms. Post-operative follow up demonstrated good patient recovery with intact neurology and no aneurismal remnant on computed tomography angiography.

**Case Conclusion:** In conclusion, we suggest that a wrap-clipping technique could be used both for prophylaxis and treatment of ruptured blister aneurysms, which could be superior to other traditional neurosurgical methods

**Vernix caseosa peritonitis: An enigmatic diagnosis presenting as right upper quadrant (RUQ) pain in post-partum period**

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**Background:** Vernix caseosa peritonitis (VCP) is a rarely documented condition, with just 23 cases reported. VCP results from amniotic fluid spillage into the peritoneal cavity during caesarean section, causing severe aseptic inflammation. The condition presents with abdominal pain, fever and leucocytosis. Diagnosis is often difficult and is invariably achieved by peritoneal biopsy. This case study reports a case of VCP occurring in Scotland and reviews this case in relation to other cases of VCP reported in the literature.

**Discussion:** A 26 year old woman presented ten days after caesarean section (LSCS) with severe RUQ pain and signs of sepsis. The diagnosis proved elusive but eventually was achieved by laparotomy and biopsy. The macroscopic appearance was of caseous white nodules which microscopically was rich in anucleate squamous cells. Literature review of the previous 23 reported cases reveals that foci of VCP in Morison's pouch and presentation with RUQ pain is common, diagnosis is frequently elusive, requiring multiple invasive investigations. Prevention by thorough lavage of the peritoneal cavity follows caesarean section, which focusses on dependent areas. VCP indicates the importance of lavage of the cavities, namely Morison's pouch.

**Conclusions:** VCP is a rare complication of LSCS and requires inadvertent opening of the peritoneal cavity. It involves aseptic immune response to intra-peritoneal vernix. The diagnosis should be suspected in women presenting soon after LSCS with RUQ pain and fever.

### First reported case of a Gastrointestinal stromal tumour concomitant with a Brenner tumour

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**Background:** Gastrointestinal stromal tumours (GISTs) as well as Brenner tumours are considered a rare malignancy. This is the first reported case in which a GIST tumour was diagnosed concomitantly with a Brenner tumour.

**Objectives:** To report a case of an undescribed association of Gastrointestinal tumour and Brenner tumour and to discuss its management.

**Design:** Case study and literature review.

**Patient and Methods:** A 64 year old woman with early satiety of 3 months duration underwent a CT scan, endoscopy and an ultrasound guided puncture which indicated a lesion suggestive of a GIST.

A videolaparoscopic partial gastrectomy was performed. During the surgery, a nodule of about 4cm in diameter in her right ovary was noted and a right oophorectomy was executed.

The gastric lesion of 2.5 cm in diameter was confirmed by immune-histochemistry as being a GIST with low malignancy risk and the ovarian lesion as a benign Brenner tumour.

Patient progressed uneventfully and was free of evidence of progressive disease in a two months post-operative follow-up.

A literature review of GIST and Brenner tumor cases was performed on Pubmed and SciELO-Scientific Eletronic Library On Line using the expressions "GIST", "Brenner tumor" and "Transitional cell tumor".

**Discussion/Conclusions:** This is the first documented case in which a GIST is found concomitantly with a Brenner tumour. The incidental finding of this ovarian tumour during the gastrectomy, emphasizes the importance of a meticulous abdominal exploration even when no metastasis of GIST are expected.

### Pamidronate as a treatment for post traumatic AVN of femoral head

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**Background:** Avascular necrosis (AVN) of the femoral head occurs when there is vascular compromise to the femoral head resulting in ischaemia to the bone. It is a recognised complication of posterior hip dislocation both in adults and children.

**Case:** A 14-year-old male patient presented with knee and hip pain after a quad bike accident. MRI revealed a fracture dislocation of the right hip with a small femoral head fragment. The patient underwent an open reduction but at 5 months post operation, he continued to have a limp and a repeat MRI showed early signs of AVN of the femoral head. Patient was started on pamidronate which controlled the progression of the disease.

**Discussion:** Various surgical options have been advocated for the treatment of AVN in young adults and children, including core decompression with or without bone graft. Bisphosphonate (alendronate) was first reported in 2001 to be an effective treatment for AVN of the femoral head as it retarded the progression of AVN, reduced the rate of collapse and led to improvement of symptoms. Evidence suggests that there is favourable outcome for early treatment of AVN using either surgical (decompression) or medical management. In young adults, medical management is preferred to avoid breaching of the growth plate.

**Conclusion:** This is the first reported case of post traumatic AVN in a young adult treated with pamidronate showing favourable early results

**Spontaneous surgical emphysema of the larynx following hyperextension of the neck**

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**Background:** A 39 year old with no ENT history presented to the ENT department complaining of hoarseness of the voice, odynophagia and the sensation of something flapping in his throat. The symptoms started following hyperextension of his neck to drink a cup of coffee. He reported hearing and feeling an audible crack over the thyroid cartilage followed by a coughing episode. On arrival he had palpable crepitus of his thyroid cartilage but no palpable surgical crepitus. Nasendoscopy revealed oedema of the arytenoid cartilage and bruising in the pyriform fossa and CT revealed moderate subcutaneous emphysema of the larynx although no fracture was seen. After conservative management with antibiotics, intravenous steroid and voice rest the patient made a complete recovery.

**Discussion:** Surgical emphysema of the larynx is rare in the absence of trauma and there are a paucity of case reports that describe such conditions. The few cases published in absence of trauma all relate to massive laryngeal tears in patients with compromised mucosal integrity due to disease or medication. We present what we believe to be an unusual, atraumatic mechanism for mucosal breach of the larynx with subsequent surgical emphysema, in absence of predisposing risk factors.

**Conclusion:** This represents an usual presentation of surgical emphysema of the larynx in the absence of trauma which resolved with conservative management. We encourage others to consider potentially significant laryngeal crepitus in patients presenting with seemingly benign laryngeal injury and to seriously assess the need for definitive anatomical imaging with a CT scan

**Bilateral Acanthamoeba keratitis: A case report**

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Acanthamoeba keratitis is a rare, acute sight-threatening infection of the cornea occurring mainly in regular contact lens-wearers. It is caused by Acanthamoeba, a free-living amoeba ubiquitously found in the environment, including fresh and sea water, soil, sewage, air and even medical equipment. The symptoms are often nonspecific, with redness, tearing, disproportional excruciating pain and photophobia being the commonest complaints. Unilateral involvement is the case in most reports in the literature, however, the much rarer bilateral infection is not unheard of. We report a case of a 17-year old female who is a regular contact lens wearer diagnosed with bilateral Acanthamoeba keratitis confirmed on corneal scrapings. Her vision never recovered completely and is now at imminent danger of going blind. Solutions for cleaning contact lens wear are not legally-bound to be tested against Acanthamoeba and to have this amended is one of the main recommendations that emerges from this report. The solution used by our patient contained neither isopropyl alcohol nor 3% hydrogen peroxide – two ingredients proved to be very effective disinfectants for soft lenses. Another factor is that very little information is given to patients when purchasing contact lenses including the advice not to wear lenses while in contact with water of any kind. The patient claims to have swam while wearing the lenses, three days prior admission and this is thought to be an important causative factor. Avoiding any water contact with the lenses/cases and ensuring the use of proper disinfecting solutions should allow adequate protection against this condition.



### A Pink Herring – A Case of Adult Onset Still's Disease

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**Background:** Adult onset Still's Disease (AOSD) is a rare form of inflammatory arthritis. The prevalence of this disease is 1.5 cases per 100,000-1,000,000. It is characterised by arthralgia, myalgia, pyrexia, a 'salmon-coloured' rash and lymphadenopathy. Diagnosis is clinical and the criteria suggested by Yamaguchi et al is the most sensitive at 96%. We describe a unique case that met the majority of these criteria, however in this case the classical rash was in fact a 'Pink-Herring'.

**Discussion:** A 47-year-old lady of Pakistani descent, was admitted with symptoms and signs suggestive of sepsis. Three months prior, she had been to Pakistan and remembered a mosquito bite during her stay. She complained of intermittent fever, myalgia, arthralgia and rash for a week and a sore throat for two days. On examination, she had tenderness in the neck with cervical lymphadenopathy and a macular salmon pink rash on the face, arms, upper back and legs.

Numerous infection screens were performed which all returned negative and she continued to spike temperatures of up to 41.5C even with antibiotic therapy.

Rheumatology opinion was sought and AOSD was considered as the possible diagnosis. Prednisolone was commenced; subsequently inflammatory markers began to subside with resolution of pyrexia. A skin biopsy showed lichenoid infiltrate with morphological features more compatible with a fixed drug eruption.

**Case Summary:** This highlights that the salmon pink rash was a coincidental finding in this case of AOSD, more related to a drug reaction even though the other symptoms were diagnostic of this disease.

### A Case of Recurrent Thrombosis and Adrenal Insufficiency

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Antiphospholipid syndrome (APS) is an acquired prothrombotic autoimmune disorder that may present with arterial or venous thrombosis in any organ or tissue. Testing for APS is recommended in patients under the age of 50 presenting with stroke, those with unprovoked DVT or PE, and those with specific pregnancy morbidity. Over 50% of patients with APS have a further thromboembolic event within 5-6 years of initial presentation. The optimal treatment strategy remains controversial but longterm anticoagulation is usually advised.

In the case reported, a 47 year old female presented with femoral artery embolism and developed acute adrenal failure during admission. High resolution MRI showed evidence of bilateral adrenal infiltration but was not diagnostic of adrenal infarction or haemorrhage. Three years following initial presentation, the patient represented with a right frontoparietal lobe infarction and developed a deep vein thrombosis. Investigations were persistently positive for lupus anticoagulant and anti-cardiolipin antibodies and a diagnosis of antiphospholipid syndrome was made.

Adrenal thrombosis is a recognised although rare feature of APS. This case highlights the necessity for suspicion of APS in young female patients presenting with thromboembolism of any vessel in the absence of thrombotic risk factors. Acute adrenal insufficiency with concurrent thromboses should guide the clinician to investigate APS as the underlying cause.

**Case Report: An unusual presentation of IgG4 disease in the neck***Quinn B**Daisy Hill Hospital, Newry, UK*

**Background:** IgG4 tubulointerstitial nephritis (IgG4-TIN) is the most common form of IgG4 renal disease. Renal pathology may be accompanied by other systemic manifestations, in which case the disease is known as IgG4 related systemic disease (IgG4-RSD). There are no published case reports of IgG4-RSD presenting as a submandibular mass, as in this case report.

**Discussion:** A 54 year old male presented to his General Practitioner with a painless lump in the right anterior triangle of the neck. An ultrasound-guided fine needle aspiration was performed. This found lymphoid infiltrate of both B- and T- lymphocytes with prominent populations of plasma cells and was consistent with the diagnosis of chronic sclerosing sialadenitis (Kuttner's tumour.) Upon routine follow up, two years later, haematological tests indicated deterioration in renal function. A renal biopsy was performed, which found extensive fibrocartilaginous fibrosis and abundant B-cells, T-cells and plasma IgG4 cells, confirming IgG4 disease. The condition responded to prolonged steroid treatment.

**Conclusion:** A case of IgG4-RSD is described, which presented as a submandibular neck lump with local lymphadenopathy. The disease eventually progressed to tubulointerstitial nephritis approximately two years later, which was confirmed on renal biopsy. While IgG4 disease can present in a number of different ways, this case report highlights an unusual presentation – a submandibular mass. It is important to reach a definitive diagnosis for a swelling in the neck and to be aware of the multisystem presentation of IgG4 disease

**A review of the effectiveness of a specialised tinnitus clinic in South Yorkshire***Xu Y**Sheffield Teaching Hospitals/Royal Hallamshire Hospital, Sheffield, UK*

**Background:** Tinnitus affects 10-15% of the general population and up to one in every three elderly. With the shift in demographics, UK's ageing population raises the problem that tinnitus will increase economic and healthcare burden. Due to the many aspects of tinnitus, a wide variation in clinical management is present and no guidelines have been published. We therefore propose that highly specialised tinnitus clinics will decrease the healthcare burden and streamline patient care.

**Method:** From 2008 to 2012, a prospective collection of data from N=452 patients who presented with tinnitus in a weekly specialised clinic was done. Every patient had hearing tests, a complete medical history taken and a full otoneurological examination. Education and reassurance about tinnitus and its innocuous nature were given, while self-help techniques were taught. Appropriate referrals to audiometry and psychology were made and all patients were booked for an imaging scan to rule out any pathology.

**Results:** 20% of patients were discharged after their initial consultation, while another 46% of patients were discharged by the second consultation. Only 11% needed more than three consultations. Results of imaging scans were informed via post and non-pathological patients were discharged back to primary care. The most common accompanying symptom was hearing loss (86%) and the most common precipitating factor was ear instrumentation (26%).

**Conclusion:** With a discharge rate of almost 70% by second consultation, we find that having specialised tinnitus clinics in district general hospitals is an efficient way of managing tinnitus in secondary care and should be encouraged

### Thiamine deficiency presenting as an acute, disabling, polyneuropathy – A rare presentation causing a considerable diagnostic challenge

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**Background:** Thiamine deficiency is an uncommon condition, which usually presents in the context of alcoholism with a Wernicke-Korsakoff type picture. This case highlights an atypical presentation with rapid onset polyneuropathy.

**Case:** A 67 year old lady presented to the gastroenterology clinic with a 2 month history of severe weight loss, persistent vomiting and epigastric pain. Following clinic review she developed a progressive paralysis and sensory loss of her left leg requiring emergency admission. Within one week this progressed to involve all four limbs. Clinical examination demonstrates a profound sensory ataxia, severe pseudoathetosis, nystagmus and bilateral weakness.

Nerve conduction studies demonstrated severe, predominantly sensory neuropathy. One week following admission the patient exhibits clear visual hallucinations, profound retrograde amnesia and marked confabulation, consistent with Wernicke-Korsakoff syndrome. Following intravenous thiamine replacement she demonstrated progressive improvement in her sensory ataxia and mild improvement in her confabulation and amnesia. Blood results ultimately confirm a marked thiamine deficiency.

**Discussion:** This case clearly depicts an atypical acute presentation of thiamine deficiency, previously labelled dry Beriberi. Few cases have been described in the literature, which are not as a result of alcohol abuse. In this lady it was felt that a combination of background peptic ulcer disease, chronic hepatitis and an acute gastroenteritis precipitated the acute clinical presentation.

**Conclusion:** Thiamine deficiency can rarely present as a rapidly progressive sensory neuropathy and this needs to be remembered in the differential of Guillain-Barre syndrome when considering this clinical picture in an individual with recent weight loss and poor oral intake.

### Subacute Subdural Haematoma – Should CT head guidelines include additional criteria?

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**Background:** Head injury is a common presentation in the emergency setting. This case highlights the pitfalls in adhering to guidelines too rigidly.

**Case:** A 90 year old man presented to A&E with a head injury after a mechanical fall. His GCS was 15, there was no history of loss of consciousness, amnesia, vomiting or seizures. He was not on any anticoagulants. On examination there was moderate left periorbital swelling and contusions but no signs of focal neurological deficit or depressed or basal skull fracture. After review of the patient with the registrar it was decided that the patient did not fit criteria for a CT head and was thus discharged with advice to his wife to bring him back if there were any signs of deterioration. Two days later he presented to A&E with a GCS of 6 and CT head showing subdural haematoma. He sadly passed away hours later.

**Discussion:** Due to objective criteria for a CT head not being fulfilled, this patient missed a potential lifesaving intervention. This patient was elderly and had recent platelet count of 84 – these are both risk factors for developing a subdural haematoma which are not taken into account by NICE guidelines unless there is loss of consciousness or amnesia.

**Conclusion:** It is important to highlight that guidelines are not a replacement for clinical judgement, both be used in conjunction. This case provides some evidence to suggest additional criteria for a CT head in patients with risk factors for developing subdural haematomas.

**"The unusual DVT"**

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A 73 year-old lady presented with a one day history of discoloration and severe pain of her left leg. She had noted to have a reduce appetite and weight loss prior to this. On examination, she had gross oedema, paraesthesia to her left foot, with an 8-second capillary refill time. Left leg was dusky in colour and cold. It was initially thought of an arterial thrombus however her risk factors were low.

An unusual presentation of a large venous thrombus, which mimics the manifestation of an arterial thrombus, known as phlegmasia cerulea dolens (PCD) was diagnosed. She was commenced on treatment dose low molecular weight heparin and urgent CT abdomen/thorax/pelvis arranged while waiting for vascular input. CT revealed a right renal tumour, pulmonary metastasis and an almost complete obstruction of the IVC, with intramural thrombus extending down to the left iliac and femoral veins.

PCD, also known as the blue phlebitis, is an uncommon but potential life-threatening form of an iliofemoral thrombosis, causing the venous outflow of the leg to be obstructed. In severe cases, approximately 25% could result with gangrenous limb. It is reported to be associated with several conditions, such as neoplasm, cardiac valvular disease, infection and oral contraceptive pill<sup>1</sup>. Treatment options for PCD are anticoagulants, thrombolytic therapy or venous thrombectomy.

This is an unusual case of a large venous thrombus that presented like an arterial thrombus. Hence it is worth further investigating as in this case it revealed the primary cause.

**Stress induced Graves' disease: a case report highlighting the pre and postoperative implications of subclinical thyrotoxicosis**

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**Background:** Graves' disease has long been associated with stress as a precipitant factor. Early recognition and management of thyroid disease in both the pre and postoperative periods is vital to minimise the risk of development to thyroid storm following acute trauma or surgery.

**Methodology:** A case report describing the rapid progression from a subclinical thyrotoxic state, to disabling Graves' disease with thyrotoxicosis and bilateral dysthyroid orbitopathy in the postoperative period. The case describes a 67-year-old female smoker, admitted electively on urgent basis for an open, high anterior resection for a rectal sigmoid adenocarcinoma who presented postoperatively with a persistent sinus tachycardia, palpitations and bilateral exophthalmos.

**Discussion:** Initial thyroid function tests demonstrated a free T4 52.3 pmol/l and TSH < 0.05 mU/l, with TPO and TSH antibody levels raised at 176 IU/ml and 9.5 IU/l respectively. A Burch-Wartofsky-Score was 35 prior to successful medical management with 10mg propranolol and 30mg carbimazole daily. Closer investigation into her medical history highlighted a 12-month history of subclinical thyroid disease in addition to a previous occurrence of thyrotoxicosis postoperatively to a total abdominal hysterectomy and bilateral salpingo-oophorectomy.

**Conclusions:** This case highlights the importance of careful preoperative assessment and appropriate management of thyrotoxicosis in addition to the implications in the postoperative period of uncontrolled thyroid disease. It demonstrates that acute trauma can precipitate clinical progression to thyrotoxicosis from a subclinical state. It also raises the question of appropriate investigation and management of subclinical thyrotoxicosis in the urgent preoperative setting.

### Hereditary Angioedema Presenting as Acute Appendicitis – A Case Report

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**Background:** Hereditary angioedema (HAE) is an autosomal dominant disease characterised by self-limiting, tissue oedema. Mutations of the C1-inhibitor gene causes unmoderated activation of the complement cascade. When this tissue swelling affects the GI tract, abdominal attacks can present with severe pain. First-line treatment is with plasma-derived C1-inhibitor (pdC1INH) but as this is not widely available fresh frozen plasma (FFP) is commonly used.

**Discussion:** We report the case of a 17 year old girl with HAE, which had previously manifested with facial and leg oedema. She presented with a 10 hour history of periumbilical pain radiating to the right iliac fossa, anorexia, nausea and vomiting. Blood tests showed a leucocytosis, white cell count of 16.5, and C-Reactive Protein of 6. A diagnosis of acute appendicitis was made and she underwent a laparoscopic appendicectomy with 2 units of FFP preoperatively. Operative findings showed a macroscopically normal appendix but extensive serous abdominal fluid and an oedematous jejunum/proximal ileum. Post-operatively her symptoms resolved and she was discharged the next day. Histology revealed a normal appendix.

**Conclusion:** We suggest that in patients with a family or personal history of HAE, an abdominal CT scan should be performed in suspected appendicitis to avoid inappropriate operative intervention. We also highlight the importance of taking a formal family history as part of a surgical workup. Surgical awareness of this medical cause of acute abdomen needs to be encouraged with greater availability of pdC1INH. In time, evidence based guidelines will need to be developed for the management of HAE

### Bilateral Facial Nerve Palsy

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**Introduction:** Facial nerve palsy (FNP) is characterised by ipsilateral facial asymmetry, loss of taste of anterior two-thirds of tongue and abnormal eye closure. In contrast to its unilateral counterpart, bilateral FNP occurs infrequently but commonly signifies more serious systemic disease.

**Case study:** We report an interesting case of acute onset of bilateral FNP in a 25 year old female patient with hypothyroidism and recently diagnosed type 1 Diabetes Mellitus. She presented with facial weakness following a non-specific prodrome and developed generalised weakness, numbness and paresthesia, affecting the upper limbs more than the lower limbs. Thorough investigation revealed the only abnormality to be elevated protein and glucose in her cerebrospinal fluid. She was therefore treated for suspected Guillian-Barre syndrome (GBS).

**Discussion:** Bilateral FNP is thought to manifest from underlying systemic disease in contrast to Bell's palsy which is usually idiopathic. The vast differential diagnoses necessitate thorough clinical evaluation and extensive investigation to exclude life threatening causes such as Lyme disease and GBS. Despite the atypical nature of her presentation, her facial paralysis and neurological symptoms slightly improved with intravenous immunoglobulins and steroids. She was discharged with residual bilateral facial paralysis with complete resolution of all her other neurological symptoms.

**Conclusion:** Bilateral FNP commonly manifests as part of an underlying systemic condition. Prognosis of Bilateral FNP is heavily influenced by the aetiology therefore thorough investigation and empirical treatment of life-threatening conditions such as GBS is fundamental to the timely, effective management of these patients



**DCIS Recurrence With Microinvasion: A Case Study**

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Breast cancer accounts for the most diagnosed malignancy in women across the globe, also being the second highest cause of cancer mortality in this sex group. Ductal carcinoma in situ (DCIS) only accounted for around two per cent of carcinomas found in the breast 25 years ago, before the National Health System began screening for breast abnormalities using mammography. Since this time the incidence of diagnosed DCIS cases has risen by over ten times this figure. A 57 year old woman with a five year history of DCIS is found to have high-grade recurrence of the condition, and is given the option of a fourth surgery to remove malignant foci discovered in her right breast. Some research suggests DCIS over time can progress to invasive breast cancer (IBC), while other studies argue otherwise, and believe too much focus is placed on low-grade DCIS cases. This case raises awareness of the concept that DCIS can often be over-treated, however sometimes as in this patient, radical surgery may be the only option to remove all risk of pathological recurrence.

**"An uncommon manifestation of Alpha-1-antitrypsin deficiency"**

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A 29 year old female presented with a 4 years history of recurrent painful nodules on her legs and arms, which worsened after she gave birth 8 months prior.

On examination, there was a deep overhung and purple edge ulcer noted on the right medial calf with indurated plaques on the legs and scars from previous lesions suggestive of either a liquefying ulcerating panniculitis or pyoderma gangrenosum.

Biopsy of a lesion showed mild fibrosis and perivascular infiltrate, composed of lymphocytes, histiocytes and eosinophils. Septal and lobular panniculitis with fat necrosis were noted in the subcutis, with foamy macrophages, histiocytes, scattered lymphocytes and eosinophils with lipophagic granulomas.

Alpha-1-antitrypsin (A1AT) level was low at 0.26g/l (1-2.1). The patient was diagnosed with panniculitis secondary to A1AT deficiency. A1AT Pi testing revealed the patient was PiZ. The patient was initially treated with steroids and subsequently doxycycline, which stopped her flare ups.

Alpha-1-antitrypsin is mainly synthesized in the liver and is a principal protease inhibitor in the serum. Its deficiency presents in different forms, typically panacinar emphysema but also as liver cirrhosis, noninfectious hepatitis and persistent vasculitis. Although the classical histopathology of A1AT deficiency associated panniculitis is neutrophilic panniculitis, late stages may present with scarring and fibrosis, as in this case.

The aim of the treatment is to correct the protease-antiprotease imbalance. Oral Dapsone is commonly used as the first-line treatment, as it interferes with myeloperoxidase which inhibits anti-trypsin. Tetracyclines can also be used, and alpha-1-protease inhibitor is commonly reserved for severe resistant cases.

### Lemierre's Syndrome secondary to Group A Streptococcus: a case report

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Lemierre's syndrome, or postanginal sepsis, is a rare clinical entity in which an oropharyngeal infection leads to thrombophlebitis of the internal jugular vein (IJV) with subsequent bacteraemia and septic embolization. The classical pathogen ascribed to Lemierre's syndrome is the bacterium *Fusobacterium necrophorum*, a gram-negative anaerobe. However, although extremely rare, other bacteria have now been cultured in isolation in patients with Lemierre's syndrome. This may reflect difficulties in culturing *F. necrophorum* or may support the role of other bacterium in the pathogenesis of this condition. The case presented here is of a 2-year-old boy with thrombophlebitis of IJV and sigmoid sinus. A diagnosis of Lemierre's syndrome was made following computed tomography imaging and Group A *Streptococcus* was the only bacterium isolated in culture. The patient was treated with antibiotics and LMW heparin and made a full recovery. The scientific literature of Lemierre's syndrome is reviewed and discussed in the context of the intriguing and rare case presented here.

### Two Interesting Cases of Takotsubo's Cardiomyopathy: Typical and Variant

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**Background:** Takotsubo cardiomyopathy, also known as stress cardiomyopathy and transient left ventricular (LV) apical ballooning syndrome, is a unique relatively rare syndrome initially described in 1991. It is characterised by transient LV dysfunction, chest pain with or without associated dyspnoea, electrocardiogram changes often ST-segment elevation, T wave inversion and pathological Q waves, and finally an elevation of cardiac enzymes importantly, in the absence of any obstructive coronary artery disease.

**Discussion:** This case report describes two interesting cases of takotsubo cardiomyopathy the first in a 60-year-old woman who was diagnosed with an 'atypical' variant; LV angiography showed moderately impaired LV function, significant ballooning and hypokinesia in left ventricular basal segments. The second in a 72-year-old woman with 'typical' takotsubo characteristics on LV angiogram; apical ballooning with marked left ventricular systolic dysfunction at the apex and apical regions. Both were admitted after stressful events and were initially treated as acute coronary syndrome (ACS) and later were finally diagnosed with takotsubo cardiomyopathy after angiography showed normal coronary arteries.

**Case summary/Conclusion:** Takotsubo cardiomyopathy is an important differential diagnosis of patients presenting with ACS which all clinicians should be aware of especially in post-menopausal women over the age of 50 with a recent stressful event. The vast majority of patients have a complete recovery and normal LV function returns within days to weeks, it also very rarely reoccurs. Treatments involve empirical medication therapy which should be tailored to patient's individual symptoms.

**New onset Schizophrenia in adolescents – A diagnostic challenge**

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**Background:** Schizophrenia has an insidious onset in childhood & adolescence and as the symptoms overlap with metabolic, developmental, behavioral, and cognitive disorders, the diagnosis can be challenging. We share our experience of such a case where schizophrenia was diagnosed with great difficulty.

**Case report:** An 18-year-old girl was referred to psychiatry, with cognitive decline, and psychotic symptoms. She was born normal with mildly delayed speech, verbal dyspraxia and problem solving difficulties. These symptoms improved with occupational and speech therapist input. There was no family history of psychiatric problem or learning disabilities. Initially parents related her symptoms to the death of her grandfather. She continued to have strange behaviors and delusions when admitted to psychiatric services. Her IQ was 57. She was started on anti-psychotics, which improved symptoms but she developed a rash and alopecia necessitating stopping of medications. She was referred to neuro-psychiatric and metabolic services and was found to have risen ANA, it was thought to be related to inflammatory disorder of CNS. She was commenced on cyclophosphamide and prednisolone for six months with plan to continue on Methotrexate. After six months, patient showed no significant improvement and the investigations were inconclusive. The case was discussed in MDT and help was sought from department of Psychiatry with learning disabilities. She was eventually diagnosed to have hebephrenic schizophrenia. The methotrexate was stopped and the patient showed symptomatic improvement with Clozapine.

**Conclusion:** A multidisciplinary approach is crucial in the early diagnosis and management of adolescent onset schizophrenia

**The 'Start Time Matrix': Did it work, or is it common sense after all?**

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Upper extremity deep vein thrombosis (UEDVT) is a rare occurrence in healthy individuals without a pre-existing anatomical abnormality or haematological predisposition. We report a case of bilateral UEDVTs in a young, otherwise healthy patient undergoing conservative management (figure-of-eight bandaging) for bilateral closed mid-shaft clavicle fractures. Four days following the initial injury he presented with increased pain and swelling around both shoulders and arms. Doppler ultrasonography demonstrated bilateral UEDVTs. He was commenced on anticoagulant therapy and his figure-of-eight bandage was removed. His symptoms settled and he made an uneventful recovery.

UEDVT can be associated with significant complications such as pulmonary emboli and post phlebotic syndrome..Cases of UEDVT have been reported previously in orthopaedic patients, but predominantly in the context of arthroplasty or trauma of the shoulder joint. This is the first documented occurrence of bilateral UEDVT in the context of clavicle fracture. Endothelial damage and a hypercoagulable state associated with the initial injury are proposed as possible aetiological factors. We hypothesise, in addition, that venous stasis resulting from an ill fitting figure-of-eight bandage is a likely contributory factor.

Clinicians treating patients with figure-of-eight bandaging should remain vigilant for UEDVT and initiate treatment promptly given its significant morbidity. Appropriate application without inadvertent constriction of the upper limb venous system must be ensured. Furthermore, use of a simple sling should be considered as treatment outcomes are comparable between.

### Undiagnosed Systemic Lupus Erythematosus in a 25 year old male requiring multi-organ support in intensive care

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This case report describes an atypical presentation of SLE and the complicated task of obtaining the diagnosis in a patient without previous signs or symptoms. Although the diagnostic conundrum of SLE is well documented, the challenges of each case are important to describe in order to improve its diagnosis.

A 25 year old male was admitted with nausea, vomiting, pyrexia, and lethargy present for 3 weeks. Over a further 1 week period he developed tachycardia, dyspnoea, hypotension, type 1 respiratory failure, tonic clonic seizures, pancytopenia, elevated bilirubin and liver transaminases, lactic acidosis, a pericardial effusion, axillary lymphadenopathy and acute kidney injury.

Investigations ruled out a pulmonary embolus, intra-abdominal and infectious bowel pathology, hepatitis, infective endocarditis, bacterial meningitis, lymphoma, malaria, EBV, HIV, CMV, syphilis, thyroid dysfunction and autoimmune haemolytic anaemia as the causative pathology.

The patient spent 4 weeks in intensive care for supportive treatment of his multi-organ dysfunction (respiratory, cardiovascular, hepatic and renal). Anti-TB treatment was commenced but a definitive diagnosis remained elusive. Immunological investigations highlighted antibodies present to dsDNA (elisa), Ro, smooth muscle and RNP, with negative antibodies to La and dsDNA crithidia. ESR was elevated, with a normal CRP. Examination did not elicit any signs of SLE and the patient denied previous symptoms of the disease. Corticosteroid treatment was initiated for a diagnosis of SLE based on the laboratory findings.

**Summary:** This case highlights an atypical presentation of SLE, one which required a lengthy intensive care stay with multi-organ support in a young, previously fit and well man.

### Lessons Learnt from Management of Chest Injuries in Gaza City

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**Background:** Chest injuries account for 20-25% of deaths due to trauma and contribute to 25-50% of the remaining trauma-related deaths.

**Aims:** To study mechanisms of injury, presentations, diagnosis, triaging, management and outcome of chest injuries at Al Shifa' Hospital.

**Methods:** We retrospectively reviewed management and survival as the main outcome measure of 183 consecutive chest injuries presented to Al Shifa Hospital between 2010 and 2012.

**Results:** 85% were males with average age of 30.53 years. 68 cases had deep penetrating chest injuries (PCI). The mechanisms of injury included gunshot- or blast- related (GSI, BRI) in 34 cases, stab injuries (SI) in 43 cases, traffic accidents in 27 cases, 46 falls from height, altercations in 28 cases and 5 others. 172 victims sustained a lateral or thoracic (T) injury, 3 patients suffered a central or mediastinal (M) injury while 8 sustained combined lateral and central injuries (T+M). 32 of the first group (T) were treated surgically with thoracotomy +/-laparotomy, and chest tube (CT). In the second group (M) the pericardium, the heart or any of the great mediastinal vessels were involved and the 3 were managed surgically. The 8 in the third group (T+M) were managed surgically. One died in the thoracic group, none in the mediastinal group and 3 in the (T+M) with overall peri-operative mortality of 2.2%. Survival in patients presented alive with recordable systolic blood pressure (SBP) on arrival was approximately 99.4%.

**Conclusions:** An expeditious surgical intervention in life-threatening thoracic trauma save lives. Mixed thoracic and Mediastinal blunt chest injuries are poor prognostic indicators.

**Macrophage Activation Syndrome presenting as a complication of Adult Stills Disease**

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Adult Stills disease (ASD) is a systemic inflammatory disorder of unknown aetiology which typically affects 16-35 year olds. Rarely, it may be complicated by the development of Macrophage Activation Syndrome (MAS), a multisystem inflammatory syndrome caused by massive cytokine release from activated lymphocytes and macrophages. This report describes the case of a 31 year old nurse who presented with a 3 week history of arthralgia, myalgia, fever and sore throat. ASD was diagnosed and the patient commenced on oral Prednisolone. The patient was readmitted 7 days later following 3 days of significant diarrhoea and deterioration in symptoms. The patient was haemodynamically unstable. Serum ferritin was grossly elevated and liver function tests significantly deranged. Haemoglobin and platelet count fell acutely with associated hypo-fibrinogenaemia and coagulopathy. A bone marrow biopsy demonstrated haemophagocytosis. A diagnosis of MAS was made. The patient was transferred to ICU where she received an IV immunoglobulin infusion and packed red cell, cryoprecipitate and FFP transfusion. IV Methylprednisolone was continued and Cyclosporine commenced. She stabilised on this therapy. To treat the underlying problem of ASD the patient was commenced on the Interleukin-1- receptor antagonist Anakinra. She improved markedly over the course of the next week and continued to remain well with ASD in remission at 4 month review.

This case adds to the growing evidence base regarding treatment of MAS and ASD. It highlights that the clinical picture of MAS may mimic sepsis and must be considered as a differential diagnosis in an unwell patient with underlying autoimmune/inflammatory disease.

**Plasmapheresis; a main treatment for Thrombotic Thrombocytopenic Purpura**

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**Background:** Although thrombotic thrombocytopenic purpura is not a common disease, it still has serious complications especially on the neurological and renal systems. The use of plasmapheresis shows a powerful effect for treatment.

**Discussion:** A 42 years old Caucasian woman patient, named H. A. A., showed neurological manifestations in the form of: heaviness of the right upper limb as well as heaviness in the tongue and then loss of consciousness. Complete blood count and other investigations were done and revealed thrombotic thrombocytopenic purpura. The patient received the usual treatment in the form of blood, fresh frozen plasma and platelets transfusion but she did not improve. After plasmapheresis, the patient showed significant improvement.

**Conclusion:** Plasmapheresis was proved by trial to be an effective method for treatment of the thrombotic thrombocytopenic purpura.



**Decidualisation of ovarian endometriomas in pregnancy: a management dilemma. A case report and review of the literature.**

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Complex ovarian masses in pregnancy are uncommon with endometriomas accounting for approximately 11.5% of these lesions. During pregnancy increased progesterone levels may result in decidualisation of endometriomas, which occasionally mimic malignancy on imaging resulting in a management dilemma.

An ovarian cyst was noted on USS in a 33 year old woman at 12 weeks gestation. Reviewed at 16 weeks, suspicious features remained on imaging and CA-125 was elevated to 77u/ml. Serial monitoring undertaken; at 18 weeks gestation, TVS and MRI showed a unilocular mass of increasing size with features suggestive of early ovarian malignancy. Extensive debate ensued at gynaecology multi-disciplinary team meeting regarding the nature of the mass and close surveillance recommended. The cyst was monitored throughout pregnancy with serial TVS 4 weekly and repeat MRI with intervention reserved if patient became symptomatic. Caesarean section at 38 weeks delivered a healthy male neonate. Frozen section of the ovary was benign and histology confirmed a decidualised endometrioma and benign dermoid cyst.

Literature search was undertaken to evaluate existing evidence for decidualised ovarian endometriomas in pregnancy. 14 papers were identified reporting on 26 cases excluding the index case.

Surgery during pregnancy offers histological diagnosis but may introduce risks to mother and fetus; conservative approach is worrisome but avoids interventions during pregnancy. Elective caesarean section following monitoring throughout pregnancy may bridge the gap between surgical and purely conservative approaches.

Limited evidence makes a definitive decision regarding management difficult; however, decidualisation should be considered as a differential for suspicious ovarian lesions in pregnancy.

## Poster Presentations

### Re-audit of potential antidepressant adverse drug

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Previously, our audit of NICE Guidelines (CG91) demonstrated that antidepressants are co-prescribed with medications that could cause adverse drug reactions. We re-audited prescribing to assess the impact of the following action points after 6 months: teaching hospital doctors about common antidepressant drug interactions; including information about potential drug interactions in discharge summaries.

Data was collected by pharmacists on one day from all patients prescribed an antidepressant using a revised audit tool. Prescribed medications and information regarding history of upper gastrointestinal haemorrhage (UGIH) or confusion in patients on certain drugs were collected from patient notes.

83/845 patients (10%) were prescribed an antidepressant. Most antidepressants were prescribed prior to admission. More patients were co-prescribed an NSAID/aspirin and an SSRI/SNRI in the re-audit. 8/83 (10%) patients had a history of an UGIH. 19/83 were prescribed an SSRI/ SNRI and aspirin or an NSAID. 2/19 (10%) of these patients had a history of UGIH and only one of these patients was co-prescribed gastro-protective cover. Fewer patients were co-prescribed an SSRI/SNRI/TCA and tramadol in the re-audit (26% vs. 18%). 23/83 patients had a history of confusion during this admission. 4/23 (17%) were over the age of 65 and taking amitriptyline.

This re-audit shows that potentially hazardous co-prescribing with antidepressant medication continues in the UHBT. This highlights the need for training GPs, since most antidepressants were prescribed before admission. By identifying potential adverse events from hazardous co-prescribing, it demonstrates the importance of auditing this practice and implementing change.

### Pre operative fluid management: Staff and patient knowledge and effect on renal function

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**Background:** With fast-track operations and discharges becoming more popular a closer look at medical care, pre and post operatively, recently changed fluid guidance. Guidance now states fasting time for clear fluids is 2 hours (1). This was an audit to assess knowledge of healthcare staff and patients regarding pre-operative fluid fasting prior to elective hip and knee replacements.

**Design:** Questionnaires to staff and patients regarding fluid fasting. For staff this included knowledge of national and local guidelines and the importance of fluid management. For patients this assessed their fluid intake pre operatively and knowledge of fasting information. Renal function was checked pre and post operation using urea and creatinine.

**Results:** Cycle one found that 81.8% of staff knew the guidelines whilst only 38% of patients understood the guidance. It found an average fasting time of 6.37 hours. Cycle two introduced a patient leaflet on admission and reduced fluid fasting times to 4.8 hours. It also found that those who fasted longest were those first on the list- usually those with greater co-morbidities. No significant correlation was found between renal function and fluid fasting though encouraging good pre-operative hydration has been shown to 'improve patient well being' (2) and aid 'enhanced recovery'. (3)

**Conclusion:** Clear information on admission regarding fasting is beneficial as pre assessment information may have been forgotten or overlooked during the waiting period.

### Do Cystic Fibrosis (CF) patients who visit the dentist regularly have a better lung function?

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**Aims:** The audit aims to determine whether CF patients under the care of the University Hospital Southampton CF team, visit the dentist regularly and it's impact on their pulmonary health.

**Background:** At annual reviews, all CF patients are asked whether they visit the dentist regularly and are offered advice on the importance of dental hygiene. Although little evidence is present on the origin of bacteria in the lungs of these patients, some theories suggest that the bacteria could be first colonised in the oropharynx and subsequently enter the lungs. Therefore, the CF team has incorporated a plan to ensure that all patients are counselled about the benefits of good oral hygiene.

**Methods and Results:** Annual reviews of 173 patients were accessed using online database. Simple bar chart was used to compare the number of patients visiting the dentist and whether they were given advice about the benefits of dental hygiene. 69% of the patients visit the dentist every 6 months (median=2.15, IQR=1.40). 31% of patients did not visit the dentist (median=2.60, IQR=1.57). 92% of the patients were counselled about the benefits of dental care. Using independent t-test, there was no statistically significant difference ( $p=0.992$ ) in  $FEV_1$  whether patients visited the dentist or not.

**Conclusion:** Most patients were successfully given advice about dental care and regular checkups. Even though, the relationship between lung function and dentist visits was not statistically significant, it is important for patients to look after their oral hygiene to prevent the oropharyngeal bacteria from entering the lungs

### Sepsis events after Transrectal Ultrasound guided (TRUS) prostate biopsy at The Royal Bournemouth Hospital

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**Background:** The British Association of Urological Surgeons (BAUS) quotes a 2% septicaemia complication rate and a 10% urinary tract infection (UTI) rate post TRUS prostate biopsy in men undergoing investigation of suspected prostate cancer. An audit of our sepsis rates for this procedure was commenced at the Royal Bournemouth Hospital (RBH), during which the antimicrobial guidelines were changed and the impact assessed.

**Methods:** Retrospective audit of 579 consecutive cases identified over a seven month period. The individual records of all cases investigated for UTI and sepsis within 30 days of their procedure were retrieved and data collated.

**Results:** Out of the total 579 patient cohort, 14 (2.4%) were readmitted with septic complications. With our original prophylactic antibiotic therapy pre-procedure (ciprofloxacin 500mg and metronidazole 400mg), 10 out of 279 (3.6%) patients were readmitted with sepsis. After increasing the ciprofloxacin dosage to 750mg this then fell to 4 out of 300 (1.3%) patients. Median interval from biopsy to hospitalisation was 48 hours. An 83% ciprofloxacin resistance was identified from the microbiology blood culture results.

**Conclusion:** The change in antibiotic prophylaxis policy appears to have lowered our sepsis complication rate to less than the BAUS standard. Currently a re-audit is being undertaken for the next cycle of data.

The high prevalence of fluoroquinolone resistance demonstrated from this audit is concerning and has also been reported in other series. To address this, data has been shared and discussions are currently underway with our microbiologists to examine this in more detail.

**A study to assess Foundation Year (FY) doctor handover procedure**

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**Background:** General Medical Council guidance states FY doctors must have formal handover and local induction at the beginning of placements. This is reinforced by the National Health Service Litigation Authority who recognise lack of inductions to new placements may lead to mistakes, ultimately compromising patient safety. This study aimed to assess first year FY doctors (FY1s) handover procedure and attitudes at a teaching hospital.

**Method:** An anonymised 9 point questionnaire was given to 36 (FY1) doctors at a teaching hospital to complete, of which 28 were returned. The results and comments were collated in an Excel spreadsheet, interpreted and relayed to both the postgraduate co-ordinators and sample group.

**Results:** All FY1s agreed that they would benefit from a handover, and all but 2 agreed a basic performa would help facilitate this. Of the 28, 92% received some sort of handover, and the majority of FY1s who did not write a handover stated it was because they didn't have enough time to complete one. 68% wished their handover documents to be kept private from postgraduate staff. Common complaints in the comments section included insufficient patient list handover. 2/3 of FY1s did not feel their predecessor had enough time to run through their written or verbal handover.

**Discussion:** This study showed the majority of FY1s want a handover, and feel they would benefit from protected time to both write and receive placement handover- be it verbal or written handover. Better handover may ensure greater confidence and reduce mistakes made in new placements

**The diagnostic work up of stable chest pain at the UHW**

Sen G

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**Background:** Chest pain (CP) needs a prompt diagnosis. NICE published new guidelines in 2010, proposing a new method for the assessment of stable CP. The aims were to compare the assessment of stable CP at the UHW with the NICE guidelines.

**Methods:** The audit was undertaken by retrospectively reading clinic letters of patients having coronary angiograms (CA). The letters were used to determine the type of CP, cardiovascular risk-factors and ECG details. The likelihood of coronary artery disease (CAD) was calculated as published by NICE.

Depending on the calculated CAD risk probability, the NICE-suggested investigation was determined: No investigations (<10% risk), calcium scoring (CS) (10-29% risk), functional imaging (30-60% risk), CA (60-90% risk), treat as angina (>90% risk). To compare the deviance from NICE, the actual investigations undertaken for each patient were noted.

**Results:** 299 patients were included. 178 met the audit criteria of having CP; 61% male; median age 65 (range 37-88) years. 97 (54%) had exercise tolerance test (ETT), 14(8%) functional testing and 67(38%) angiogram, a large deviation from the NICE guidelines. According to NICE 4% should have had no investigation, 8% CS, 11% functional imaging, 23% CA and 53% should have been treated as angina.

**Conclusion:** If the NICE guidelines were implemented at the UHW, functional imaging and CA would be the main investigations required for assessing stable CP, and ETT would be disregarded. This would mean a dramatic change in how stable CP is being assessed and would be a huge financial burden on the NHS.

### Impact of trainee involvement with robotic-assisted radical prostatectomy

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**Background:** Robotic-assisted surgery has been rapidly adopted within urology. The challenge is to effectively train residents and fellows to perform robotic-assisted surgery without compromising outcomes. We evaluated the perioperative outcomes of trainee involvement with robotic-assisted radical prostatectomy (RARP) within our institution.

**Methodology:** We retrospectively reviewed RARP cases performed between 09/2008-12/2010 using a single da Vinci robotic platform. Trainees consisted of urology residents and fellows who operated with staff surgeons on select operating days, whereas two staff surgeon teams performed RARP on alternate days. We compared clinicopathologic variables: operating time, estimated blood loss, surgical margin rates, complication rates between the trainee and staff-only surgeon groups.

**Discussion:** Overall, 1019 RARP surgeries were performed within this period and trainee participation was 16% (162 cases). Clinical characteristics were similar between both cohorts. Positive surgical margin rates were lower for patients with pT2 disease for cases with trainee involvement (11 vs. 19 %,  $p = 0.02$ ), although overall margin rates and margin rates for patients with pT3 disease were similar between the groups ( $p = 0.34$ ). Cases involving trainees were longer (241 vs. 200 min,  $p < 0.001$ ), resulting in higher estimated blood loss (190 vs. 120 mL,  $p < 0.001$ ) than the two staff surgeon cases. However, transfusion rates, intraoperative and postoperative complication rates didn't differ significantly between groups.

**Conclusions:** Surgical margin rates were lower in teaching cases for patients with pT2 disease. Importantly, trainee involvement in RARP is safe with similar perioperative outcomes to staff-only surgical cases. This information may be useful for training and surgical planning.

### Rosai-Dorfman disease and oligoarthritis: a case report

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Sir, we submit a case report of a 41-year-old woman with sinus histiocytosis with massive lymphadenopathy (SHML, Rosai-Dorfman disease), who presented with cervical lymphadenopathy and inflammatory joint pain for 2 weeks. Her history included spiking fevers with profuse night sweats, and travel to Asia in the last 3 months.

On examination, she had gross cervical lymphadenopathy, and boggy swelling around her right elbow and ankle, which were both hot and tender on palpation. Aspiration of the elbow showed numerous leukocytes with no crystals or organisms seen. Histological examination confirmed large histiocytes with abundant foamy cytoplasm engulfing lymphocytes and plasma cells (emperipolesis). Immunohistochemistry illustrated these to be CD68- and S100-positive, indicating so-called SHML cells.

This is a rare, but well-defined disorder with only a handful of case reports showing association between SHML and clinical joint disease. The aetiology is unknown, and although the clinical manifestations and histological appearance are suggestive of an infectious process, no micro-organisms have yet been identified. The clinical picture suggests a reactive arthritis, T-cell lymphoma or a systemic inflammatory condition leading to arthropathy.

Given the rarity of the condition, the non-specific symptoms affecting multiple sites and frequent absence of cervical lymphadenopathy, clinicians often do not consider SHML in their differential diagnosis. This results in inappropriate treatment of this benign but sometimes progressive disease. In our patient, her symptoms improved with a course of naproxen and she was discharged 5 days later.



**Polypharmacy in a Scottish District Hospital**

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Polypharmacy is defined as co-prescription of  $\geq 4$  drugs. 80% of people aged  $>75$  years take a prescription medicine and 36% receive polypharmacy. Adverse drug reactions (ADR) are implicated in 5–17% of hospital admissions, and are particularly common in frail older adults. Three important areas in drug review are high-risk combinations, drugs poorly-tolerated in frail adults and drugs that may require discontinuation when dehydrated.

We reviewed admission and post-admission prescriptions for 100 consecutive admissions to an Acute Medical Unit in January 2013. For all patients taking  $\geq 12$  drugs on admission, we recorded age; gender; likelihood that an ADR caused admission; high-risk drug combinations; drugs poorly-tolerated in frailty; and drugs for review in dehydration. These last three were defined by the 2012 Polypharmacy Guideline.

2 patients died and 5 were discharged before data verification, leaving 93 complete sets. 45 (48%) were male. Mean age was 66 years: 58 (62%) were  $\geq 65$  years and 38 (41%) were  $\geq 75$  years. Median prescriptions at admission were 8. 76 (82%) were taking  $\geq 4$  drugs and 17 (18%) were taking  $\geq 12$ . 1/17 (6%) had an ADR: acute-on-chronic kidney disease triggered by fever whilst taking an ACEI with diuretic. 4/17 (25%) had high-risk combinations (NSAID, ACEI and diuretic; Warfarin plus azole; Warfarin plus macrolide; Warfarin plus Aspirin and Clopidogrel). 15/17 (88%) had drugs poorly-tolerated in frailty, including combination analgesics and anticholinergics. 13 (76%) dehydrated patients were prescribed drugs requiring review (ACEI, ARB, NSAID, diuretics and Metformin).

This review highlights the importance of careful drug review at admission.

**Ipsilateral Translaminar Screws inserted Bilaterally with Rod-to-Rod Connectors in Occipitocervical Fusion: A Technical Note with Case Series**

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**Objective:** We describe a novel technique of C2 translaminar screw insertion which is simple to execute, safe and enables rigid fixation with a rod construct. A case-report of 2 patients that underwent this technique was compiled to assess technical issues and patient outcomes post-operatively.

**Technique:** With a posterior approach, the spinous process of C2 vertebra is decorticated and used as an autograft for fusion. Translaminar screws are then inserted bilaterally in an ipsilateral fashion. This method improves accuracy by enabling direct visualization of the screw pathway during drilling. As the screw heads lie very medially, this makes it difficult to incorporate into the usual Occiput to C3 (or distal) rod. The use of a screw to rod connector makes this easy without having to contour the rod excessively. The risk of a laminar breach into the canal is less likely. For added stability, crosslinks are used in the construct. Iliac crest bone graft was used to promote speedy union.

**Case Report:** Two patients who underwent Occipitocervical fusion with this technique were reviewed. One had a combined occiput-C1 and C1-C2 dissociation while the other had a displaced C1/C2 fracture dislocation.

**Conclusion:** Occipitocervical fusion with bilaterally inserted ipsilateral translaminar screws into C2 vertebra was demonstrated to be safe, less technically demanding than the crossed technique, with improved accuracy in screw insertion due to better visualization. This lowers the risk of laminar breach and resultant damage to the spinal cord. Stability and rigid fixation is rendered by the screw-to-rod connector, thereby promoting fusion.

### Reversal of loop Ileostomy – A review of outcomes

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**Aims:** Major complications following loop ileostomy reversal can occur in up to 9% of cases. The aims of the study were to assess outcomes following loop ileostomy reversal in our unit.

**Methods:** Retrospective review of consecutive patients undergoing elective loop ileostomy reversal between Jan 2006 to Jan 2013. Demographic data, anastomotic technique, length of stay, complications and 30-day mortality were recorded.

**Results:** 67 patients underwent elective loop ileostomy reversal over the time period. 45 were male and 22 were female. Median age was 65 years (range 20-83). Indication for the ileostomy formation was low anterior resection for rectal cancer in 54 cases, ileo-anal pouch formation for Inflammatory Bowel Disease in 7 cases, and 6 miscellaneous cases. Median length of wait between ileostomy formation and reversal was 266 days (range 49-1317 days). Length of wait for reversal was not affected by post-operative chemotherapy, radiological leak or stricture formation requiring repeated dilatation ( $p=0.4555$  unpaired t-test). Hand sewn anastomosis was performed in 13 cases and stapled in 54 cases. Median post-operative length of stay was 5 days (range 1-23). 4 patients had anastomotic leaks and 2 had bowel obstruction requiring intervention; resulting in a major complication rate of 4.02% (Clavien-Dindo Classification III-V). No statistically significant difference was seen between anastomotic technique and major complication ( $p=0.5743$  fisher exact test). 30-day mortality rate was 0%.

**Conclusions:** Median length of wait between loop ileostomy formation and reversal was eight months. Our major complication rate following reversal of loop ileostomy was comparable to published data. There was no significant difference in major complication rate comparing anastomotic techniques

### Beyond the ABC approach: A preliminary cross-sectional study highlighting gaps in understanding of paediatric trauma management

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**Background:** Most training for Paediatric trauma is focused on the Airway, Breathing, Circulation (ABC) approach; a clinical model for resuscitation in emergencies. In many hospitals, the Paediatric trainee doctor has a key role in trauma management, but their level of understanding has rarely been investigated before.

**Method:** This cross-sectional study examined the working knowledge of trauma management in a cohort of 25 Paediatric trainees. Each participant completed a timed, unannounced question paper before a teaching session on trauma. The test was designed to examine areas of the ABC model and beyond, including mechanisms of injury and coagulopathy. The tests were marked anonymously by an invigilator with a defined mark scheme, as agreed with a Paediatric Intensive Care consultant.

**Results & Discussion:** The results showed strengths in airway and breathing management as emphasised in the ABC model with an average mark of 76%. However, significant gaps in knowledge were identified in basic mechanisms of injury, coagulopathy in trauma, and C-spine management (average mark of 40%). For example, 9/25 responses stated they would unnecessarily delay giving platelets in trauma until they had a platelet count. A lack of knowledge on *trauma-specific* resuscitation guidelines should be addressed in the trainees' teaching to ensure good patient outcomes.

**Conclusion:** Despite the preliminary nature of this work, it suggests important gaps in the understanding of trauma pathophysiology and management amongst paediatric doctors. Further baseline assessment and re-appraisal is urgently required to guide training and revalidation in these areas, especially around coagulopathy and management of bleeding.

**Investigating the Role of Matrix Metalloproteinases (MMPs) and Heat Shock Proteins (HSPs) in Postpartum Uterine Involution**

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**Background:** Following labour, the uterus rapidly returns to its pre-pregnancy state in a dynamic process known as postpartum uterine involution. Exact mechanisms underlying labour and postpartum involution are not fully understood but inflammation is understood to play a key role. It has been hypothesised that rather than initiating or propagating labour, inflammation may prime the uterus for extensive postpartum tissue repair and remodelling, in a manner akin to repair in exercising skeletal muscle. MMPs and HSPs are known to play a role in skeletal muscle remodelling after injury. Little is known about their role in the postpartum myometrium and this study aims to examine the expression of mRNA for MMPs (MMP2, MMP8, MMP9) and HSPs (HSP70, HSP27, HSP60, HSP90) in the postpartum mouse uterus.

**Methods:** Uterine tissues of C57BL/6 mice were collected at Day 1 (n=5), 4 (n=6) and 7 (n=5) postpartum. Virgin females (proestrous stage) were used as non-pregnant controls (n=5). mRNA expression was determined by qRT-PCR. Differences were analysed by Kruskal-Wallis test, followed by Dunn's Multiple Comparison Test.

**Results:** A 3-fold increase in expression of Hspb1 (HSP27) at Day 7 postpartum (p=0.04) and Mmp8 at Day 4 postpartum (p=0.03) compared to non-pregnant samples was found. Expression of all other genes examined remained unchanged throughout the postpartum period.

**Conclusion:** HSP27 and MMP8 may have a role in postpartum uterine involution. This study provides a foundation for future research into the potential role of these proteins during the physiological process of uterine involution and muscle damage repair and remodelling

**RIF pain an unusual presentation of stercoral perforation of the sigmoid colon: Case report and extensive literature review.**

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**Aims:** We recently treated a 45 year old woman who presented with acute right iliac fossa (RIF) pain. At laparotomy she was found to have stercoral sigmoid perforation secondary to chronic constipation. Stercoral perforation is considered rare and information on best management is limited. This paper aims to systematically review the literature on stercoral perforation, reporting on demographics, aetiology, risk factors and management.

**Methods:** A MEDLINE search was performed using the PubMed interface and the search terms: Search (stercoral perforation) AND "case reports"[Publication Type]. Information on age, gender, predisposing factors, anatomical site, surgery, hospital stay, and mortality was extracted.

**Results:** 74 publications matched the search criteria. After exclusion of papers and cases that did not fit the inclusion criteria the data in this paper are based on the information extracted from 55 publications describing a total of 90 cases of stercoral perforation. The median age was 63.2 years (range 4 – 94), 62 were female and 28 male. The most common anatomical site of perforation, was the sigmoid (72%) and least common in the ascending colon (2%). In 58 cases predisposing causes were proposed: 23% were on NSAIDs, 14% taking opioids, 11% anticholinergics, and 5% calcium channel blockers. Fifty cases reported chronic constipation due to: inactivity (14%), neurological (9%), and medications (30%). The majority underwent a Hartmann's procedure and there was an associated mortality of 30%.

**Conclusions:** Stercoral perforation is not as uncommon as is often thought and can present with RIF pain. Most cases are associated with severe constipation and the associated mortality is high

### Patient recruitment and experiences in a randomised control pilot study of supervised exercise training in patients with small abdominal aortic aneurysm

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**Background:** The purpose of this research was to outline the experiences gained from recruiting into a randomised controlled pilot study of supervised exercise training for patients with small AAA, with a view to informing recruitment strategies in future clinical trials. We also invited 6 individuals from the exercise group to take part in a focus group to share their experiences from participating in the study.

**Methods:** The pilot study aimed to recruit 60 patients with early AAA disease, to receive a 12-week programme of moderate intensity exercise or standard care control. Potentially eligible patient were identified at clinics where details were passed on by their clinician or via aneurysm surveillance list from a large NHS trust (Sheffield teaching Hospitals). Consequently they were sent a postal invitation to participate in the study followed by a telephone call if there was no reply to the letter.

**Results:** We identified 545 potentially eligible patients via our recruitment strategy. The response rate to invitation letter was 81.7% (N=445/445), of patients who responded and remained available and interested (N=108) 25.9% (N=28) were eligible to be randomised. 25 patients (89.3% of consenting patients) completed the study over the 12 week period. On the basis of recruitment via invitation letters we estimated the trial recruitment rate amongst eligible patients to be 13.8%.

**Conclusions:** The number of patients randomised was significantly lower than anticipated. We were able to identify and highlight valuable information for planning the recruitment of future trials involving similar populations

### Continuous subcutaneous hydrocortisone infusion in patients with poorly controlled adrenal insufficiency

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**Background:** Three patients with poorly managed adrenal insufficiency were trialled on continuous subcutaneous hydrocortisone infusion pumps on compassionate grounds. All three had previously required numerous hospital admissions for problems associated with inadequacy and adverse effects of oral hydrocortisone therapy.

**Methodology:** Hydrocortisone solution was infused using an insulin pump, and the delivery method was identical to that for continuous subcutaneous insulin infusion into the abdominal wall. Hydrocortisone doses were initially calculated based on body weight and previous oral dose requirements, and subsequently adjusted over a period of weeks, based on initially serum, and then salivary cortisol profiles.

**Discussion:** All three patients reported improved symptom control and had reduced hospital admissions through an eight month follow-up period to date. All reported a significant improvement in symptom control and quality of life. Unlike oral replacement therapy, which fails to mimic the normal circadian rhythm in serum cortisol concentration, continuous subcutaneous infusion delivers near-physiological cortisol replacement, with the added benefit of bypassing first-pass hepatic actions. Delivery pumps can however impose physical restrictions, and are costly. Nonetheless; the reduction in costs associated with less frequent hospital admissions may financially justify the use of such devices.

**Case summary/Conclusion:** In patients with poorly managed adrenal insufficiency, continuous subcutaneous cortisol infusion can be considered as an effective measure to help improve patient quality of life and reduce frequency of hospital admissions .

**Multicomponent Analysis of the Tumour Microenvironment of Early Stage NSCLC Patients Reveals Tenascin-C Expression in Fibroblasts as a significant risk factor in Shortened Post-Operative Survival**

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**Background:** The role of the Tumour microenvironment (TME) in NSCLC remains poorly defined. Nevertheless, the radical success of early trials of PD1/PD-L1 immunotherapy suggests that the TME has a guiding influence on NSCLC disease outcome and points the way for further exploration of TME-targeted therapies. Central TME constituents, cancer-associated fibroblasts (CAFs), can modulate tumour progression through induction of epithelial-mesenchymal-transition (EMT) and subversion of the immune system. Here we investigate correlations between the expression of proteins implicated in CAF pathogenesis (Caveolin-1 [Cav-1] and Tenascin-C [TNC]), markers of EMT (E-cadherin and vimentin) and overall patient mortality.

**Methods:** Immunohistochemical staining for Caveolin-1 and Tenascin-C expression was performed using FFPE sections of NSCLC tumour tissue. Proportions of stromal staining were determined using a blinded semi-quantitative method and staining intensity scores were determined by image analysis (ImageScope). Proportion and intensity of staining were correlated with tumour EMT status (E-cadherin and vimentin expression) and density and location of immune cells (T-cells, T-regulatory cells, and macrophages) as well as with overall patient mortality.

**Results:** We identified a reciprocal expression of TN-C and Cav-1 in CAFs. Furthermore, following multicomponent analysis, patients with identified EMT, and those patients with the highest grade of TNC staining had significantly reduced overall survival ( $p=0.0242$ , and  $p=0.0035$  respectively).

**Conclusion:** This study suggests that the TME, and CAFs in particular, can significantly influence NSCLC behaviour. There are also implications in the identification of patients with significantly shortened survival due to aggressive TME driven disease which may benefit from adjuvant TME targeted therapy

**Alcohol use in Major Trauma Patients in the Midland Region, New Zealand: An Institutional Review**

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*Research performed at Waikato Hospital, New Zealand*

The incidence, characteristics and context of alcohol related injury in major trauma patients in New Zealand is not well defined. A retrospective cohort study from prospectively collected trauma registry data from the Midland Region, New Zealand, was performed. Major trauma patients with International Severity Score (ISS)  $\geq 15$  admitted to Midland region hospitals between 01/01/2009 to 31/12/2010 were included. Patients were categorised into alcohol positive and negative groups. Variables examined included demographics, mechanism of injury, day and time of injury. 5,887 trauma admissions were recorded, 531 having an ISS  $> 15$ . The incidence of alcohol related major trauma cases were 24%. There was a statistically significant difference in age groups ( $p<0.001$ ), ethnicity ( $p<0.001$ ), days of the week ( $P<0.05$ ), time periods ( $P<0.001$ ) and mechanism of injury ( $P<0.001$ ) between alcohol positive and alcohol negative groups. Alcohol use was highest in the 20-24 age group, accounting for 54% of patients. Maori ethnicity had the highest alcohol positive rate (44%) followed by Europeans (17%) and other ethnic groups (7%). Alcohol was involved in more weekend (28%) than weekday (20%) major trauma admissions and between the hours of 00:00-03:59 (78%). Regarding mechanism of injury, assault only contributed to 6% of all major trauma admissions however, showed 76% alcohol positivity rate; 3.6 times that of Road Traffic Collisions. These findings highlight potential targets for public health interventions regarding alcohol consumption in the context of major trauma in New Zealand.



### First Aid for Epistaxis – the layman scratches his head!

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**Introduction:** Nosebleeds are a common occurrence, and generally well controlled by simple first aid measures. This study aims to evaluate the extent and influences on the knowledge of first aid for epistaxis, amongst members of the public in Malta.

**Methods:** Volunteers, recruited according to a probability quota sample, submitted to a structured interview detailing demographics, experiences, training and knowledge relevant to immediate care for epistaxis. Individual chi-squared tests were performed to relate knowledge to expected influences.

**Results:** 500 participants (47% male) were interviewed, of whom 34% (n = 169) had previously received formal training in first aid, and 9% had previously suffered a nosebleed requiring medical attention. Only 22% (n = 108) of participants indicated the appropriate site for application of direct pressure in an attempt to control a nosebleed, whilst 52% (n = 257) correctly indicated that the patient's head should be in a neutral or slightly tilted forwards position. Attendance to formal first aid training resulted in a higher incidence of correct head positioning (63% vs 45%,  $p < 0.001$ ), but registered no improvement in the ability to identify the point at which to apply pressure. Previous epistaxis requiring medical attention was not associated with any improvement in knowledge.

**Conclusions:** Much of the general population remains unable to provide effective simple first aid for nosebleeds. Previous first aid training is not associated with an improvement in management, and neither is a history of presentation to medical practitioners with epistaxis.

### Cost comparison between Robot Assisted Partial Nephrectomy and Cryoablation in patients with renal masses

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**Background:** Since the introduction of the Da Vinci, robot assisted partial nephrectomy (RAPN) has been rapidly adopted as the future in minimally invasive surgery. Few comparative studies comparing its purported advantages to other minimally invasive surgeries such as cryoablation have been adopted despite literatures indicating similar oncological outcomes. With advancements and vast implementations between both modalities, the cost differences remain unclear.

**Method:** A total of 100 consecutive patients which underwent RAPN or cryoablation from June 2008 to February 2012 were reviewed. Cost data for hospital length of stay (LOS), operating room (OR) time, surgical costs and professional fees were obtained from the institution to establish a cost model. Each modalities purchase cost and maintenance were also amortized to be included within the study.

**Results:** Both RAPN and cryoablation had 50 patients reviewed respectively. Mean OR time was 152 and 142 minutes ( $P = 0.207$ ); mean LOS was 2.46 and 1.73 days ( $P = 0.536$ ); mean mass size was 31.7 and 26.12mm ( $P = 0.004$ ); mean age was 61.74 and 69.80 ( $P < 0.05$ ) respectively.

**Conclusion:** Preliminary results indicate that cryoablation is more cost effective due to its lower instrumentation costs despite similar OR and LOS times. Significant differences in mass size and age correspond to the differences in patients eligibility for RAPN or cryoablation. The high cost of purchase, maintenance and instrumentation of the RAPN should be re-evaluated with its long term patient outcome and usage to warrant its future role

**Improving confidence in prescribing through practically focussed teaching**

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**Background:** Over 86,000 medication errors were reported to NPSA (National Patient Safety Agency) in 2007.(1) Almost 20% of these were made by Foundation Doctors, even though safe prescribing is a core component of the GMC's undergraduate curriculum.(2-4) A lack of training is associated with increased rates of prescription errors.(4)

**Methodology:** Current Foundation Trainees delivered a practical prescribing course to 8 final-year medical students, focusing on improving students' confidence in prescribing. Over 5 weeks, sessions covered Acute Coronary Syndrome, antibiotics, anticoagulation, fluid balance and hyperkalaemia.

Subjective feedback (measuring confidence out of 10 both before and after the session) was collected each week before the course was repeated to 9 different (but similar stage) students.

**Discussion:** Overall confidence improved by 4.4 and 3.9 points in Groups 1 and 2 respectively. Confidence improved most in treating hyperkalaemia. Feedback was positive, with students finding the course a useful addition to their other lectures.

**Conclusions:** Students still lack confidence in prescribing common medications at the end of the undergraduate courses. Many students have not used a BNF or written on a drug chart before sitting their final exams. Short courses focussed on the practical aspects of prescribing can significantly increase students' confidence in common prescriptions.

**Redesigning the Intensive Care Unit Discharge: A Quality Healthcare Improvement Project**

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Discharge from the intensive care unit (ICU) is a complex process. Patients discharged from ICU to wards have an increased incidence of clinical deterioration and mortality. Similarly readmission to the ICU is associated with poor outcomes and increased costs. Transfer from the ICU to wards involves the exchange of information among ICU and ward staff, often foundation doctors, which has been shown to be fraught with errors. NICE has published guidelines for the transfer of patients from critical care to wards.

Phase one consisted of a prospective audit of patients discharged from a large 30 bed ICU in a tertiary referral centre for compliance with NICE guidelines. Phase two involved a questionnaire to determine how many foundation trainees had been responsible for review of patients discharged from ICU and their experience of transition of care between ICU and ward.

69% of patients discharged from ICU had a formal structured handover with 62% having a written handover plan, easily located within medical notes. 75% of foundation trainees reviewing patients that had been discharged had received a verbal handover. An average time from discharge to ward review of patients' was 3-4 hours. Foundation doctors were concerned about reviewing patients discharged from ICU with the majority finding discharge summaries useful.

### Socioeconomic variations in access to smoking cessation interventions in primary care: insights using the Mosaic classification

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**Background:** Smoking is the leading cause of preventable illness in the UK, with prevalence being highest amongst more deprived social groups. Using Mosaic classification, a novel measure of socioeconomic status, socioeconomic variations in the delivery of smoking cessation interventions in primary care in the UK were explored.

**Methods:** 460,938 smokers registered in The Health Improvement Network database between July 2008 and June 2010 were analysed. Logistic regression was used to calculate the odds of smokers receiving cessation advice/prescription, by Townsend Index of Multiple Deprivation, the 11 Mosaic groups and 61 Mosaic types. Characteristics of smokers were described qualitatively to suggest ways to target those least likely to receive cessation interventions.

**Discussion:** The odds of smokers receiving cessation support increased with increasing Townsend deprivation. Using the Mosaic classification, smokers with uncertain employment, living in social housing, in deprived areas were 35% more likely to receive advice than successful professionals living in desirable areas (OR 1.35; 95% CI 1.20-1.52). Furthermore, smokers in low-income families were 50% more likely to receive a prescription than successful professionals (OR 1.50; 95% CI 1.31-1.73). Smokers less likely to receive interventions were well educated, married with no children, and had broadband access.

**Conclusion:** Wide socioeconomic variations exist in the delivery of smoking cessation interventions in UK primary care. Analysis using Mosaic classification suggests that groups with low intervention rates may be best targeted through broadsheet media and the internet, to increase their awareness of the cessation support available in primary care

### A systematic study of the use of aggressive sales techniques by cosmetic surgery providers in the United Kingdom

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**Background:** Cosmetic surgery is a large and growing industry in the UK. Sir Bruce Keogh, NHS Medical Director, led the review of the regulation of cosmetic interventions in 2012. This included a Call for Evidence involving professional bodies and patient groups. The majority of respondents called for bans on free consultations and time limited promotional deals for cosmetic surgery.

This study aims to examine the extent by which these sales techniques are currently being used by cosmetic surgery providers.

**Methods:** The keywords 'cosmetic surgery UK' were entered in the online search engine google.co.uk. The top 50 websites that provided cosmetic surgery were systematically searched for the following criteria: i) free consultations ii) promotional offers, including discounts and 'multibuy' deals (e.g. "two-for-one") and iii) whether these offers are time limited.

**Results:** Out of 50 cosmetic surgery providers, 29 (58%) offered free consultations. 25 (50%) offered promotional deals, of which 7 (28%) were time limited.

**Conclusions:** This study has demonstrated that there is wide use of aggressive sales techniques by cosmetic surgery providers in the United Kingdom. Tighter government regulations and increase in public awareness of these issues may help in safeguarding patients.

**How does expression of the cancer-associated protein, survivin, regulate motility and adhesion of cultured mammalian cells?**

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Survivin expression is upregulated in human cancers and is involved in metastasis. It is crucial in mitosis and is involved in inhibiting apoptosis, through preventing caspase action. Mutations at threonine 34 can affect the phosphorylation state of survivin, as survivin-T<sub>34A</sub> is constantly unphosphorylated, whereas survivin-T<sub>34E</sub> is constantly phosphorylated. These mutations affect cell behaviours involved in metastasis, such as proliferation and apoptosis inhibition. This project aimed to determine whether these mutations also affected other behaviours involved in metastasis, cell motility and cell adhesion.

Experimental methods included a wound healing assay to measure cell motility, a cell spreading assay to assess cell adhesion, and fluorescence microscopy. Non-transformed fibroblast cells (MRC5 cells) were used.

MRC5 cells expressing survivin-T<sub>34A</sub> showed increased motility compared to survivin-T<sub>34E</sub> expressing cells, which showed reduced motility. Survivin-T<sub>34A</sub> expressing cells showed faster initial adhesion, but reduced adhesion efficiency overall. Survivin-T<sub>34E</sub> expressing cells showed the opposite: slower initial adhesion, but enhanced adhesion efficiency overall. These results indicate that the T34 phosphorylation state is essential in the influence of survivin on cell behaviour related to metastasis. It was suggested that the survivin-T<sub>34A</sub> mutant caused increased activation of  $\alpha_5$  and  $\beta_1$  integrins, causing upregulation of the Akt pathway which led to increased cell motility.

**A potential novel objective measurement of wheeze is not a good measure of severity in bronchiolitis**

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**Background:** In infants with bronchiolitis a clinical score (CS) is used to assess severity and treatment response. It is subjective and does not correlate with measures of pulmonary resistance or clinical outcomes. Acoustic sound analysis has shown potential as an objective monitoring tool. A new handheld device, the Wheezometer®, is designed to assess wheeze at the bedside. We aimed to determine if the Wheezometer® could be used as an objective measure of airway obstruction in bronchiolitis.

**Methods:** Children <1 year with acute bronchiolitis had paired CS and WheezeRate (WR = %respiratory cycle with acoustic wheeze) recordings. Agreement between repeated measurements and correlation between the WR and CS was tested.

**Results:** The study was terminated after N=7 (of planned N=100). Mean age = 9 weeks (range 3 to 40). The Wheezometer **did not detect** clinically relevant 'wheezing' (WR >10%) in any infant despite a range of CS (2 to 7 out of total 12). There is no relationship between WR, as measured by the Wheezometer®, and CS. There was barely adequate intra-observer agreement in repeated CS measurements (Kappa=0.49, 95% confidence intervals 0.18 to 0.79).

**Conclusion:** The Wheezometer® cannot detect clinically significant wheeze in infants with bronchiolitis and therefore is not a useful objective tool in bronchiolitis. While infants with bronchiolitis may have audible wheeze there is a different range of acoustic noise, than true wheeze in older children (notably crackles and low-pitched wheeze), which may not be compatible with the Wheezometer®. Further research is required to develop useful acoustic devices in bronchiolitis

### Role of GPR103 in the regulation of human adrenal steroidogenesis

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QRFP exerts its effects via the G protein-coupled receptor 103 (GPR103) and is recognised for its metabolic role in regulating energy balance and appetite. A high expression of GPR103 in rat adrenal glands has been reported by one study, which suggested it might play a role in the regulation of adrenal function following the observation of aldosterone production after intravenous administration with QRFP (Fukusumi et al., 2003). However, the role of GPR103 in regulating adrenal steroidogenesis in humans has not yet been explored. The present study aimed to investigate the role of GPR103 in human adrenal steroidogenesis by using H295R human adrenocortical cells. By employing Western Blotting, PCR and immunohistochemistry, our study is the first to provide a detailed characterisation of the presence of functional GPR103 receptor in human adrenal glands. We showed that H295R cells expressed both QRFP and GPR103 mRNA and protein. We also demonstrated a direct biological effect of QRFP on human adrenocortical function. Long-term incubation with QRFP over a 24h period increased aldosterone and cortisol production, and this was accompanied by a parallel change in the expression of key steroidogenic genes (StAR, CYP11B1, CYP11B2) involved in human adrenal steroidogenesis. Taken together, our results suggest that QRFP and GPR103 work in an autocrine and/or paracrine manner to regulate adrenal steroidogenesis in humans. This could have important physiological and/or pathophysiological significance that merit further investigation. Considering the metabolic role of QRFP, it may provide a functional link between adrenal malfunction and obesity related disorders.

### Neural Stem Cells: Novel Therapy or Not? Alzheimer's Disease

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**Background:** Alzheimer's Disease (AD) causes multiple neuropathologies (amyloid plaque build-up, neurofibrillary tangle formation and widespread neuronal and synaptic loss). Neural stem cell (NSC) could be a possible therapy for AD treatment yet NSCs need to be multipotent in order to combat the multiple neuropathologies.

**Objectives:** The principle objective of this work was to determine if neural stem cell therapy is a potential treatment for AD.

**Design/ Methodology:** This study contains a literature review regarding developments made in the use of NSC technology to treat AD and clinical trials that have stemmed from this.

**Results:** Discovery of APP and MAPT genes which encode plaque and tangle proteins, respectively, lead to transgenic animal models of AD [1]. Cognitive function improvements have been seen with NSC transplantation in AD animal models [2, 3], however, this does not significantly alter AD pathology [2]. With NSC having no significant effect on AD pathology other factors determine improved cognitive function; animal studies have shown that neurotrophic factors (NFs) improve cognitive function [2, 4, 5]. Two cell based therapy clinical trials in AD have taken place [4, 6]; these focused on neurosurgical implantation of cells that express neurotrophic factors (NFs). The studies show the procedures to be safe with some improvement in cognitive function.

**Conclusion:** Cell based therapy may provide a potential short-term treatment for AD yet further work is needed for longer term therapies. Overall, stem cell and cell based therapy could still be a novel therapy for AD yet it is in its infancy with further research in animal models needed to improve its efficacy.



### A retrospective audit of biologic treatment for patients with psoriasis in a District General Hospital in the United Kingdom

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Due to the cost and uncertain long-term effects of biologic agents used in psoriasis, NICE have published guidance to ensure treatment only takes place if it is cost-effective and safe for the patient.

An audit was undertaken to assess use of biologics in treatment of patients with moderate to severe psoriasis and determine adherence to these NICE guidelines.

We retrospectively reviewed medical notes and electronic discharge summaries for 45 patients currently on biologic treatment for psoriasis. This data was collected on an audit form, the results analysed, conclusions reached and actions agreed following discussion at a departmental audit meeting.

45 (100%) patients were on biologics for psoriasis. At some stage 31 (68.9%) patients had been prescribed Etanercept, 21 (46.7%) patients prescribed Adalimumab, 13 (28.9%) patients prescribed Ustekinumab and 2 (4.4%) patients prescribed Efalizumab before it was withdrawn from the market. First-line agents used; varied from 29 (64.4%) for Etanercept, 9 (20%) for Adalimumab, 6 (13.3%) for Ustekinumab and 1 (2.2%) for Efalizumab. 23 (51.1%) of patients had the severity of their psoriasis documented using an objective severity score.

Treatment with biologics at a District General Hospital was often not in keeping with NICE guidance. Consequently, a pre-assessment proforma was introduced to record; medical history, severity of disease, previous treatments, contraindications, relevant investigations and patient consent. This document could be adapted by other Dermatology Departments to improve and clarify clinical decision making. The utility of this proforma will be assessed with future audits and hopefully establish an improvement in clinical practice

### An Audit of Pre-operative Checks

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**Background:** Pre-operative checks, broadly outlined in local guidance, were performed on each patient the day before surgery by a junior doctor.

I found difficulty in knowing precisely what was required.

#### Experimental Design:

- Determine whether the checks were being performed according to the guidance.
- Create an advice document and checklist.
- Re-audit performance after implementation.

**Methods:** Using the WHO Surgical Safety checklist I selected 9 ideal checks (standards). Records of 39 gynaecological surgery patients were analysed for documentation of these checks. An advice document and checklist were created, circulated and presented at an audit meeting. Following this implementation 50 further patients were audited.

**Results:** Before implementation only 4/9 standards were met in >50% patients and 4 were met in fewer than 20%. Most frequently missed checks were MRSA status, allergies, drug chart completion and VTE assessment. After implementation 6/9 were met in 100% patients. The 3 unmet in 100% of patients were: availability of blood for transfusion (88%) VTE assessment (92%) and allergies (96%).

#### Conclusion

- The advice document and checklist markedly improved documentation of pre-operative checks. This improvement in clinical practice should enhance patient care.
- Junior Doctors indicated:
  - a. the advice document clarified their role.
  - b. the checklist was a useful "to do list" highlighting outstanding checks and a good learning tool.
- It is realistic for further continuous audit to aim for 100% documentation of all checks.
- These tools could be used by all surgical specialties.

### An audit into the efficiency and efficacy of a tertiary level paediatric dysphagia service

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**Background:** There are no national guidelines for paediatric dysphagia. This is the case for many neurodisability services, particularly at a tertiary service level. At Great Ormond Street Hospital, efficacy and efficiency of the dysphagia service has not been previously audited. A 2012 GOSH outpatient survey showed patient and parent satisfaction was lower amongst those with special needs and disabilities.

**Aims:** To develop outcome measures for the dysphagia service and compare clinical practice to these standards.

To identify areas for improvement in the service.

**Method:** The audit was split into two parts: firstly reviewing national outpatient recommendations, interviewing staff, using departmental targets and observing clinics to create audit criteria for the service; secondly collecting the data using a two year retrospective study of clinic reports, letters and appointment records to compare against the criteria. All new patients seen in 2010 and 2011 were included in the audit.

**Results:** The criteria were measured against a 95% target to allow for unavoidable clinical circumstances preventing criteria being met. Of the 15 audit criteria, only 5 had more than a 95% compliance rate. The criteria with the worst compliance rates were recording patient/parent satisfaction and giving written information.

**Conclusions:** The efficacy and efficiency of the service is lower than it should be. This could be because there have not previously been any guidelines to work towards. Improvements in information recording, provision of information and patient administration are needed. This audit provides a baseline and should be repeated yearly to measure improvement in the service

### Patient safety in nasogastric tube placement: an audit pre and post interventions to improve adherence to safety guidance

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Feeding through nasogastric tubes misplaced into the lungs has serious consequences for patient safety. The National Patient Safety Agency (NPSA) alert to reduce this risk recommends using pH testing first line to check NG tube position, with x-ray second line after failure of aspirate. This service evaluation at York Hospital aimed to improve NPSA alert compliance using a behaviour change approach, as part of a Health Innovation and Education Cluster (HIEC) region-wide project.

A retrospective baseline audit of 44 sets of case notes was conducted to assess current practice regarding NG tubes. Questionnaires were completed by multi-disciplinary staff identifying barriers to using pH first line. Two focus groups addressed these barriers. Strategies included using an e-learning package, an NG tubes awareness day, posters/screensavers, new documentation and a radiology system change. This was followed by a re-audit to evaluate the impact of the interventions.

Between baseline and post-intervention, there was a significant increase (14-33%) in use of pH first line for checking tube position ( $\chi^2 = 4.38$ ,  $p < .05$ ), a significant decrease (36-10%) in tubes placed in radiology ( $\chi^2 = 6.64$ ,  $p < .05$ ), but no decrease in the use of x-ray (41-40%;  $p > .05$ ).

The behaviour change methods deployed effectively increased use of pH testing first line for NG tube placement. Documentation also improved. Communication with staff and improving awareness have been beneficial in achieving adherence to the NPSA alert guidance at York Hospital, however the improvement is not as great as at two trusts with similar intervention.

**A Retrospective Audit of the Management of Open Fractures at a Major Trauma Centre**

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The BOA and BAPRAS guideline on the management of open fractures outlines the current standards in the treatment of this orthopaedic emergency. This retrospective audit compares the acute management of open fractures at a major trauma centre to the standards set out in this guideline. We reviewed the notes of open fracture cases in a 6 month period between May and October 2011 and compared the management received by these patients to the clinical guideline, aiming for 100% compliance with standards. 29 cases were eligible. Photography was used in only 10% and none had correct wound coverage. 71% had the affected limb splinted and neurovascular status was examined repeatedly in 79%. Correct antibiotic prophylaxis was given in 53%. 10 cases met criteria for urgent surgery but only half of these were taken theatre within 6 hours. An antibiotic bead pouch or a VAC dressing was not applied to any of the 6 wounds left open for delayed primary closure. Only two cases had plastic surgery input. Surgery was performed by a senior surgeon in 97% and definitive wound closure was achieved within 72 hours in 90%. Overall, current practice is somewhat short of best practice. To implement change we have created a trust guideline for the management of open fractures with an attached audit proforma to be completed prospectively for new open fracture admissions. A teaching session will be organised to update staff. These measures will ensure that the audit cycle is completed and that improvements in practice are sustained.

**HbA1c league tables: Does selection policy encourage foul play to support promotion to the “premier league”?**

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The National Paediatric Diabetes Audit (NPDA) provides a benchmark of performance for Paediatric Diabetic services across the UK. Whether intentional or not, a league table is created comparing units based on their overall mean HbA1c. Although the coordinators suggest submitting the patients most recent HbA1c, this may not necessarily be a universally adopted phenomenon. We examined the effect of selecting patient best, yearly average, and latest HbA1c on our unit's overall mean HbA1c and its impact on our position in the “league”.

All patient HbA1c values were collected for the NPDA periods, January 2010 - March 2011 and January 2011 - March 2012. The patient best, yearly average and latest HbA1c results were used to calculate our unit's mean HbA1c and then compared to regional and national data to assess the impact on our ranking.

For 2010-2011, our mean HbA1c varied significantly from 8.0% using the best HbA1c results to 8.5% with yearly average HbA1c, moving us from 2<sup>nd</sup> to 13<sup>th</sup> in the league. Similarly, for 2011-2012, there were significant variations from 7.8 % to 8.2% and 8.3% using the best, latest and yearly average HbA1c variables.

Therefore, these significant differences in our clinic overall mean HbA1c could see us as champions or candidates for relegation in the league table! The system is potentially open to foul play and tighter regulation of selection policy is required as HbA1c is increasingly used as a performance indicator and in some cases the basis for quality payments.

### Making 'Nil By Mouth' Time for Gastroscopy Patients More Palatable

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**Background:** Fasting prior to endoscopy aims to maximise visualization during the procedure and minimise the risk of aspiration. National guidelines advise patients should be fasted six hours for food, and two hours for clear fluids. The aims of this audit were to introduce measures whereby fasting times met current guidelines, and prevent fasting in excess of these recommendations.

**Method:** Patients included were all on the emergency endoscopy list; data regarding the time patients were made NBM, and the time of the actual procedure was collected and compared. Cycles of data collection were repeated after interventions were made on two surgical wards and one medical ward - these included educating nursing and endoscopy staff, and introducing a revised NBM sign. Currently on our third cycle, whereby further interventions are being made and data is being collected. The PDCA method was used to analyse results.

**Results:** The mean baseline NBM time (prior to intervention) was 22 hours. After the first cycle (with nursing education and an NBM sign), the mean NBM time was 10.2 hours, a 56.6% reduction in NBM time relative to pre-intervention. Nursing staff knowledge of NBM protocol improved from 40% to 60%. The second cycle involved a revised sign and further education; the mean NBM time was 9 hours, a 41% reduction in NBM time relative to the first intervention.

**Conclusion;** NBM timings have been much improved with ongoing staff education, and implementation of a revised sign with clear guidelines.

### Role of CD32b in the internalisation of monoclonal antibodies

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**Background:** Internalisation of type-I anti-CD20 monoclonal antibodies (mAbs) is thought to be one of the underlying mechanisms of treatment resistance in B-cell malignancies as only surface-bound antibody is effective for tumour destruction. Internalisation was shown to correlate with expression of CD32b on Chronic Lymphocytic Leukaemia cells.

**Aims:** Determine whether internalisation of a variety of other mAb is dependent on CD32b and if differences exist among lymphoma subtypes.

**Method:** Internalisation was quantified using a fluorescence quenching flow cytometry assay; firstly with Ramos cell lines (control/CD32b-transfected) then primary clinical samples (Mantle Cell Lymphoma (MCL), Follicular Lymphoma (FL), and Diffuse Large B-cell Lymphoma (DLBCL)). Cells were treated with Alexa-488 conjugated antibodies against CD19, CD20 (both Type-I and-II, of varying isotypes) CD22, CD37, CD38 and MHCII. Anti-CD32b mAb, AT10, was used to block CD32b in clinical samples.

**Results:** Dependence on CD32b for internalisation was demonstrated with cell lines. Clinical samples varied in CD32b expression levels, however, type-I mAbs consistently internalised faster than type-II, agreeing with previous data. Internalisation sometimes did not correlate with CD32b expression in FL; however, the effect of AT10 was largest in high expression samples, potentially suggesting different FL subtypes. Data from other antigens suggest CD19 and CD37 may prove better therapeutic targets as less internalisation occurred in comparison with CD22.

**Conclusion:** Continued investigation of all antigens in different lymphoma groups is needed. The present data may demonstrate the existence of specific FL subtypes more or less susceptible to internalisation. The addition of anti-CD32b mAb may improve treatment of certain lymphomas

**Overcoming barriers to the Ottawa ankle rules in a tertiary UK hospital**

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Ankle sprains account for over 300,000 A&E attendances per year in the UK. Whilst over 80% of ankle injuries reporting to emergency departments (ED) undergo radiography, fewer than 15% have a fracture. The Ottawa ankle rule (OAR) is a validated clinical decision rule for determining whether radiographs are required for acute ankle trauma.

An online survey was distributed to ED clinicians at a tertiary UK hospital to assess knowledge, compliance and barriers to implementation of the OAR. A retrospective audit was then conducted of all ankle x-rays for acute, traumatic ankle injuries in the ED during January 2013. Compliance of the OAR was measured from electronic requests and clinical notes. Strategies for change included education, a proforma, patient leaflets and an OAR electronic ankle order request reminder. A re-audit was then conducted.

Over 90% of ED staff answered they had heard of the Ottawa ankle rules, however, fewer than 15% could state the complete rule. Primary barriers cited to using the Ottawa ankle rules included meeting patient expectations and medico-legal implications of missing a fracture. The audit identified 33% of ankle x-rays were justified using the OARs. Preliminary results of the re-audit have showed a 25% increase in the use of the Ottawa ankle rule by ED staff and a 15% increase in proportion of x-rays showing an ankle fracture.

Knowledge and compliance with the Ottawa ankle rules amongst emergency department providers is poor. Compliance in a tertiary UK hospital has been improved with a multi-strategic approach



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