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Editorial

'All changed, changed utterly'

Michael Trimble

This has not been an auspicious time to take over as editor of the journal. I had been asked before, had tried to avoid it, but then eventually gave in. I had met with my predecessor for a brief handover just before lockdown, before it all changed. "Changed, utterly changed", Yates' words, of course, refer to Easter 1916 but they seem appropriate to describe life in light of Covid-19. And what changes we have seen, particularly in the realm of our work, in healthcare and healthcare education and training. Whether in General Practice or hospital specialty it is 'utterly changed'.

We have also witnessed how the profession has risen to this challenge: hospitals re-profiled, staff re-deployed, volunteers returning from retirement. We have all become amateur virologists. It would churlish to mention only the medical teams as we have seen nurses, allied healthcare professionals, and carers all step up to the mark.

Our trainees have seen their training programmes and research projects suspended as they are sent to cover acute wards. Our students have found themselves sent home from placements, while educators rapidly devise novel distance-learning programmes and discover how to teach on Zoom.

The pandemic has raised many questions about how to manage coronavirus cases, both clinical and ethical. Concerns regarding the fair allocation of critical care support and the establishment of ceilings-of-care lead to the establishment of the COVID-19 HSC Clinical Ethics Forum. The resulting guidance, the COVID-19 Guidance: Ethical Advice and Support Framework can be found online. Thankfully, the worst-case scenario with rationing of ICU beds did not arise but there have been many other issues to consider: the effect of the coronavirus response on patients with other healthcare needs, the reciprocal duty of care of Trusts towards their staff, e.g., in the provision of adequate Personal Protective Equipment. The over-riding emphasis of the guidance is that ***everyone matters***. The work of the Forum is far from over and it has been reconstituted as the HSC Regional Clinical Ethics Forum.

And so, to the Journal; I must first thank my predecessor, John Purvis, for his work in editing the UMJ for the past five years. I now have an inkling as to how much work this involves. I am reminded of the words of the teacher in Ecclesiastes – "Of making many books there is no end, and much study wearies the body." I must thank those who have continued to submit manuscripts, those who have reviewed manuscripts and also my sub-editor, editorial assistant and the team at Dorman and Sons printers. I must apologise to those who have been waiting to see their work in print. The lockdown period has meant that we have missed the May edition and so this year there will only be two issues. This means that some material that would have appeared in May has been pushed into the September issue and therefore other material will have to wait until next year before it can be published. I hope you will bear with me on the learning curve of editing the journal and hope too that the next six months will seem more normal than the last.

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Guest Editorial

The Economy of Wellbeing

Anna Mckeever

By its very nature, wellbeing is a slippery beast. Generally, it describes a holistic picture of wellness encompassing various attributes; physical, social and emotional. As such, it is difficult to differentiate specific components, and even harder to nail down as a quantifiable measure.

The fundamental purpose of medical professionals; to care for the health and wellbeing of their patients, is an increasingly impossible task. Doctors are expected to fix people, quickly, and at as low a cost as possible. Management and professional practices emphasise process and productivity, but fail to acknowledge the need for a much wider systems based approach to health and wellbeing.

Non communicable diseases (NCDs) are cited by the WHO (World Health Organisation) as the leading cause of death, disease and disability in the European Region.[1] These lifestyle related diseases put significant strain on the health systems working to treat patients, well-being of the population, and overall economic development. As such, doctors can play their role as efficiently and effectively as possible, but until there is recognition that the health and wellbeing of our population is a system wide problem that requires a system wide solution, they are fighting a losing battle.

Good wellbeing has been recognised as a positive predictor of health, as well as protective against all-cause mortality.[2] The health sector has historically focussed on diagnosis and treatment of illness, and timely intervention. Whilst acknowledging the need for specialist intervention for illness, there is a requirement to move from a deficit based model of health and wellbeing, to one where it is viewed as a universal asset to be strengthened and protected. This requires a change in conversation about health and wellbeing, and most importantly, where responsibility lies.[3]

So how do we place wellbeing on the political agenda?

There are several obstacles:

1. Intersectoral/interdivisional collaboration
2. Evidence the impact of wellbeing on economic productivity
3. Measurement/indicators of population wellbeing

Intersect oral/interdivisional collaboration

Enhancing wellbeing is not as simple as equipping individuals with a personalised "toolkit" to help withstand adversity. We must also work to build systems and design policies with the common goal of enhancing this core principle. Amongst many others, wellbeing relies on good working environments, accessible public transport, green spaces, social support and inclusion across the life course. This requires a comprehensive systemic approach and a wide recognition of the shared responsibility to enhance population wellbeing; which spans numerous government departments and sectors.

The WHO have voiced their support for member states to strengthen their health system response to NCDs; highlighting the importance of enhanced analytics and technical assistance to facilitate a new policy dialogue and knowledge exchange.[1] Once accepted as a strategic imperative across all government departments, it is a potential common concept from which to unite policies and actions across agencies.[4] The responsibilities for health and wellbeing cannot, and must not, belong solely to the health sector.

Evidence the impact of wellbeing on economic productivity

The need for an alternative measurement beyond GDP (Gross Domestic Product) to measure economic performance and societal success is well recognised.[5] In 2018 the ONS (Office of National Statistics) began it's "Beyond GDP" initiative, part of which looks at economic wellbeing indicators. Organisations such as the OECD (Organisation for Economic Cooperation and Development) have played a prominent role in the development of "multi-dimensional well-being" measures, through creating instruments such as the OECD Well-being Framework as a means of conducting research and allowing for comprehensive measurement. The New Economics Foundation recently published a report[6] describing the positive impact personal wellbeing can have on the nation's health, work and productivity, as well as being linked to outcomes such as a strong society and economy. It is estimated that that for every 10% increase in NCD mortality, economic growth is reduced by 0.5%[1].

There is a need for robust evaluation and measurement to generate evidence is required in order to secure wellbeing's place on the political agenda. There have been nods towards a strategic approach to wellbeing in the UK, with the widespread adoption of the "Five Ways to Wellbeing" framework, but fundamentally, there has been no evaluation of the impact of the initiative.[7] There is reluctance from any one department to take ownership of the wellbeing beast. As a result, many hands are in the mix, but without a firm steer there remains a fragmented, disjointed approach to a holistic problem.

Measurement/indicators of population wellbeing

The development of a wellbeing index does not mean reinventing the wheel. A large amount of routinely collected data can be interpreted via a wellbeing lens, and used to provide strategic direction for health improvement work; such as the Early Years Collaborative in Scotland.[8] By pointing out existing win-win situations out with the health sector, we can agree indicators that are not mutually exclusive and work towards a common goal. This allows large-scale population interventions (that lie out with the health sector) and individualized health services to work from the same data set; pooling resources and aligning strategies. A renewed shift of focus toward enhancing wellbeing requires improving literacy in the public sector; particularly in sectors that are not used to viewing wellbeing as part of their remit. There is a role for organisational "spanners" or professionals whose responsibility is to work to facilitate collaborative working between sectors; driving a shift in policy toward prevention and research generation.

Putting wellbeing on the political agenda is as much a cultural shift as it is an economic and political one. Particularly at this time of political and social unrest, it is both a moral and economic imperative that decision makers are the first to start the conversation about the need to invest in the wellbeing as a means of building a happier, healthier, and more prosperous UK. The common goal of enhanced wellbeing should not be a hastily conceived considered afterthought, but has the potential to fundamentally challenge the way in which policy is conceived. Wellbeing is good for business, and that makes it *everyone's* business.

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Research today: Diagnostics in the future

Presidential address to the Ulster Medical Society on 3rd October 2019

Mary Frances McMullin

Hippocrates argued that the causes of diseases (or the diagnosis) were physical and could be determined by observing a patient's symptoms. Disease was the result of an imbalance between the four humours or fluids in the human body: black bile, yellow bile, phlegm and blood. Thus, for example if you were lethargic you had too much phlegm and the suggested treatment, citrus fruit (figure 1).

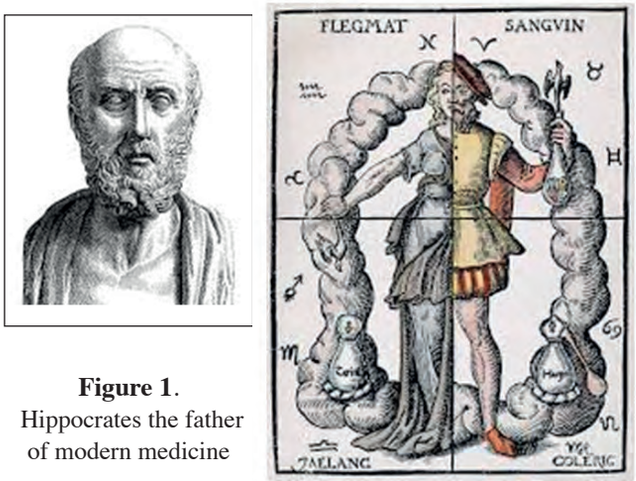

Figure 1.
Hippocrates the father of modern medicine

These ideas of diagnosis and treatment still underpin medicine today.

As doctors we are first of all diagnosticians. I am the doctor in my house and my grown-up children have great faith in me as a diagnostician. From anywhere in the world if you notice any observed symptom or sign you ring Mum for a diagnosis.

Therefore, I have had: "I was out last night and I think I bit my tongue and now my face looks funny". I instruct him to smile at the mirror. "My face is all twisted" he responds. I reassure him "you have a Bell's palsy". The same child aged 25 yrs. rings complaining of an severe pain the chest after playing football and his friends are about to take him to hospital (I am in Portugal, he is in England!).This is followed by a text communication, 'sorry to tell you but they say I am having a heart attack as the heart tracing is abnormal'. I text back: 'You have pericarditis' which was promptly shown to unfortunate attending junior doctor.

And the worst one from a university in England: "Mum I have felt awful and shivery all night and now I have little bruises all over me." I manage to instruct her to urgently get help. She did have meningococcal meningitis (and is fine) but of course as a haematologist I first wanted to know her white cell count and actually had an even worse diagnosis in mind (acute leukaemia).

This is all about making a diagnosis from signs and symptoms. Recognising the pattern and putting it together to come up with the diagnosis.

On entering medical school, we practise the mantra: inspect, palpate, percuss, auscultate and learn to recognise signs and make working diagnoses. Eventually it becomes second nature. (figure 2) In order to develop our examination skills, we have various aids. A prime example is the stethoscope - an

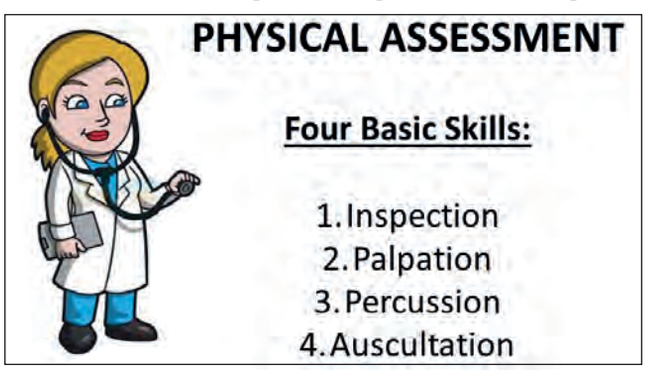

Figure 2. The pathway for detection of signs

aid of the 20th century doctor used to listen to the chest and heart. Interpretation of the findings helps to make a diagnosis.

In former times, the diagnostic process involved careful description of the clinical findings. Ronald Ross in his memoirs describes fever characterised by regular recurrences on a daily basis or every two or three days (quotidian, tertian or quartan) [1]. Starting with chills and followed by high temperatures, the disease was recognised from the pattern of the fever in endemic malarial areas and treatment with quinine was instituted. In the second half of the nineteenth century, with pathological science, the malaria parasite and life cycle was described and to this day in a case of suspected malaria the first step is microscopic examination of a blood film in order to make a diagnosis (figure 3).

Typhoid fever is another example where doctors described the rose-coloured spots and the high fever. Typhoid is one of the

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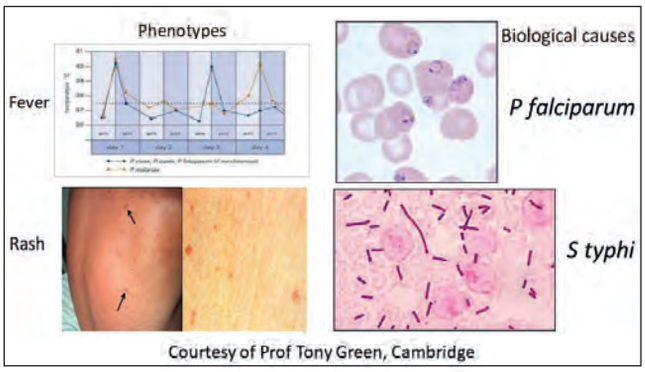

Figure 3. From clinical signs to microscopic pathology in malaria and typhoid.

possible pathogens which killed one third of the population of Athens including Pericles in 430BC and after this disaster the balance of power shifted to Sparta. It was the 1880s before the causative organism *Salmonella typhimurium* was identified. Identification led to an understanding of bacterial transmission and incidents such as the 26-year quarantine of 'Typhoid Mary' who refused to have her infected gall bladder removed.

The diagnostic process proceeds from careful description of the symptoms and signs to formulate possible diagnoses to pathological investigations which reveal the diagnosis.

After entering medicine, I was captured by haematology as a subject when in my fourth year of medical school. I decided that I wanted to be a haematologist and never changed my mind. The attraction of haematology was the mixture of investigative science and medicine leading to a diagnosis. From seeing and examining the patient, the haematologist proceeds to the microscope where the blood is examined and diagnostic findings revealed. I found and have continued to find this fascinating. Not only do you see the patient, take a history and examine them, but the same doctor then observes the blood and the diagnosis may be revealed.

This process is seen going back to the nineteenth century. John Bennett was reputed to be the first person to describe leukaemia as a blood disorder in 1845 (although Virchow published similar results 6 weeks later). John Bennett in 1845 at the age of 33 was already a fellow of the Royal Society, although he was described as 'a man of brilliance but short temper, certain of his own virtues, pugnacious and unable to suffer fools'. He described the microscope findings in a very sick patient. There appeared to be huge numbers of colourless corpuscles (or cells) which resembled pus. In those days no counterstain was used when looking at a blood film so cells did appear colourless and he was looking at the large numbers of white cells seen in a patient with the white cell proliferation of leukaemia [2]. This was a case of chronic myeloid leukaemia.

Following this initial description, leukaemia was subtyped and defined by the microscopic findings as were many other haematological disorders.

Acute myeloid leukaemia was subclassified by the FAB group (French/ American/ British) in 1976 where a number of the 'great and the good' in haematology sat round a multi-headed microscope looked at a large number of cases and divided them into seven different subgroups depending on the morphological appearance [3]. Acute promyelocytic leukaemia or the subgroup M3 is perhaps the clearest example of this. There is a definitive picture of heavily granulated promyelocytes where the distinct morphological appearance defines the subtype.

There are many other examples of the use of the microscope to arrive at a definitive diagnosis. One fascinating piece of research in a different area is that of peptic ulceration. When I was a junior house officer in surgery in the Mater hospital in 1980, we had a surgical ward full of people who had had major invasive surgery for duodenal ulcers. Medical therapy in the form of H_2 blockers and later protein pump inhibitors initially came along that year. However, it was the work of Barry Marshall and Robin Warren for which they won the Nobel prize in 2005 which shows that *helicobacter pylori* infection was the cause. Barry Marshall drank *H. pylori* and developed symptoms of peptic ulceration within 5 days and had inflammation and *H. pylori* in his stomach. This linked the long described clinical findings with the causative organism.

In haematology, the process of linking clinical findings and patterns in the blood picture to define disease continued. In 1951 the preeminent American haematologist William Dameshek published a very short paper describing and identifying the myeloproliferative diseases. These were individuals with elevated red cells, white cells and/or platelets. He described these as polycythaemia vera (PV), when the red cells were primarily the issue; essential thrombocythaemia (ET) when it was the platelets and chronic myeloid leukaemia when it was primarily a white cell problem [4]. To further define these, complicated clinical and laboratory criteria developed which had to be fulfilled to make a diagnosis of PV or ET.

Included in this classification were those with who appeared to have proliferating white cells, termed chronic myeloid leukaemia. This diagnosis was clarified over subsequent decades as new investigation revealed more of the malignant process. Chronic myeloid leukaemia is characterised by a markedly raised white cell count and a packed bone marrow, full of white cell precursors. Cytogenetic investigation reveals a small chromosome 22 in these patients, the so called 'Philadelphia chromosome' because it was initially described in Philadelphia. Over the decades this chromosomal change was dissected at the molecular level where the reciprocal translocation between chromosomes 9 and 22 takes place leading to a new fusion gene, *BCR-ABL*-1. This leads to a fusion protein made from the new gene (Figure 4). This abnormal protein (tyrosine kinase) drives the disease. However, the discovery of the disease pathway led on to a definitive treatment. A drug to block the tyrosine kinase protein was developed and a number of tyrosine kinase inhibitors are now available [5].

Sir John Dacie was considered to be the father of British

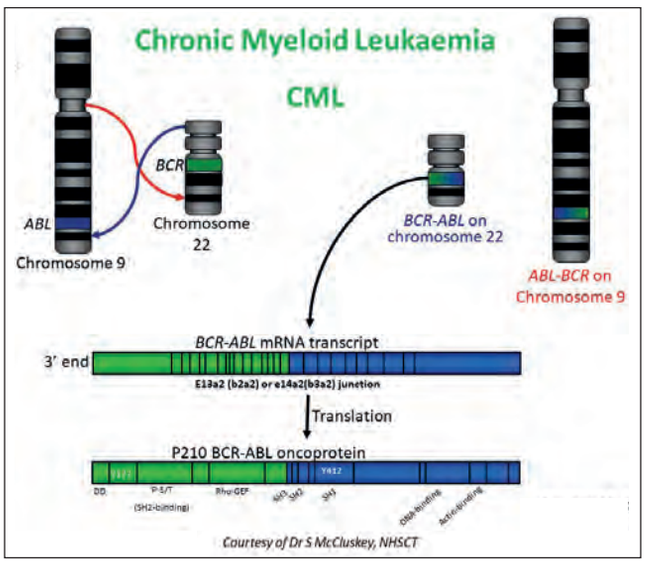

Figure 4. The *BCR-ABL-1* reciprocal translocation of chromosomes 9 and 22 in chronic myeloid leukaemia

haematology. I went to work in the Hammersmith hospital (Royal Postgraduate Medical School) in 1989 as a senior registrar. Sir John Dacie was occasionally still around and a great influence. One of the things that he and colleagues had described world- wide was the rare and fascinating disorder paroxysmal nocturnal haemoglobinuria (PNH) where rare patients were seen who produced red urine in the early morning and had devastating haemolysis. Extensive laboratory studies showed that these patients' red cells lysed in acidified serum along with other complicated patterns of biochemical abnormality. However, Sir John Dacie and his collaborators have been described as 'stamp collectors'. They collected rare cases and studied them in great depth clinically and in the laboratory and recognised patterns of disease making diagnostic groups.

In the 1980s and early 90s the molecular lesion was described in individual cases of PNH where mutations were seen in the *phosphatidylinositol glycan Class A* (*PIG*a) gene. This mutated gene produced a mutated protein on the surface of the red cell which does not function normally. This results in failure of binding of other proteins to the red cell surface. Therefore, the red cell becomes unstable in the presence of complement and the cell lyses resulting in catastrophic haemolysis. Thus, in PNH the diagnostic pathway began with careful clinical description but it is with molecular diagnostics that the disease mechanism is explained. Understanding of the molecular lesion led to the development of a treatment to control the haemolysis. Eculizumab, a humanised monoclonal antibody specific for the human plasma component C5, binds to it and thus blocks the complement pathway. This blockage of complement activation protects the red cell from complement-mediated lysis and stops haemolysis [6]. The pathway here is from clinical description, to accurate molecular diagnosis to effective treatment.

Another haematological example as to how diagnosis developed is one of the types of acute myeloid leukaemia described on morphological appearance by the FAB group. This is acute promyelocytic leukaemia, M3, the one with the obvious morphological appearance with large numbers of these needle-like structures (Auer rods) in the promyelocytes. This disorder was recognised by this appearance and classified on this basis by the FAB group. The clinical pattern of disease with patients who were seen to have a bone marrow full of this type of blast cell often presenting with catastrophic bleeding. Further investigation revealed that the patients with disease with this morphological appearance had a particular chromosomal abnormality, a t(15;17) translocation. The molecular lesion associated with the translocation was discovered. The *promyelocytic leukaemia* (*PML*) gene and the *retinoic acid receptor alpha (RARA*) gene was found to be fused together and this new fusion gene produces an abnormal protein which drives the disease. Explaining this mechanism led to treatment with all- trans-retinoic acid (ATRA) which leads to blockage of the fusion protein reducing the incidence of life threatening bleeding and ultimately chemotherapy treatment of the disease [7]. Full diagnosis therefore leading to effective treatment.

Similarly, with acute myeloid leukaemia, cytogenetics and molecular diagnostics have led to much greater understanding of acute myeloid leukaemia with many different subgroups defined on a molecular basis. This has had many iterations and expansions since the original 1976 description of 6 subgroups defined on the basis of the microscopic picture only. The 2016 WHO classification of acute myeloid leukaemia extends for many pages with some different types defined on the basis of recurrent genetic abnormalities [8]. Current work is addressing the issue of finding specific therapies effective against all of these genetic abnormalities leading to 'precision medicine' where there is a specific drug for each molecular lesion. However, there remain many types where the genetic lesion is not yet defined.

In my area of interest, the myeloproliferative neoplasms molecular genetics have taken classification a lot further that the original definitions originally formulated by Damashek [4]. In 2005 it was discovered that many patients with myeloproliferative neoplasms had a single point mutation in the *Janus kinase 2* or *JAK*2 gene. The amino acid at position at point 617 is highly conserved across species from bacteria to man suggesting it in highly important functionally and this proves to be the case (figure 5). When the amino acid is changed it leads to a constitutively activated protein on the receptor which signals even in the absence of a driver ligand. This ultimately results in increased cell production and as the JAK protein is on multiple receptors it would account for increases red cell, white cell or platelet production as seen in the myeloproliferative neoplasms [9].

The discovery of the *JAK*2 mutation and then subsequently mutations in *myeloproliferative leukemia virus oncogene* (*MPL)* and *calreticulin (CALR)* genes meant that diagnostic criteria for polycythaemia vera and essential thrombocythaemia could be simplified and clarified. However, these discoveries give rise to further questions. Is the presence

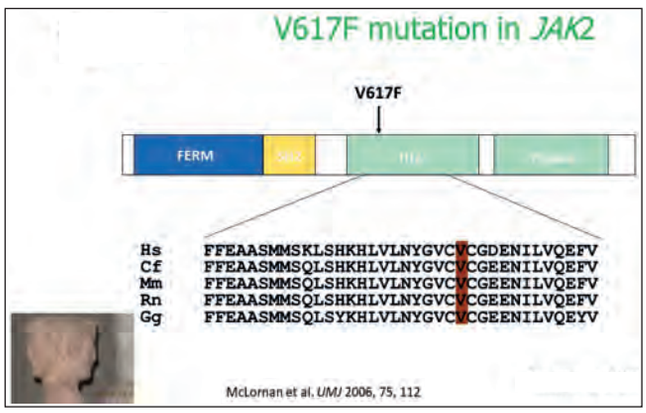

Figure 5. Mutation in the *Janus Kinase* 2 gene is highly conserved across species

of a mutation and an abnormal blood count enough to make a diagnosis rather than the previous diagnostic criteria based on a description of phenotype alone? What other factors, genetic or otherwise, influence the ultimate diagnostic picture and need to be considered in the diagnosis? And is it valid to split up disease into these different subgroups or is the molecular detection of an acquired clone indicative of a unified diagnosis?

These are some of many examples where the diagnostic process has proceeded from clinical description, investigation often microscopically to molecular definition which then leads to development of effective treatments. However, there are other clinical situations where there is nowhere near this degree of diagnostic definition. Many of my haematology patients complain of a lot of aches and pains. They tell me they have fibromyalgia. NHS websites give criteria for diagnosis as severe pain in 3 to 6 different areas of the body or milder pain in 7 or more areas with symptoms at a similar level for at least 3 months in the absence of any other explanation for the symptoms[10]. That is very non-specific. Surely, a much better diagnostic test is needed to classify and understand the phenomenon.

Another example seen microscopically is the phenomenon of haemophagocytosis where there is consumption of cells seen in the bone marrow and other organs. In this haemophagocytic lymphohistiocytosis, a rare immune disorder, the body reacts inappropriately to a trigger usually infection. The microscopic phenomenon of haemophagocytosis is associated. In children this reaction is associated with specific genetic abnormality but in adults it is now described with many different triggers. Diagnostic criteria are complicated and convoluted. Extreme hyperferritinaemia is considered to be a marker but this is a very non-specific test [11]. Recognising the disorder early and attempting treatment are required given the catastrophic clinical course and the high associated mortality. However, the pathological process and triggers of that process in individuals are not really understood. More definitive and specific diagnostic tests are needed to sort out these presenting signs and symptoms.

Having seen how the diagnostic process has developed and evolved over time, I would like to consider how current and future developments may aid the evolution of diagnosis although of course this will always be speculative.

It is interesting to reflect in general how technological development changes revolutionise our world. In little over a hundred years the motor car has gone from a new but revolutionary means of transport to the object which every young person aspires to on reaching 17 years of age. In the future cars will certainly be electric and may be something to hire or rent whenever we have need. The telephone similarly has transformed from an object present only in the houses of the rich to the ubiquitous small device from which we cannot be parted and of which we only use a tiny fraction of the available computing power at any time. There are many other examples of technological advances which change how we navigate our lives, such as moving from paper maps to the GPS (global positioning system) device on mobile phone as the only way to get around (or diagnose how to get to a destination !).

In medicine new methods are rapidly changing the diagnostic process. The stethoscope has been central to a physician's identity. The stethoscope of the 21st century is point of care ultrasound (POCUS) which enables us to look rather than listen and the patient can share the experience. Use of the ultrasound will become a core competency for physicians [12]. Imagine a future where you have a small ultrasound machine in your pocket instead of a stethoscope.

Returning to the microscope, with computer technology many thousands of cells can be rapidly examined , patterns recognised and cells classified without the need for a person to look and count. This raises a point about which many haematologists are passionate. When will the microscope be obsolete? With the microscope a phenotypic diagnosis is made but with computers scanning and evaluating patterns in vast numbers of cells will this replace the need for simple morphology? Whereas we are all trained in the use of the microscope is the time coming when this is unnecessary and machines will be able to make the diagnosis.

The future of diagnostics will embrace molecular genetics. These tests are now part of the routine workup. No matter what the area of medicine, we look to the genetic code for the diagnosis, either by using specific next generation sequencing panels aimed at looking for specific defects or perhaps in the future more frequently investigating the whole genome. This can be seen in a recent study looking for clonal defects in blood samples from normal populations. The number of recurrent somatic mutations or clones detected increases exponentially with increasing age [13]. This is termed age-related clonal haematopoiesis (ARCH) but what does it mean in diagnostic terms. Will these clones develop into malignant disease? Surely not in all cases and is there any treatment to supress the clonal disease?

Computer assisted data collection of clinical and laboratory information and pattern recognition is now occurring on a grand scale. This is the same process as our early

'stamp collecting' haematologists but with vastly more power. Country wide collection of clinical, laboratory and molecular data is in the planning process and this will give an enormously rich source for evaluation. This leads to the development and use of algorithms where large amounts of data are processed and then used by following algorithms to make a diagnosis and then one step further to artificial intelligence. Can the analysis of large amounts of data and its use in diagnostic algorithms improve the making a diagnosis?

Will new and better pattern recognition lead to clearer diagnostic classification ?

Better diagnostics are crucially important as this leads to better treatment. The example of chronic myeloid leukaemia where the understanding of the diagnosis led to the development of a tablet to treat the disease and the patient diagnosed with CML today would expect to have a similar life expectancy to their age and sex matched peers [14].

However, that is not the case with many of the diseases treated today. We regard our forbearers who bled and purged patients in order to get rid of the 'Bad Humours 'as administering barbaric treatment but perhaps much of what is done today in treating malignancy will appear equally barbaric in the future. In haematology we treat leukaemias by destroying all bone marrow cells with chemotherapy and then try to keep the patient alive through infection and bleeding waiting for the normal blood cells to grow back. Perhaps with more accurate diagnosis in the future, better and much more targeted treatment would avoid such blunderbuss management.

The development on new diagnostics is an ongoing process but as I write up this inaugural lecture in the middle of the COVID 19 pandemic, astounding advances have been incorporated into practice in an astonishingly short period of time. Practice has rapidly switched to online and telephone consultation and we have adapted to changes in practice which would have seemed impossible just a very few weeks ago. There are many technologies available which have facilitated the changes in our practice.

And it is with this in mind I invite you to consider fundamental and clinical research and to think how diagnostics in the future will lead to new and more precise diagnosis.

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Review

Masked Hypertension: Lessons for the Future

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Key words: Masked hypertension, mechanisms, classification, outcomes.

Abstract

Masked hypertension (MH) is a commonly overlooked phenotype of hypertension in practice. Lifestyle factors and conditioned stress response specific to out of clinic blood pressure readings may be the mechanisms leading to this phenomenon. 24-hour ambulatory blood pressure monitoring or home blood pressure monitoring in an out of office setting are required for its reliable diagnosis. MH has a high risk of progressing to sustained hypertension with comparable cardiovascular and mortality risk. In this review, we discuss current evidence-based perspectives on definition, pathological mechanisms, risk factors, screening, clinical implications, and treatment of MH.

Introduction

Blood Pressure (BP) is a fluctuating phenomenon that was historically quantified exclusively by static measurements in the physician's office. Variability of BP values when the subject's measurement was done in a medical environment using mercury or aneroid sphygmomanometer led to the advent of out of office BP measurement techniques. The validity of office blood pressure measurement (OBPM) was first questioned by Ayman and Goldshine in a landmark paper published in 1940 which revealed differences between office blood pressure and home blood pressure readings before treatment, signifying the role of home blood pressure monitoring (HBPM) to improve the precision of diagnosis and treatment of hypertension.[1] In 1962, the first device for non-invasive ambulatory blood pressure monitoring (ABPM) was developed by Hinman and colleagues.[2] Subsequent pioneering work by Sokolow et al showed that ambulatory blood pressure values correlated more with cardiovascular damage compared to casual office BP values and established the role of ABPM in hypertension management.[3,4] The spectrum of BP values measured across different modalities of measurement led to the identification of four BP phenotypes (Figure 1):

	Office BP **HIGH**	Office BP **NORMAL**
Out Of Office BP **HIGH**	Sustained Hypertension	Masked Hypertension
Out Of Office BP **NORMAL**	White Coat Hypertension	Normal Blood Pressure

Figure 1 - Blood Pressure Phenotypes

1.Normal or Controlled BP - Normotensive BP measured in office and in out of office setting.

2.Whitecoat hypertension (WCH) -High office BP but normal out of office BP.

3.Masked hypertension (MH) – Normal office BP but high out of office BP.

4.Uncontrolled or sustained hypertension (SH) – High office and out of office BP.

BP that is normal at a physician's office but higher in other settings is known as Masked hypertension (MH). Pickering first coined the term masked hypertension for the entity which was previously referred to as reverse white-coat effect, isolated clinic normotension, isolated ambulatory hypertension.[5,6] It is a commonly overlooked phenotype of systemic hypertension.

Pathomechanisms

Mechanisms leading to MH may be classified into two groups which may not be mutually exclusive:[7]

1.Low office BP relative to ambulatory BP – The exact cause of low office BP compared to ambulatory BP is unknown. But extrapolating our understanding that WCH may in part be a conditioned anxiety response that is relatively specific to the clinic setting, the reverse could be true in MH, where the anxiety or stress response is higher out of the doctor's office. Office BP in some elderly hypertensives measured after meals may show significant post-prandial reduction leading to a diagnosis of MH.[8]

2. Selectively high ambulatory BP – Lifestyle factors such as smoking, alcohol, physical inactivity, interpersonal

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conflicts, mental anxiety, and job stress could selectively increase ambulatory BP. Sedentary, obese individuals may have poor exercise tolerance through daily activity showing pre-hypertensive BP values in office when measured at rest. Exaggerated BP response to exercise (EBPR) is also associated with MH. Kayrak et al studied sixty-one normotensives with EBPR by ABPM. The prevalence of MH in subjects with EBPR was 41%. Diastolic BP measured at peak exercise was an independent predictor of MH in subjects with EBPR.[9] Because of these factors, measurement of BP should rely on anxiety neutral approaches like automated office blood pressure (AOBP) in office and ABPM or HBPM out of office.

Incidence, Prevalence & Risk Factors

Data on the incidence of MH is scarce. In the Ohasama study from Japan, which included 649 normotensive subjects by conventional and HBPM measurements, the incidence of MH requiring treatment was found to be 11.3% after a follow-up of 8 years.[10] This correlated with the more recent study by Trudel et al where 1836 normotensive patients by ABPM were followed for 2.9 years with the cumulative incidence of MH at 10.3%.[11] Current data on the prevalence of MH is highly variable due to differences in ethnicity of study groups, the heterogeneous definition of MH, and measurement tools used (ABPM/HBPM/Daytime/Nocturnal/24 Hour ABPM) for its diagnosis. Overall, the prevalence of MH in the general population ranges from 8.5% to 16.6%.[12] The prevalence increased to 30.4% in populations with high normal clinic BP.[12] In a systematic review by Thakkar et.al, the prevalence of MH was significantly higher in patients of African ethnicity with prevalence as high as 52.5% in African-Americans as compared to lower values in patients of Korean (5.7%) and Omani (6%) descent.[13] The presence of comorbidities also influenced the prevalence of MH, with 30% in obstructive sleep apnea (OSA), 13.3% to 66.4% in diabetes, 7% to 32.8% in chronic kidney disease (CKD), 15% in haemodialysis and 16% to 39% in renal transplant recipients.[13]

In a prospective study, risk factors for MH identified are male gender, age > 40 years, body mass index (BMI) > 27, smoking, and alcohol intake > 6 drinks/week.[14] Interestingly, people with a habit of smoking, substance abuse, and alcoholism had a high prevalence of MH as they are often abstinent when visiting doctors and record lower or normal clinic BP.[13] Another issue for accurate estimation of MH prevalence is the reproducibility of MH in subsequent measurements. There is limited evidence in this aspect. De la Sierra et al reported the reproducibility of MH diagnosis over a median period of 3 months was only 47%.[14] In this study, the authors concluded that MH phenotype is reproducible only in the short term and frequently shift towards SH in the long term.[15]

Screening

The 2018 European Society of Cardiology/European Society of Hypertension (ESC/ESH) blood pressure guidelines suggest screening for MH in these populations:

1. Individuals with clinic systolic blood pressure (SBP) 130-139 mmHg or diastolic blood pressure (DBP) 85-89 mmHg.

2. Patients with hypertension-related target organ damage (arterial stiffening, peripheral vascular disease, retinopathy, proteinuria, CKD, left ventricular hypertrophy (LVH).

3. Subjects with high cardiovascular risk (calculated 10-year systematic coronary risk evaluation of >5%). The method of out of clinic measurement is by validated HBPM device or ABPM.[16]

Diagnosis

Accurate diagnosis of MH hinges on the reliable measurement of the clinic and out of clinic BP measurement. In a systematic review and meta-analysis by Roerecke et al, AOBP, when recorded with the patient sitting alone in a quiet place, is more accurate than office BP readings in routine clinical practice and similar to awake ambulatory BP readings with mean AOBP negating white coat effect.[17] Health care providers must ensure clinic BP measurement using a device validated by British and Irish Hypertension Society[18] and manually exclude conditions with pulse irregularity like atrial fibrillation as automated devices may not measure BP accurately in these conditions.[19] An appropriate cuff size to the person's arm should be used. In individuals who have normal BP (<140/90 mmHg) during clinic measurement may be stratified into 3 categories:

1. Optimal office BP (<120/80 mm Hg)

2. Normal BP (120-129/80-84 mm Hg)

3. High normal BP (130-135/85-89 mmHg)[16]

In persons with high normal BP, a possibility of MH should be considered and an out of office BP measurement by HBPM or ABPM should be pursued. In all categories, focused evaluation with history, physical examination, and diagnostics for hypertension mediated target organ damage (HMOD) should be done. Basic screening tests include the 12-lead electrocardiogram (ECG) to look for LVH, urine albumin to creatinine ratio (ACR), blood creatinine and estimated glomerular filtration rate (eGFR) to detect possible renal disease and optic fundoscopy to detect hypertensive retinopathy.[16]

Cardiovascular (CV) risk has to be estimated based on risk factors using the QRISK3 score to assess 10-year CV risk.[9] Individuals with high CV risk (>5%) should be further evaluated with out of office BP measurements to screen for MH. The National Institute for Health and Care Excellence (NICE) guidelines of 2019 for diagnosis and management of hypertension in adults define MH as normal blood pressure (<140/90 mm Hg) during a clinic visit, but higher than 140/90 mm Hg when measured outside the clinic using average daytime ambulatory blood pressure monitoring (Day-ABPM) or average HBPM measurements.[19]

Classification

The positive difference between office and out of office BP measurements further identifies 3 subtypes of MH.

1. Masked Effect – BP in an untreated subject measured with ABPM or HBPM is higher than the corresponding normal clinic BP but within the target. A study from the Netherlands in healthy volunteers by Aksoy et al showed that home BP can be significantly higher compared to office BP although both values can remain in normotensive range.[20]

2. Masked Hypertension - BP in an untreated subject measured with ABPM or HBPM is higher than the corresponding normal clinic BP and target out of office BP threshold.

3. Masked Uncontrolled Hypertension (MUCH) – BP in patients on antihypertensive treatment where office BP is on target and out of office BP is not on target.

MH can also be classified based on ABPM into two types [21]

1.Masked daytime hypertension – This pattern is observed in individuals with job stress, smoking, poor exercise tolerance, or heavy alcohol consumption.

2. Masked night-time hypertension- This is seen in the context of OSA, diabetes, CKD, sleep deprivation, or metabolic syndrome.

Many patients with MH will show both daytime and night-time MH. Among the out of office BP measurement modalities, there is little evidence to determine whether HBPM, ABPM, or both should be used for accurate diagnosis of MH. HBPM is more readily available, easier to perform, and easier to monitor. ABPM is cumbersome and more costly, though 24-hour ABPM is the gold standard for out of office BP measurement. Out of office BP measurement should be done preferably by ABPM. If ABPM is unsuitable or the person is unable to tolerate it, HBPM should be offered for diagnosis of hypertension.[19] When using ABPM, at least 2 measurements per hour should be taken during the persons waking hours and the average value of at least 14 measured values noted during the persons usual awake hours should be used to diagnose hypertension.[19]

When using HBPM, it must be ensured that for each BP recording 2 consecutive measurements are taken at least 1 min apart with a person seated. Additionally, HBPM should be recorded for at least 4 days and ideally 7 days with BP recordings twice daily in the morning and in the evening. If hypertension is not diagnosed by the clinic and out of office BP measurement, but target organ damage is evident, consider work up for alternative causes of target organ damage. BP should be measured annually in adults with type 2 diabetes, and at least every 5 years or more frequently in persons without hypertension or target organ damage. Preventive lifestyle advice should be reinforced.

There are considerable variations among various guidelines regarding the technique of out of office measurement of BP and the threshold values for the diagnosis of hypertension. (Figure 2) In contrast to the NICE UK 2019 and American College of Cardiology/American Heart Association (ACC/AHA) 2017 hypertension guidelines which prefer day BP, the ESC/ESH 2018 consider either day, night, or 24 hours mean BP for diagnosis of hypertension. In a study by Anstey et al which evaluated the overlap between HBPM and ABPM for diagnosis of MH, majority of untreated hypertensive subjects had hypertension by ABPM with an associated increase of left ventricular mass index (LVMI) compared to a diagnosis of hypertension by HBPM which did not correlate with increased LVMI suggesting that ABPM is essential for identifying individuals with MH who are at high CV risk.[22] Inferences from the Jackson Heart Study suggest that night time BP is an overlooked component of 24-hour ABPM which correlated not only with MH more than day-ABPM, but also the progression of CKD and poor CV outcomes in the African-American population.[23,24]

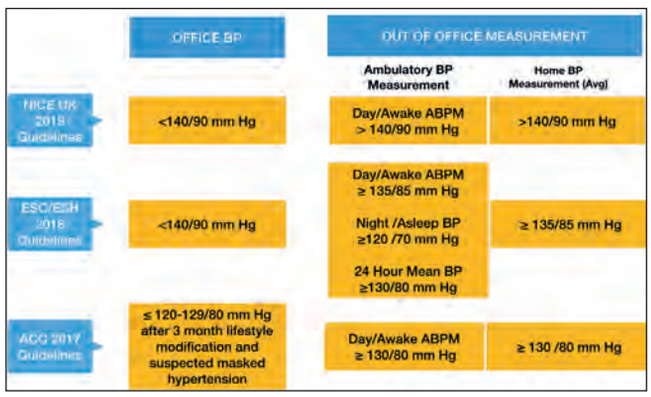

Figure 2 - Definition of Masked Hypertension

In summary, based on current evidence, ABPM is the preferred out of office method to screen for MH with emphasis on considering night ABPM measurement in individuals with African ancestry.

Adverse outcomes

Observations from the Finn-Home study revealed MH phenotype had the highest risk of progression to SH compared to normotension or WCH during an 11 year follow up.[25] Robust data from meta-analyses support MH association with increased risk of CV events, target organ damage, and mortality which is comparable to the risk of having SH. Re-analyzed cross-sectional analysis of several studies showed that patients with MH have higher left ventricular (LV) mass often comparable to SH.[26] This correlation was also found in patients treated with antihypertensive medications. Meta-analyses by Cuspidi et al showed that MH is also associated with increased LVMI and increased carotid intima-media thickness which is a presumed indicator of early atherosclerosis.[27,28]

In a systematic review and meta-analysis by Palla et al,[29] CV events and all-cause mortality were higher in patients with MH compared to normotension and WCH. Though composite CV events were low in MH compared to SH, the all-cause mortality due to MH did not show a significant difference compared to SH.[29] In patients who underwent treatment with antihypertensives, there was no significant difference in composite CV events and all-cause mortality between the patients with MH and SH. However, in treated patients, MH was associated with higher rates of CV events compared with normotension and WCH.[29]

A large observational cohort study from Japan which included 4261 hypertensive outpatient participants, where MH was defined based on HBPM and median follow-up was for 3.9 years, showed that MH was associated with greater risk of stroke compared to a group with controlled BP independent of CV risk factors like urine ACR and circulating B-type natriuretic peptide levels.[30] Analysis of the Dallas Heart Study showed an increase in aortic pulse wave velocity, cystatin C and urine ACR in persons with MH and conferred a 2.03 times increased risk of CV events compared to normotensives at 9-year median follow-up after adjusting for traditional CV risk factors.[31]

Clinical implications in special patient groups

Diabetes – The prevalence of MH is higher in patients with diabetes compared to those without diabetes.[32] In untreated diabetics followed for a median duration of 11 years, the adjusted risk for CV events for masked hypertensive patients was higher, compared to sustained normotensive subjects (HR: 1.96; 95% CI: 0.97–3.97; *P*=0.059) and similar to untreated stage 1 hypertensives (HR: 1.07; 95% CI: 0.58–1.98; *P*=0.82) but less than stage 2 hypertensives (HR: 0.53; 95% CI: 0.29–0.99; *P*=0.048).[32]

CKD – Cross sectional data from the Chronic Renal Insufficiency Cohort (CRIC) study by Drawz et al[33] showed MH measured by ABPM was independently associated with low estimated glomerular filtration rate (eGFR -3.2ml/min/1.73m2 ; 95% CI – 5.5 to -0.9 ml/min/1.73m2), greater LVMI (2.52 g/m2.7; 95% CI, 0.9 to 4 g/m2.7), pulse wave velocity (+0.92 m/s; 95% confidence interval,0.5 to 1.3 m/s) and higher proteinuria (+0.9 unit higher in log2urine protein; 95% CI, 0.7 to 1) compared with controlled BP.

Persons of African ethnicity – The Jackson Heart Study showed a high prevalence of MH in African Americans. Specifically, isolated nocturnal hypertension was noticed in 19% subjects by ABPM with mean office BP of 124/76 mm Hg.[34] They also had greater left ventricular mass and 3 times higher odds of left ventricular hypertension compared to normotensives.[34]

Outcomes of Masked Uncontrolled Hypertension (MUCH)

In a meta-analysis by Pierdomenico et al, patients with MUCH had a significantly higher risk of CV events and all-cause mortality compared to those with controlled hypertension.[35] The prognostic effect of MUCH was similar, whether the measurement was done by ABPM or HBPM. The overall adjusted hazard ratio was 1.80 (95% CI, 1.57–2.06) for MUCH versus controlled hypertensives.

Treatment

MH is a high-risk phenotype of hypertension and should not be left untreated. Unfortunately, many patients with MH have been excluded from hypertension trials due to normal office BP values leading to a paucity of data regarding the best way to treat MH. There have been no prospective clinical trials to evaluate the effect of treating MH and its impact on CV events and mortality. However, consistent evidence pointing to CV risk in patients with MH suggests prompt treatment of MH despite lack of evidence.

It is reasonable to consider pharmacological management in identified MH patients after optimizing their metabolic profile by treating the modifiable risk factors like obesity, diabetes, OSA, avoidance of alcohol, smoking, addressing work-related issues if any, and psychosocial factors. Another approach is to use antihypertensives to reduce ambulatory BP despite the absence of elevated office BP and monitor response to treatment by periodic ABPM.

Retrospective analyses of JMS-1 (Japanese Morning Surge-1) study and J-TOP (Japanese Morning Surge -Target Organ Protection) study showed treatment of MH targeting morning home BP was associated with regressions in surrogates of target organ damage like urine ACR, pulse wave velocity and LVMI over 6 months.[36] Effective CPAP in patients with OSA was shown to reduce MH.[37] The Spanish Registry Study which followed 2115 treated hypertensive patients for 4 years noted that night time, but not daytime SBP predicted CV events (hazard ratio per SD increase, 1.45: 95% CI, 1.29–1.59) suggesting the need for good nocturnal BP control.[38] Inferences from Spanish registry study and Jackson Heart Study show isolated nocturnal hypertension as a variant of MH and poor control of nocturnal BP is twice more common than daytime ABPM control and favour the importance of using 24-hour ABPM to monitor BP control during treatment both during daytime and night especially in high-risk patients.[39]

A double-blinded placebo-controlled randomized controlled trial (RCT) by Hare et al studied the impact of fixed-dose spironolactone (25 mg daily) in 115 untreated individuals without hypertension but with a hypertensive response to exercise (exercise SBP >210 mm Hg in men or >190 mm Hg in women, or DBP >105 mm Hg).[40] In the subgroup analysis of the 40% of participants with MH by daytime ABPM using a cut off of 135/85 mm Hg, the spironolactone group showed significantly greater reductions in exercise systolic BP (–10.0±12.9 vs 0.3±8.7 mm Hg, *P*<0.01) and 24-h ambulatory pulse pressure (–2.4±4.7 vs 2.1±8.4 mm Hg, *P*<0.05). However, no difference in LVMI reduction was observed between the spironolactone and placebo groups after 3 months.

Several ongoing clinical trials are investigating the impact of antihypertensive treatment in MH. Results are awaited from an RCT evaluating the effect of anti-hypertensives on the clinic and ambulatory BP, proteinuria, and target organ damage in patients with MH (ClinicalTrials.gov NCT02142881). Another large multicentric, randomized, 4-year prospective study aims to understand MH treatment based on office and out of office ABPM measurements and differences in outcome with a focus on cardiovascular (LVMI), and renal (Urine ACR) endpoints and events including all-cause mortality, CV morbidity, and mortality, cerebral morbidity and mortality (ClinicalTrials.gov NCT02804074). An interventional trial from China aims to study the role of allisartan isoproxil in the treatment of MH for target organ protection (ClinicalTrials.gov NCT02893358).

Conclusion

MH is often an occult phenotype of hypertension, the possibility of which should be considered in individuals with high normal office BP, lifestyle risk factors, and African ethnicity. 24-hour ABPM is the preferred method for diagnosis and comprehensive long-term management of MH. Individuals with MH are at high risk for progressing to SH with an equal risk of target organ damage and CV risk. RCTs to identify the optimal degree of day and night-time BP control which translates to a reduction in the CV and target organ damage risk are currently lacking and are required for future perspectives.

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Review

Diverticular Disease: A Review on Pathophysiology and Recent Evidence

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Keywords: Diverticular disease, Diverticulitis, SCAD, diet

ABSTRACT

Diverticular disease is common condition globally, especially in Western countries. Diverticulitis, Symptomatic uncomplicated Diverticular disease and Segmental Colitis associated with diverticula constitute diverticular disease. Although most patients with diverticula are asymptomatic, around 25% of patients will experience symptoms whilst 5% of patients have an episode of acute diverticulitis.

The prevalence increases with age with more than one theory being put forward to explain its pathogenesis. Faecolith entrapment in diverticula results in colonic mucosal damage and oedema, bacterial proliferation and toxin accumulation leading to perforation. This mechanism may explain diverticulitis in elderly patients with multiple, larger diverticula. Ischaemic damage could be the cause of acute diverticulitis in younger patients with sparse diverticula where more frequent and forceful muscular contractions in response to colonic stimuli occlude the vasculature leading to ischaemia and microperforation.

Chronic colonic active inflammation in the presence of diverticular disease is termed Segmental colitis associated with diverticulosis. Its pathophysiology is still indeterminate but together with its clinical picture, may mimic Inflammatory Bowel Disease. Treatment includes a high fibre diet together with antibiotics and/or salicylates with surgery in severe cases.

Indications for elective surgery in diverticular disease have changed over the past decades as this may not suggest a reduction in morbidity and mortality. Prophylaxis with probiotics, laxatives, anti-spasmotics, anticholinergic drugs and salicylates are at the centre of recent studies. Studies are also challenging previously believed facts regarding dietary fibre, nuts and seeds whilst emphasizing the effect of healthy lifestyle and smoking on the increasing incidence of DD.

Key words: Trauma, Ischaemia, Segmental Colitis associated with diverticula, Surgery, Prophylaxis.

1. Introduction

Diverticular disease is a common condition in the Western world and is defined as clinically significant and symptomatic diverticulosis due to Diverticulitis, uncomplicated Diverticular disease (DD) and Segmental Colitis associated with diverticula.[1] It is present in around 10% of people aged less than 40 years and increases up to more than 70% in people aged more than 80 years, with prevalence being similar in both men and women. [2] Around 25% of people with diverticula will experience an episode of symptomatic DD. [3]

Diverticulitis may be sub-classified as complicated or uncomplicated, with the former comprising fistulas, abscesses, obstruction and perforation (Figure 1).[1]

Historically, inflammation leading to diverticulitis was thought to be due to a primary infection of the diverticular task. However, no pathogens were actually found to cause diverticulitis. Because of this, the combination of broad spectrum antibiotics together with metronidazole was the mainstay of treatment for an acute episode. More recently, 2 main theories have been recognized as hypothesis for the pathogenesis of diverticulitis.[4]

2. Pathophysiology

The pathophysiology of DD is not completely understood. Many factors have been thought to contribute to its pathogenesis including colonic wall structure, colonic motility, diet and fibre intake, obesity and physical activity as well as genetic predisposition. [1,3]

"TRAUMATIC THEORY"

The most accepted current theory that describes the underlying mechanism in acute diverticulitis is "traumatic" damage to the diverticulum and subsequently bacterial proliferation. Increased pressure within the colon leads to faecoliths present within the lumen being pushed into the diverticuli, especially larger ones, resulting in stool impaction in the diverticular task. The entrapped faecolith causes trauma by abrading the mucosa of the diverticular sac leading to local inflammation and bacterial overgrowth. If the proliferating bacteria breach the mucosal wall to involve the full bowel wall, their toxic and gas production may eventually lead to bowel perforation. Furthermore, the irritation and inflammation caused by trapped faecoliths lead to vascular congestion and oedema, which in turn cause further obstruction, with secretions from

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the proliferating bacteria accumulating in the diverticular sac, thus increasing the risk of perforation (Figure 2). This theory could well describe the sequence of events leading to acute diverticulitis in older patients with larger diverticula, and since bacterial overgrowth is the most important pathological factor, antibiotics are the basis of treatment.[4]

"ISCHAEMIC THEORY"

In younger patients, where the finding of colonic diverticula may be sparse, acute diverticulitis may be the result of ischaemic damage. Studies have demonstrated neuromuscular differences in the affected colonic areas leading to more prolonged and forceful contractile impulses.[4] The activity of choline acetyltransferase was shown to be lower in circular muscle of patients with DD, whilst there was an increase in the number of M3 receptors. Furthermore, patients with DD showed increased sensitivity when administered exogenous acetylcholine, when compared to controls.[5] All these factors lead to increased sensitivity to cholinergic denervation leading to excessive contractile impulses in response to normal stimuli in the diverticular wall.[4] The "ischaemic" theory suggests that long-standing contractile impulses of the colon cause persistent compression of blood vessels at the diverticular neck. The neck is found in the colonic circular muscular muscle wall, which may be compressed by muscular spasm, triggering ischaemia at the mucosa and micro-perforation (Figure 2). This theory therefore puts forward another possible mechanism for the pathophysiology of acute diverticulitis where faecal entrapment is unlikely and the role of bacteria is not so prominent. Treatment with antibiotics is used more as prophylaxis against opportunistic infections on the damaged colonic mucosa rather than to treat the primary infection itself.[4] In fact, The American Gastroenterology Association (AGA) suggest that 'antibiotics should be used selectively, rather than routinely, in patients with acute uncomplicated diverticulitis'.[6]

Whenever abdominal pain is present in patients without the acute symptoms of diverticulitis, this is defined as symptomatic uncomplicated diverticular disease (SUDD). [1] Interestingly, 22% of patients with SUDD describe left lower quadrant pain lasting more than 24hours. This could be produced by the sustained spastic state of the bowel wall which predisposes to mucosal ischaemia in the diverticulum. [4] Clemens et al studied the underlying mechanisms which may be implicated in SUDD and it was found that such patients have hypersensitivity in the sigmoid colon bearing diverticula, which is similar to the pathophysiology in irritable bowel syndrome (IBS). More studies on the two diseases are required in order to be able to confirm whether patients suffering from IBS are more likely to have diverticulosis and hence be identified as SUDD in view of the chronic abdominal pain.[7]

SEGMENTAL COLITIS ASSOCIATED WITH DIVERTICULOSIS (SCAD)

DD, with its underlying inflammatory process, may closely mimic inflammatory bowel disease (IBD). Segmental colitis associated with diverticulosis (SCAD), or Diverticular colitis, is nowadays recognized as an independent entity. It describes areas of the colon affected with DD which demonstrate chronic active inflammation, irrespective of diverticular inflammation. Symptoms usually consist of diarrhoea, abdominal cramps and fresh/altered rectal bleeding.

The exact pathogenesis of SCAD remains unclear, but it is most likely to be multifactorial (Figure 2).[8]

In contrast to IBD, it is believed that SCAD runs a more benign and self-limiting course with patients achieving remission without treatment and recurrence. Management includes a high fibre diet in combination with antibiotics and/or salicylates. As suggested by Rampton, a 7 day course of Ciprofloxacin 500mg BD together with Metronidazole 500mg TDS may be used to treat patients with SCAD. Furthermore, 2.4g-3.2g of Mesalazine may be added daily in cases of incomplete response to antibiotics or recurrent symptoms. [8] An alternative antibiotic regime used in patients who are unable to tolerate Ciprofloxacin and Metronidazole is an Ampicillin-based antibiotic regime.[9]

Recently, Tursi et al have demonstrated how acute mild to moderate diverticular colitis can be treated with a combination of beclomethasone dipropionate (BDP) and the probiotic VSL#3, as shown in Table 1. The probiotic was administered for a total of 15 consecutive days whilst BDP for 4 weeks with the great majority of patients achieving symptomatic remission by week four. Immunosuppressants, such as systemic steroids, may be used in severe cases as 3rd line agents. Steroid-dependent or steroid-refractory cases may then require surgical interventions, with decisions being taken according to each individual case.[8] Table 1 summarises the management algorithm for patients with SCAD.

3. The Role of Surgery

In the past, patients with recurrent episodes of diverticulitis generally underwent elective surgery after the second acute episode. [3] This was based on the fact that there was thought to be an increased risk of complications and reduction in response to treatment after the second acute episode. Recently however data shows that the indication for elective surgery should not be based on the number of acute episodes alone, but should take into consideration the patients' risk factors, age, comorbidities, severity of the episodes and any complications. One major benefit with respect to elective surgery is the removal of symptoms that are experienced with acute diverticulitis. However this does not guarantee a reduced risk of emergency surgery or colostomy, reduction in septic complications of acute diverticulitis or a general reduction in morbidity and mortality.[10] Therefore, the decision for surgical intervention should be based on the benefits and risk exposure to each individual patient, once the patient has recovered from an episode of acute diverticulitis.

4. Prevention of Diverticulitis

DRUGS

Studies and advances in medical treatment have demonstrated that a number of drugs may be used in the prophylaxis of DD and therefore further reducing the need for surgery. Laxatives prevent constipation by reducing faecolith formation and the risk of traumatic damage to the diverticulum by stool impaction. Conversely, the administration of spasmolytics in patients with abdominal pain lasting more than 24 hours interrupts the colonic contractions and relieves the ischaemic injury. Anticholinergic drugs also reduce the contractions in colonic circular muscle hence reducing vascular ischaemia. [4] Interestingly, aminosalicylates particularly Mesalazine have been used as maintenance of remission in patients with diverticulitis. In a study by Rampton, a maintenance dose of Mesalazine 1.6g daily was administered to patients with the addition of probiotic VSL#3 in patients with more severe disease to maintain remission (Table 1).[8]

Although Mesalazine is used in patients with ulcerative colitis, there is no clear evidence that Mesalazine alone reduces the symptoms of DD.[11] There is also no clear evidence that Mesalazine reduces the risk of acute episodes of diverticulitis and, in fact, the AGA advices against the use of Mesalazine after an acute episode of uncomplicated diverticulitis.[6,11] Similarly current guidance suggests that probiotics are effective in reducing symptoms is lacking. Several studies have been conducted aiming at evaluating the clinical efficacy of probiotics. However, no definitive results have yet been achieved, mainly due to the diversity of the available studies.[12]

5. Recent Evidence

Multiple factors have been identified as risk factors for DD and its complications, which are amongst the most common gastroenterological indication for hospitalisation. Amongst the major risk factors there are aging and lifestyle diverticulitis and diverticular bleeding. Physical activity, obesity, diet (including fibre content and nut, corn and popcorn consumption), smoking status are being analysed for their impact on disease symptomatology.[11]

5.1 Physical activity

Physical activity has been shown to reduce the risk of diverticulitis by 25%.[13] In a study by Strate et al where physical activity and DD were followed-up over 18 years, it was demonstrated that men performing the most vigorous activity had a 25% reduction of risk of diverticulitis in addition to a 46% risk reduction in diverticular bleeding when compared to men who exercised less.[14] Various mechanisms may describe this risk reduction including reducing intracolonic pressure, reducing colonic transit time and neuroendocrine alterations.[13] In fact, current guidance advises patients diagnosed with DD to engage in vigorous physical activity.[6]

5.2 Fibre intake in an Asymptomatic Patient

The theory that lack of dietary fibre is associated with an increased risk of diverticulosis has always been popular. [1] Painter and Burkitt had put forward that dietary fibre deficiency results in high colonic pressure in view of constipation that in turn results in mucosal herniation [15]. Their studies however have not proven that elevated intracolonic pressures are present in patients with diverticulosis and more recent studies are further confirming this.[16] Studies are suggesting that a high fibre diet may not protect against the development of diverticulosis, but it may protect against DD. In a small study, patients who on average consumed less fibre (21.4 g/day vs 41.5 g/day; $p<0.001$) were more likely to have DD. This study has been challenged by 2 studies by where both studies did not find an association between fibre intake and DD.[11] However, limitations to these studies are : the study by Song et al was performed in Asia, where in contrast to that in Western populations, colonic diverticula are more frequently found on the right side of the colon and the pathophysiology is different to that in Western populations[17]. In the other study by Peery et al, who carried out a short-term investigation of dietary habits before colonoscopy, failed to identify clear-cut pathogenetic elements.[18]

Data with regards to diet and DD originated from the European Prospective Investigation into Cancer and Nutrition (EPIC) Oxford study, where 47,033 healthy individuals were followed-up for 5 years and the risk of hospitalization secondary to DD was evaluated. Crowe et al found a reduced risk of DD complications, including a lower hospitalization risk and lower risk of death from DD with increased intake of fibre (25.5 g/day in women and 26.1 g/day in men), with a relative risk of 0.58 (95% CI 0.46–0.73) when compared to those with the low intake of fibre (<14 g/day).[19]

Similarly Aldoori et al analysed data from a prospective cohort of 47,888 US men over 4 years. It was found that there was an inverse relationship between the risk of DD and total dietary fibre intake after adjusting for age, energy-adjusted total fat intake and physical activity. This was mostly attributed to fruit and vegetable fibre. The relative risk for men on a low-fibre, high-total-fat diet was 2.35 (95% CI 1.38, 3.98) compared with those on a high-fibre, low-total-fat diet whilst the relative risk for men on a low-fibre, high-red-meat diet was 3.32 (95% CI 1.46, 7.53) compared with those on a high-fibre, low-red-meat diet.[20] Similar results were obtained in a retrospective study of 56 patients admitted with SUDD, where those with a high fibre intake (>25 g/day) had a reduced risk of symptoms (19% vs 44%) and diverticular complications (6.5% vs 32%).[21]

5.3 Fibre Intake in a Patient with a History of Acute Diverticulitis

Though current guidance suggests that a fibre-rich diet or fibre supplementation in patients with a history of acute diverticulitis, this is a conditional recommendation with very low quality of evidence.[6] In fact, there are no studies that

address whether dietary or supplemental fibre intake reduces the risk of recurrent acute diverticulitis. The benefits of fibre for chronic abdominal pain in patients with diverticulosis are inconsistent and do not necessarily imply benefit in terms of recurrent diverticulitis. A differential benefit of dietary fibre intake compared with fibre supplementation is unknown, as is the optimal daily dose of fibre necessary to achieve benefit. The benefit of fibre in patients with recurrent or complicated diverticulitis is also undefined.

There are controversial results in terms of symptom relief from fibre supplementation alone.[11] A meta-analysis analysed the therapeutic effect of fibre supplements and it was noted that there is minimal high-quality evidence for a high-fibre diet in the treatment of DD, and that most suggestions are based on inconsistent level 2 and mostly level 3 evidence. It is important to note that in this meta-analysis, one randomized controlled trial documented an improvement in clinical symptoms and a marked reduction in pain, whilst another documented only a reduction in constipation without a positive effect on symptoms with fibre supplementation.[22]

Type of fibre is also regularly discussed. Studies were performed to analyze the type of fibre supplements that relieve symptoms. In one study, administration of bran or ispaghula husk over 16 weeks or methylcellulose administration over three months did not result in less symptoms when compared to placebo. Similarly, 12 weeks of lactulose supplementation was no more effective than high fibre.[11] Thus, methylcellulose and lactulose are not effective in reducing symptoms.

Rifaximin in addition to fibre has shown to reduce more symptoms than administration of fibre alone. Rifaximin is a non-systemic antibiotic with a vast antibacterial action covering multiple organisms including gram-positive, gram-negative, aerobe and anaerobes. It is almost not-absorbed so its bioavailability within the gastrointestinal tract is relatively high.[11] In a meta-analysis assessing Rifaximin and fibre treatment, the pooled risk difference (RD) for symptom relief was 29.0% (rifaximin versus control; 95% CI 24.5–33.6%; $p<0.0001$) and the number needed to treat (NNT) was 3. Rifaximin in addition to fibre was also more effective in preventing acute diverticulitis than fibre alone, albeit with a low therapeutic advantage. The pooled RD in the treatment group was –2% (95% CI –3.4 to –0.6%; $p=0.0057$) and the NNT was 50.[23] Recently, a multi-centre, randomised, open trial analysed the result of administration of Rifaximin in addition to a high fibre regimen in secondary prevention of acute diverticulitis.

Recurrence of acute diverticulitis occurred in 10.4% of patients given Rifaximin together with fibre experienced in comparison to 19.3% of patients who received fibre alone ($p=0.033$).[24]

5.4 Smoking

Smoking is a well-known risk factors for diverticulitis, in a dose-response relationship.[13] In a Swedish mammography cohort, 36,000 females were followed-up from 1997 – 2008. It was found that the risk of hospital admission from DD was increased by 24% when compared to non-smokers. No significant dose-response relationship was demonstrated in this study. Furthermore, in a Swedish cohort study of 7500 men over 28 years, it was found that patients smoking during the period of study had a relative risk of 1.89 (95% CI 1.15–3.10) for perforated DD when compared to people who do not smoke.[11] In the EPIC-Oxford cohort, there was a relative risk of 1.34 in people who smoked less than 15 cigarettes per day and a relative risk of 1.86 in people who smoked 15 or more cigarettes per day of hospitalization for diverticular disease when compared to non-smokers.[19]

5.5 Body Mass Index (BMI)

An increasing problem is obesity which has been shown to increase the risk of diverticulitis by up to 80%.[13] Associations between acute diverticulitis and waist circumference, waist-to-hip ratio and body mass index have been identified.[1] The pathogenesis of these associations is still unclear however the difference in microbiology of the gastrointestinal tract observed in obese patients is currently being studied as a possible link to increased risk of diverticular disease, together with the fact that cytokines secreted from adipose tissue might play a role in the inflammatory process of diverticulitis. [25]

A cohort study by Rosemar et al recruited 7500 men in Sweden and these were followed-up for 28 years. This study found a x4 fold increased risk of diverticulitis in men with a BMI of more than 30, when compared to men with BMI of 20-22.5.[26] Strate et al also demonstrated this relationship when 47,000 men were followed-up for 18 years; there was a 78% increased risk of diverticulitis in males with BMI of more than 30 as well as a x3 times greater risk of diverticular bleeding when compared to men with BMI <21.[27]

5.6 Non-Steroidal anti-inflammatory drugs

Another identified risk factor for complicated DD is the use of nonsteroidal anti-inflammatory drugs (NSAIDs).[1] The regular use of such drugs was found to increase the risk of an initial episode of acute diverticulitis by 70%, whilst regular aspirin use by 25%.[13] Furthermore, a large meta-analysis has demonstrated a significantly raised risk of diverticular bleeding, perforation and abscess formation in patients with NSAID use when compared to nonusers.[28] Because of this, the AGA advises patients to avoid the use of non-aspirin NSAIDs in case of a history of diverticulitis, albeit with a very low level of evidence.[6]

5.7 Nuts, seeds and Corn

A subject which is increasingly being challenged recently is the result of nuts, seeds and corn intake on the prevalence of DD. For decades, patients with DD were advised to avoid foods such as nuts, corns and seeds. This was based on the

hypothesis that these particles might obstruct a narrow-necked diverticulum leading to a cascade of events similar to that of the "traumatic" theory. In a landmark study by Strate, a prospective cohort of 47,228 male health professionals were evaluated for administration of dietary nuts, corn and seeds for 18 years. Results showed that there was no increased risk of complicated diverticulitis and no significant relationship with diverticular bleeding. Instead, consumption of these types of food may inversely be protective against diverticulitis.[29] Hence, the idea that consumption of these foods is a risk factor for diverticular disease is not proven and suggestions to avoid nuts, seeds and corn should be re-evaluated.

6. Conclusion

Although the "traumatic and ischaemic" theories describe different mechanisms as to the pathophysiology of diverticulitis, both may act in the same patient and both act differently amongst different patients. Lifestyle practices especially physical activity, obesity, smoking and NSAID use play a very important role in the incidence of diverticulitis and more research is concentrating on this. Research is also questioning knowledge that was believed for a long time pertaining to dietary practices and is continuously revealing new facts to help understand risk factors and pathophysiology related to DD.

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Clinical Paper

Vertebral Artery Injury in Cervical Spine Fractures: A Cohort Study and Review of the Literature

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ABSTRACT

BACKGROUND: The risk of vertebral artery injury (VAI) secondary to cervical spine fracture is increasingly recognised in the literature. The aim of this study was to determine the incidence of VAI amongst patients presenting to the Royal Victoria Hospital (Northern Ireland's regional trauma centre with emergency surgical spinal services) with acute cervical spine fractures, and to identify fracture patterns associated with the highest risk of VAI.

METHODS: A retrospective review of 1,894 computed tomography (CT) reports of patients who underwent imaging of their cervical spine and/or vertebral arteries over a 12-month period, from June 2018 to June 2019, was conducted.

RESULTS: Sixty-eight patients (3.59%) with a confirmed cervical spine fracture were identified. These patients had an age range of 18-97 years and included 39 males (57.4%) and 29 females (42.6%). The fractures were then classified according to the AOSpine Cervical Spine Fracture Classification. Of the 68 patients with a confirmed cervical spine fracture, five (7.35%) were diagnosed with VAI, all involving fractures of their upper cervical spine. Two involved fractures extending into the transverse foramen, two involved subluxation of the vertebrae and one involved both. In all five cases, these fractures resulted from high-energy injuries. Regarding management, the patients with VAI in this study were either monitored and given no specific treatment or treated medically with antiplatelet therapy. None underwent surgical intervention.

CONCLUSIONS: Fracture patterns associated with increased risk of VAI are fractures involving the upper cervical spine, fractures with associated subluxation, and fractures of the transverse process extending into the transverse foramen - urgent CT-angiography in these cases is recommended. Further work should develop a targeted set of criteria for screening for VAI in cervical spine fractures, with consideration of high-risk fracture patterns.

INTRODUCTION

Vertebral artery injury (VAI) is a potentially serious complication of cervical spine fractures. The artery is at high risk due to its passage through the transverse foramina of the cervical vertebrae. The incidence of VAI in patients with blunt cervical spine trauma ranges from 0.53% to 39% in the literature. [1,2,3] This wide variation in incidence is most likely due to differences in sample size and the imaging modality used, as well as patient selection bias. Recently, there has been a higher incidence of VAI reported, most likely due to advances in imaging technology.[4]

The types of cervical spine fractures most associated with vertebral artery damage are fractures of the transverse process extending into the foramen transversarium, upper cervical spine fractures involving C1-C3 and facet dislocations/subluxations.[5] The mechanisms of injury involve direct impingement of the artery in the foramen, or stretching of the vertebral artery between adjacent vertebrae.[6]

Clinical symptoms of VAI may include dizziness, vomiting and vertigo due to ischaemia of the cerebellum, which is responsible for balance and coordination. Ischaemia of the primary visual cortex may result in visual disturbance and damage to the brainstem may result in focal weakness.[7] Vertebral artery injury can have devastating consequences for patients, causing neurological deficits, stroke and death, although the majority of patients are initially asymptomatic.[8] De Souza et al reported that 70% of cases showed neurological symptoms within the first 24 hours. Biffl et al reported a period of 18 hours between time of injury and neurological symptoms in 44% of cases.[9,10] Explanations for this delay in symptoms include thrombus progression and progression of the vascular injury to a higher grade, such as a pseudoaneurysm or dissection.[1] The overall mortality of VAI is reported as 4% to 8%.[9] Therefore, it is important to consider the possibility of VAI in patients presenting with cervical spine trauma. Early diagnosis will allow prompt management

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and improved patient outcomes.

Diagnostic techniques for VAI include Digital Subtraction Angiography (DSA), Computed Tomographic Angiography (CTA), Doppler Ultrasonography (USS) or Magnetic Resonance Angiography (MRA).[11]

Regarding VAI management, treatment options range from observation to medical or surgical intervention. The choice of treatment depends on both the grade and site of the injury[9], as well as associated injuries and bleeding risk. Medical management, involving the use of antiplatelets or anticoagulants, may decrease the risk of thromboembolic mechanisms, resulting in ischaemic events.[12] Endovascular intervention, including stenting, artery occlusion and embolization, may be indicated if medical therapy is contraindicated or has failed.[13] Surgical intervention on the vertebral arteries is technically challenging and tends to be reserved for patients unsuitable for anticoagulation, who have failed with endovascular options or who have uncontrollable haemorrhage.[9,11]

The aim of this retrospective cohort study was to determine the incidence, clinical features and management of VAI amongst patients with cervical spine fractures presenting to Northern Ireland's regional trauma centre, and to identify fracture patterns most commonly associated with VAI.

MATERIALS AND METHODS

Study population

A retrospective review was carried out involving patients who presented to the Royal Victoria Hospital (RVH) Emergency Department (ED) and underwent subsequent CT imaging of their cervical spine and/or CTA of their vertebral arteries, arranged by the ED. The study involved patients who presented over a 12-month time period, from June 2018 to June 2019. The CT reports of 1,894 patients who underwent a CT scan of their cervical spine or a CTA of their vertebral arteries in this time period were obtained. The reports were then reviewed to determine the number of patients who had a confirmed cervical spine fracture. Of these 1,894 patients, 68 were found to have an acute cervical spine fracture. Patients without a confirmed fracture were then excluded from further study.

Information was collected regarding patient sex, age at injury, mechanism of injury, type of fracture and whether subsequent CTA was undertaken.

The Northern Ireland Online Electronic Care Records System (NIECR)[14] was used to assess patient outcome and follow up. For those patients with VAI, further data on associated injuries, neurological status and treatment were collected. The purpose of gathering this extra information was to compare the VAI patients in this study with those in previous studies.

Radiography

The imaging of patients with a cervical spine fracture was reviewed and classified according to the AOSpine Cervical Spine Fracture classification system (Types I-III).[15] In cases where CT angiography was undertaken, the results were reviewed to determine if the patient had VAI. This was classified by the segment of the vertebral artery involved and also by the Blunt Carotid and Vertebral artery Injury (BCVI) grading system.[10]

Statistical Analysis

Due to small patient numbers, meaningful statistical analysis was not possible, thus descriptive analysis of the data using Microsoft® Office Excel® 2007 was performed.

RESULTS

Overall, 1,894 patients presenting to the RVH ED from June 2018 to June 2019 underwent CT imaging of their cervical spine and/or vertebral arteries. Sixty-eight patients were found to have a cervical spine fracture (3.59%). There were 39 males (57.4%) and 29 females (42.6%), mean age 60.4 years (range 18-97 years, standard deviation ± 22.8 years).

Mechanism of Injury

The most common mechanism of injury was a fall, which accounted for 41 (60.3%) of the 68 cases (**Table 1**). This included both falls from standing and falls from height. Road traffic collisions (RTC) caused 23 cases (33.8%). Two patients sustained a cervical spine fracture following assault, one due to a rugby tackle and one in a go-karting accident.

Table 1.
The mechanisms of injury for the 68 patients with acute cervical spine fracture are outlined.

Mechanism	Number of patients
Fall	41 (60.3%)
Road traffic accident	23 (33.8%)
Assault	2 (2.9%)
Go-karting accident	1 (1.5)
Rugby tackle	1 (1.5)

Fracture Pattern

Of the 68 patients with cervical spine fractures, 37 (54.4%) had a fracture of their upper cervical spine and 31 (45.6%) had a fracture affecting the subaxial cervical spine. When classified by injury morphology as per the AOSpine Fracture Classification System[15], 41 patients (60.3%) had Type A injuries (i.e. bony injury only), nine (13.2%) had Type B injuries (i.e. tension band injuries) and 18 (26.5%) had Type C injuries (i.e. translation injuries).

Of the patients with upper cervical spine fractures, four patients (10.8%) had Type I injuries (i.e. involving the occipital condyle/ occipital-cervical joint complex injuries), 11 (29.7%) had Type II injuries (i.e. C1 ring and C1/C2 joint complex injuries), and 22 (59.5%) had type III injuries (i.e. C2 and C2/C3 joint complex injuries) as per the AOSpine classification. When classified by injury morphology, 16 patients (43.2%) had Type A injuries, six (16.2%) had Type

B injuries and 15 (40.5%) had Type C injuries.

Of the patients with subaxial cervical spine fractures, the most common injury morphology was Type A as per the AOSpine classification, accounting for 80.6% of cases (**Table 2**).

Table 2.

Subaxial cervical spine fracture morphology as per AOSpine Fracture Pattern Classification.

AOSpine classification	Key features	Number of patients
A0	A fracture not significantly affecting spinal stability	22 (68.8%)
A1	Compression fracture involving a single endplate without involvement of the posterior vertebral body wall	3 (9.7%)
A2	Coronal fracture of the vertebral body involving both endplates but not the posterior wall	0
A3	Incomplete burst fracture involving a single endplate and the posterior wall	0
A4	Complete burst fracture involving both endplates and the posterior wall	0
B1	Disruption to the osseous posterior tension band	1 (3.2%)
B2	Complete disruption of the posterior capsuloligamentous or bony capsuloligamentous structures together with a vertebral body, disk, and/or facet injury	2 (6.5%)
B3	Disruption of the anterior tension band	0
C	Failure of anterior and posterior elements leading to displacement or translation of one vertebra compared to another in any axis	3 (9.7%)

Sixty-two (91.2%) of the 68 patients were neurologically intact following their injury. Five patients (7.35%) were diagnosed with an incomplete spinal cord injury and one patient (1.47%) with a complete spinal cord injury. Of note, all three of the Type C subaxial spine fractures resulted in neurological damage.

Thirty patients (44.1%) were found to have fractures of the transverse processes. Further study was undertaken as these can potentially involve the foramen transversarium, posing a risk to the vertebral arteries. The foramen transversarium were involved in ten (33.3%) cases, and three (30%) of these patients were found to have vertebral artery injury.

Vertebral Artery Injury

Fifteen patients of this cohort underwent CTA, eleven (73.3%) of whom had fractures involving the upper cervical spine and nine (60%) of whom had fractures involving the foramen transversarium. Five patients were found to have VAI (i.e. 7.35% of the overall cohort with a confirmed cervical spine fracture). All five of these patients had fractures involving the upper cervical spine resulting from high-energy injuries (**Table 3**).

Table 3.

Clinical and radiographic features corresponding to the five patients with VAI.

Sex	Age (years)	Mechanism of injury	AOSpine Classification	Significant associated injuries	Neurological status	VAI grade	Follow-up CT-angiography	Fracture management	VAI management
M	33	RTA	Type I, A, F3, fracture extends into TF	Haemorrhagic cortical contusions	Intact	II	Day 6; injury unchanged	Aspen collar	Observation
M	50	RTA	Type II, C	SAH	Intact	I	Day 10; injury not seen	Doll's collar	Observation
M	26	RTA	Type III, C	SAH, base of skull fracture	Intact	IV	Day 3; partial recanalisation	Minerva jacket	Aspirin
M	83	RTA	Type III, C, fracture extends into TF	Thoracic vertebral body fracture	Unknown	I	Day 7; injury unchanged	Posterior stabilisation C4-T4	Aspirin
F	58	Fall off horse	Type III, A, fracture extends into TF	Nil significant	Incomplete spinal cord injury	IV	Day 10; injury unchanged	Aspen collar	Aspirin

Abbreviations: M=male, F=female, RTA=road traffic accident, TF=foramina transversarium, SAH=subarachnoid haemorrhage,

All cases of VAI were found to involve the right vertebral artery in either the V2 (foraminal) or V3 (extraspinal) segments. As per the BCVI system, two patients had grade I injury (i.e. luminal irregularity or dissection with intraluminal haematoma occluding <25% of the lumen), one patient had grade II injury (i.e. luminal irregularity or dissection with intraluminal haematoma occluding >25% of the lumen) and two patients had grade IV injury (i.e. total occlusion of the vessel). All five patients underwent follow-up CTA within ten days of injury. Of note, none of the five patients was confirmed to have a neurological deficit resulting from the VAI. In one case, it was impossible to accurately determine neurological status due to severe sepsis from which the patient later died, and one patient was found to have signs suggestive of central cord syndrome presumed to have resulted from acute cervical hyperextension.

Regarding management, only one patient underwent surgical stabilisation. Three patients received antiplatelet therapy; in the remaining two cases this was deemed not appropriate due to acute intracranial haemorrhage.

DISCUSSION

First described by Carpenter et al in 1961[16], cervical spine fractures are well documented in the literature as being a risk factor for VAI.

This study found a 7.35% incidence of VAI in patients diagnosed with acute cervical spine fracture in Northern Ireland over a 12-month period. The incidence of VAI in the literature varies greatly, perhaps reflecting differences in study populations.[2,10,17] Fleck et al[17] found the VAI incidence to be almost three times greater than ours, however we note the median age was 45 years, 16 years lower than that of the current study, where the median age was 61 years. We suggest that as younger patients are more likely to experience cervical spine fractures from high impact trauma, and VAI is associated with high impact trauma, this may explain why our incidence is lower.

In this study, falls were the most common mechanism of injury leading to a cervical spine fracture. However, in keeping with previous studies, we found RTC to be the most common mechanism associated with fractures resulting in VAI.[11,17,18]

Fracture Pattern

In keeping with findings by Leucht et al[19], we found that type A injuries were the most common (60.3%) and type B injuries the least common (13.2%).

The most common cervical spine fracture type associated with VAI is a fracture of the transverse process extending into the foramen transversarium. In this study, three of the ten patients with fractures involving the foramen transversarium were found to have VAI. Although our numbers are small, this is felt to be in keeping with other studies, reporting VAI in approximately 20% of cases of fractures involving the foramen transversarium.[2,10]

The current study found that 37 (54.4%) of the 68 patients had a fracture of their upper cervical spine, five (13.5%) of whom were diagnosed with VAI. These findings are in keeping with the findings of Mitha et al[7], who found the incidence of VAI in patients with upper cervical spine fractures to be 18%. The vertebral artery is most mobile as it passes through the transverse foramen of C2 and moves laterally to pass through the transverse foramen of C1, putting it at risk of damage during mechanical injury.[13]

The third fracture type associated with VAI is dislocation or subluxation of the vertebrae. Eighteen (26.5%) of the 68 patients in this study were found to have subluxation of their cervical spine. Three (16.7%) of these patients were diagnosed with VAI. Mueller et al[2] found the incidence of VAI in patients with cervical spine subluxations to be as high as 31%.

Vertebral Artery Injury

The V2 (foraminal) and V3 (extraspinal) segments of the vertebral artery are most at risk of damage due to their passage through the foramina transversaria[8], with injuries located in the second and third parts in 26% and 55% of cases respectively[11]. In keeping with this, we found all cases of VAI to involve the V2 or V3 segments.

As the dominant vertebral artery provides a greater contribution to the basilar artery than its non-dominant counterpart, this may influence clinical signs and also long-term outcomes[9]. For example, damage to the dominant artery, which in most cases is the left, may be more likely to result in a posterior circulation stroke, whereas damage to the non-dominant vertebral artery may not produce any clinical symptoms due to sufficient collateral blood supply[20]. Biffl et al[10] reported that 88% of posterior circulation ischaemic events occurred in patients with a left dominant vertebral artery injury. In the present study, all patients experienced injury to the right vertebral artery, which, in most cases, is non-dominant. This may explain why none of the patients was found to suffer ischaemic complications resulting from the VAI.

The risk of a thrombotic stroke after VAI varies in the literature but rates of up to 24% have been reported[21]. None of the five patients with VAI in this study had a subsequent stroke. Bonney et al[22] noted a mortality of 4-8% for VAI. One patient with VAI in this study died, however this was as a result of chest sepsis.

Diagnostic Techniques

In this study, the only imaging modality undertaken to look for VAI was CTA.

The gold standard method for diagnosis of VAI is digital subtraction angiography (DSA), which can detect very subtle intimal injury. However, this is an invasive procedure with a complication rate of 4-8% which may include contrast induced nephropathy and stroke. Therefore DSA is no longer in widespread clinical use.[8,11]

Other diagnostic methods include Doppler Ultrasonography (USS) and Magnetic Resonance Angiography (MRA). Doppler USS is widely available and the least invasive, however it is user dependent and has a reported sensitivity of 38.5% for detecting VAI. MRA is often regarded as impractical for initial screening of the trauma patient due to scan duration.[11]

CTA has been shown to have a sensitivity and specificity for VAI of 68% and 92% respectively.[11] Thus, it is now the most widely used method to investigate for VAI[4]. However, CTA exposes the patients to radiation and to potentially nephrotoxic contrast.[22] Given the sensitivity of CTA for VAI, it is possible that in our cohort some cases of VAI were missed, however the clinical relevance of this remains unclear.

Selection Criteria for Screening

Initially, the screening criteria for VAI were broad and were felt to subject many patients to unnecessary imaging.[23] Recently, there has been an emphasis on determining a more specific set of criteria. Biffl et al[10] produced the Denver Screening Criteria for Blunt Cerebrovascular Injury. However, this screening criteria also includes carotid artery injury, which differs from VAI in presentation, prognosis and treatment.[9] Therefore, further investigation is warranted to determine a set of screening criteria specific to VAI.

Fracture patterns deemed to be at highest risk for VAI are facet joint dislocations, fractures involving the transverse foramen, and fractures of the upper cervical vertebrae.[8,24] Knowledge of these fracture patterns has allowed clinicians to limit their screening procedures to those with the highest risk. In keeping with this, we found that of the ten patients with fractures extending into the transverse foramen, nine underwent subsequent CTA.

Of the patients in this study who underwent CTA, one third were found to have VAI. None of these patients was documented as being symptomatic at the time of presentation, thus highlighting the need for appropriate screening amongst patients with high-risk fracture types in the absence of clinical signs.

Treatment

In this study three patients with VAI were commenced on antiplatelet (aspirin) therapy following discussion with the local stroke team. The remaining two patients experienced acute intracerebral haemorrhage; therefore, antiplatelet therapy was not felt appropriate and these patients were closely monitored for neurological deterioration. No patients underwent endovascular or surgical treatment for their VAI.

To our knowledge, no randomised controlled trials comparing the efficacy of different treatment strategies have been conducted to date. Several studies have reported no difference between patients treated with heparin and those treated with antiplatelets.[25,26,27] However, there is a lack of evidence in the literature regarding the efficacy of endovascular treatment when compared with medical treatment. The optimum duration for antiplatelet therapy also remains unclear.

Subsequent imaging

It has been suggested that patients with VAI should undergo a second CTA within one week.[28] In this study, all five patients with VAI underwent repeat CTA within ten days from initial imaging. For the three patients commenced on aspirin therapy, CTA findings demonstrated stability of the injury in two cases and partial resolution in one case. Regarding the two cases for whom antiplatelet therapy was contraindicated, one patient was found to have unchanged appearances, and in the other patient's case, the injury was no longer visualised, perhaps reflecting the sensitivity of CTA in detection of VAI. In both these cases, no neurological deterioration was observed, therefore no further imaging was undertaken.

The importance of follow-up CTA has been documented in other studies. Biffl et al[29] reported that improvement was noted in 57% of patients with grade I injury, allowing cessation of their treatment. Conversely, 8% of grade I injuries progressed to pseudoaneurysm requiring endovascular stenting. In the present study, no change to management was made for any of the five patients. Thus, we believe further work is warranted regarding optimal timing of repeat imaging to affect clinical practice.

Limitations

Limitations to our study include sample size, with only five cases of VAI identified over a one-year period. The data were collected in a retrospective manner from a single trauma centre. Retrospective data collection using administrative databases with potential coding discrepancies may have caused cases to be overlooked. Furthermore, as this study only included patients who underwent initial CT imaging arranged by the RVH ED, patients undergoing CT imaging following admission may have been missed.

CONCLUSION

This study found the incidence of VAI in patients presenting with cervical spine fractures to the RVH ED to be 7.35% between June 2018 and June 2019. In all cases, these fractures resulted from high-energy injuries. Fracture patterns associated with increased risk of VAI are fractures involving the upper cervical spine, fractures with associated subluxation, and fractures of the transverse process extending into the transverse foramen, and therefore urgent CTA is recommended.

Further work should focus on developing a more targeted set of criteria for screening for VAI in cervical spine fractures. Further study is also warranted regarding the efficacy of current treatment options for VAI, including optimum duration for medical therapy.

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Medical Education

"The Brain Society": The First Two Years of an Undergraduate Neuroscience Society in Northern Ireland

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Abstract

The Queen's University Belfast Brain Society was set up in September 2018 to promote interest in the human brain. There were three main goals: firstly to provide opportunities for medical students to learn from neurologists and neurosurgeons outside their formal curriculum; secondly the Brain Society aimed to organise events that included students from other disciplines and to members of the general public who were interested in learning about aspects of neuroscience; thirdly to tackle neurophobia.

In the last two years, there have been 14 events, ranging from formal lectures, to practical sessions and to patient-focused information evenings. We have sold over 1,600 tickets. This article covers how the Brain Society was set up, to inform students in other universities about the Belfast experience.

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Introduction

Clinical neuroscience is perceived to be difficult among medical students and trainee doctors[1,2,3]. Short undergraduate placements in neurosciences with reduced extra-curricular exposure to neuroscience contribute to neurophobia[2,4]. The consequence is a limited number of people advancing to a career in clinical neuroscience and reduced confidence in the management of neurological disorders in the postgraduate stages of training and independent practice[5].

Undergraduate neuroscience societies provide an opportunity to spark curiosity in neuroscience and tackle neurophobia.[6,7]. In this paper, we describe how the QUB Brain Society was founded and detail its organisation and events. We hope this informs students elsewhere wanting to set up an undergraduate neuroscience society and confront neurophobia.

"How something physical yields the abstract and the intangible, how structure leads to function. I am in awe by how the brain gives rise to consciousness, character and purpose"

David Seong Hoon Lee, Founder and 2018-2019 President

Founding of QUB Brain Society

The idea for an undergraduate neuroscience society at Queen's University, Belfast (QUB) was conceived in 2018 by two QUB medical students, David Lee (Seong Hoon Lee) and Kah Long Aw, whilst enrolled in an intercalating MSc in Neuroscience at King's College London. The extensive opportunities provided by London's undergraduate neuroscience societies and research groups provided the initial inspiration for the QUB Brain society, and it was evident this approach could help to redress neurophobia [8].

The QUB Students' Union council members welcomed the proposal for the new society enthusiastically. The next step was engagement with local clinicians, (in particular Dr Stanley Hawkins, Dr Michael Kinney and Mr Vashisht Sekar) as well as other local students who shared the same vision for neuroscience in Northern Ireland.

The 'Brain Society' was named to reflect its interdisciplinary nature and to appeal to the wider community including such areas as diverse as social sciences, computer science, and philosophy. We also wanted to encourage the involvement of people living with neurological disorders. A name like QUB "Neuroscience Society" may have appeared too exclusive and 'potentially could have deterred people from' attending events.

Events Organised

The content and style of events were chosen to have an interdisciplinary appeal with academic and non-academic events organised to get interest from the wider student body. Non-academic events explored topics not traditionally taught in the curriculum – for instance, emotional aspects of brain function (See Table 1)

The Unique Selling Point

Despite QUB's geographic isolation, being far away from the abundant neuroscience societies and research groups present elsewhere in the United Kingdom, we saw potential novel opportunities unique to Belfast.

Northern Ireland has one of the world's highest prevalence rates of multiple sclerosis (MS)[9], providing a valuable

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platform to conduct epidemiological and basic disease mechanisms research. QUB has world leading researchers such as Prof. Denise Fitzgerald, working in MS and remyelination mechanisms. There is a historical legacy of seminal observations in the neuroscience disciplines such as from the late Prof. Dame Ingrid Allen, who was instrumental in the discovery of the

Table 1: Brain Society events organised in 2018-2020

Event name	Speakers	Event description	Attendance
The Inaugural Event: What is the Brain to You? (15/10/18)	Dr Stanley Hawkins, Professor Denise Fitzgerald, Dr Ciaran Mulholland (All QUB)	Lecture series by a neurologist, neuro-immunologist, and a psychiatrist about how they view the brain from their respective fields.	242
Memories (3/11/18)	Dr Stanley Hawkins, Peter Rogan, Caitlin O'Callaghan, Chloe Gilkinson, Emma McIvor (All QUB)	A neurologist speaking about the neural basis of memories followed by 'History of Neuroscience' SSC module student presentations on the neuroscience of language, vision, law, and savant syndrome.	83
I am Not MS (29/1/19)	Sean O'Callaghan, Anna Magennis, Dr Stanley Hawkins, Dr Gavin McDonnell, Dr Stella Hughes, MS Society NI (QUB, Belfast Trust)	Individuals sharing their personal stories on living life with MS. Joined by their neurologists and the national MS society speaking about their work. Held in a talk-show question and answer format.	165
Beyond the Scalpel: Life of a Neurosurgeon (26/2/19)	Mr Vashisht Sekar (Belfast Trust)	A neurosurgeon sharing his day-to-day experience of neurosurgery. Followed by careers advice and neuro-imaging tutorials.	113
Psilocybin, Epilepsy & God: The Neuroscience of Belief (26/3/19)	Professor Alasdair Coles (University of Cambridge)	An academic neurologist speaking about the neural basis underlying religious experiences and belief.	300
Neurosurgery Bootcamp (27/4/19)	Mr Vashisht Sekar, Mr Jonathan Poots (Belfast Trust)	A practical neurosurgical workshop with stations on suturing, burr-holes, dural patching, microsurgery, and neuroanatomy.	11
Through The Looking Glass: An Evening with a World-leading Neurologist (14/10/19)	Professor Allan Ropper (Professor of Neurology Harvard University and Author of 'Reaching Down The Rabbit Hole')	A world-leading academic neurologist sharing his day-to-day experience of neurology and teaching medical students at Harvard. This was delivered virtually online.	60
More Than Human – A.I. and Neuroscience (29/10/19)	Dr Barry Devereux (QUB lecturer)	A computer scientist speaking about the link between artificial intelligence and neuroscience, the use of computers and robotic devices in the future medical profession.	95
Mental Health – The Blurred Lines Between Neurology and Psychiatry (13/11/19)	Dr Stanley Hawkins and Dr Conor Barton (Both QUB and Belfast Trust)	A neurologist and a psychiatrist sharing their insights into the impact of mental health and how mental health is treated in both professions. Followed by case studies and career advice.	75
What Can We Do With Sound? (3/12/19)	Dr Matthew Rodgers (QUB Lecturer)	A psychologist sharing his insight into research in the use of auditory-motor and auditory-visual advances and their uses in the medical profession.	Cancelled due to Union Strike restrictions.
The Evolution of Human Consciousness (29/01/20)	Dr Derek Tracy (King's College London)	An academic neuropsychiatrist speaking about the neural basis underlying the evolution of human consciousness.	216
Half The Battle: Neuroscience Behind The Northern Ireland Troubles (10/02/20)	Dr Ciaran Mulholland (QUB Lecturer) and WAVE (Widows Against Violence Empower) representatives	A psychiatrist sharing his research into the psychological trauma of the NI Troubles, followed by two personal experiences of living with the trauma	127
Life Beyond Epilepsy (4/03/20)	Dr Michael Kinney (Belfast Trust) Dr Jim Morrow Ms Sue Wilde Maeve Cassidy Sharon Karatas (All Epilepsy Action)	A neurologist sharing his research into advances in Epilepsy treatment, followed by four personal experiences of living with Epilepsy.	39
A Day in The Life of a Neurologist (27/03/20)	Dr Thomas Peukert (Belfast Trust)	A neurologist sharing his day-to-day experience of neurology and his career advice.	Cancelled due to COVID-19 restrictions.

neurological complications of the measles virus. Northern Ireland's cultural and historical context yields important perspectives for neuropsychiatry and psychology, and its interaction with neurology. Important contributions were also made in the field of neurotrauma in the context of the NI troubles.

Undergraduate students in other locations wanting to set up a neuroscience society should identify relevant local research groups and the principal investigators. Each university has its own research strategies and strengths and they focus resources towards them. Identifying a university's unique selling point in neuroscience research will help to organise events which are relevant and meaningful to the local community.

Putting a Face to Neurology and Neurosurgery

Medical students are quite rightly focused significantly on assessment driven learning, but we sought to bring out the personal stories and experiences of patients for students. This gives a deeper insight of how neurological diseases affect patients, promoting a biopsychosocial view.

In collaboration with the Multiple Sclerosis Society, we hosted a popular event ("I am Not MS"), with two patients with MS and their consultants (See figure 1). It was in the format of a talk show, with significant audience participation. Anna (one of our volunteer patients) spoke about her personal struggles and victories as an undergraduate student with MS. One audience member found this useful reflecting the comfort of knowing her own daughter was not alone in her struggles.

Later that year working with Dr Mulholland we invited the organisation Widows Against Violence Empower (WAVE), Trauma Centre to speak at our event 'Half The Battle'. We heard about the issue of post-traumatic stress disorder (PTSD) in victims of the NI Troubles and how it continues to affect their everyday lives. The issue of PTSD, no matter what the context, has a financial burden on the National Health Service (NHS). Additionally, WAVE Trauma and other organisations helping people affected by the NI Troubles have also been affected by recent budget cuts. QUB Brain Society was able to provide representatives from WAVE Trauma with a valuable platform enabling them to speak about their personal experiences from the Troubles and how they continue to affect their lives. We, unknowingly, brought together a victim of the NI Troubles and their neurologist who played a part in saving their life many years previously.

Figure 1 - Brain Society 2018-2019 Committee members at MS event. Back row - (Maran Fearon, Peter Rogan, Caitlin O'Callaghan and Ger Mullan), Marian Mawhinney (MS Society representative), Dr Gavin McDonnell, Dr Stella Hughes and Dr Stanley Hawkins (Belfast Trust). Front row - Sean O'Callaghan and Anna Magennis (MS speakers) and David Lee (President)

In March 2020, we held a joint event with Epilepsy Action called 'Life beyond Epilepsy'. Dr Jim Morrow, retired neurologist and epilepsy advocate, spoke about developing epilepsy and limbic encephalitis whilst working as a consultant neurologist (we would encourage all students to read his own fascinating account of his illness[10]). He was instrumental in setting up a specialist epilepsy service in Northern Ireland and was the principal investigator of the globally respected UK Epilepsy and Pregnancy Register. Dr Morrow's wife, Sue, gave an account of working with Epilepsy Action and living with Dr Morrow at the time he was diagnosed with epilepsy. Other fascinating and moving stories were told by a university student with epilepsy and the mother of a child with epilepsy.

Epilepsy not only affects the individual but family members and friends. Our event created a unique platform for the speakers to connect with the audience in sharing personal experiences with epilepsy. Many memorable comments were made but one that stands out was from a student who delayed their medical studies after being diagnosed with epilepsy. Dr Morrow was able to provide reassurance that they should not let epilepsy hold them back from medicine.

Personal engagement events with patients and students need careful design, being sensitive to the needs of the participants. Wireless microphones and a coffee table seating arrangement can create a more relaxed environment to promote active audience participation. Events like these help to put a face to neurological conditions so students can appreciate how brain diseases impact people's personal lives.

Tackling Neurophobia

Apart from Student Selected Components (SSCs), undergraduate clinical neuroscience exposure at QUB is limited to a two-week attachment. This poses a challenge to explore neurology and neurosurgery at a deeper level. Studies have indicated limited clinical exposure and short clinical rotations to be a major contributing factor towards neurophobia[2,3,8,11,12]. By giving students extracurricular opportunities to further explore the field and interact with experts, we strove to foster an atmosphere and academic culture of learning. We promoted our events to high school students, patient support groups, and families of patients, as we feel it is essential to tackle neurophobia in the wider community. Events focusing on the personal or emotional aspects of neuroscience not taught within the medical curriculum (e.g. "Psilocybin, epilepsy & God: The neuroscience of belief") attracted large diverse audiences, including students with little exposure to neuroscience.

Practical Academic Learning Opportunities

Academic-focused events were organised to allow keen students with a passion for neuroscience to further their interests. These events provided opportunities for revision for examinations and exposure to more in-depth material.

Previously, an evaluation of the contribution of attendance at operating theatres in medical undergraduate neuroscience teaching at QUB, proposed a need to explore medical student perceptions of clinical neuroscience teaching[13]. Our practical events complemented traditional theatre-based learning, by allowing students to perform basic neurosurgical procedures. This year we collaborated with 'Scrubs', a student surgical skills society, and ran a full-day surgical skills conference for medical students. The neurosurgery section was run by Mr Tom Flannery and "Tekno Surgical". The Neurology and Neurosurgery Special Interest Group (NANSIG) sponsored this event and provided the neurosurgical equipment. This allowed 40 students to perform burr holes, craniectomies, micro-suturing, dural closures and the insertion of pedicle screws (See figure 2). This provided tangible experience with surgical tools and a unique opportunity to consolidate neuroanatomical knowledge. We hope events like these

Figure 2 - Medical students demonstrating neurosurgical skill

provide a useful learning platform for students to understand neurosurgical conditions that they may not otherwise encounter in training.

With support from NANSIG we set up a mentorship scheme for medical students in Northern Ireland. We recruited 15 consultants from neurology, neurosurgery and neuroradiology who were paired with a student to give them clinical and research opportunities.

We have also facilitated networking opportunities with leading experts in international centres of excellence. Dr Allan Ropper, Professor of Neurology at Harvard University, spoke about his career in neurology through a video link. In 2019, we hosted Alasdair Coles, Professor of Neurology at the University of Cambridge who spoke about the neural basis underlying religious experiences.

Publicising The QUB Brain Society

Effective promotion is key for the success of a student society. Great promotion leads to large audience numbers and in turn society membership but more importantly, it leads to a shift from us contacting potential speakers to them contacting us. Creating contacts is beneficial not only for the events but for future (medical) opportunities. As QUB Brain Society is still relatively new, we explored various methods of publicising our events to both potential speakers and future audience members.

Reaching Out To Speakers

Particularly in our first year, reaching out to speakers was a daunting experience. We picked relevant and interesting topics, after carefully selecting one or two potential speakers based on availability. Understanding that clinicians and academics have busy schedules, it was important to have numerous options available. Recently we have been contacted by local experts wanting to promote their research areas, which is a great privilege to be able to showcase their work.

Collaborating with The MS Society, WAVE Trauma and Epilepsy Action, allowed us to further promote our society to the general public. Social media promotion and informing members of these organisations played a key role in promoting the events. We are indebted to these organisations for the success of the events.

Reaching Out To A Potential Audience

Having secured a speaker, it was vital to promote the event and the speaker. In our second year, we organised all of the events in advance of the respective academic year in order to create a programme which we could then promote.

The publicity team created posters and speaker profiles for each event. These were then disseminated on social media platforms (Facebook, Instagram and Twitter) on a regular basis running up to the event. We also informed all the grammar and secondary schools within Belfast, faculties/

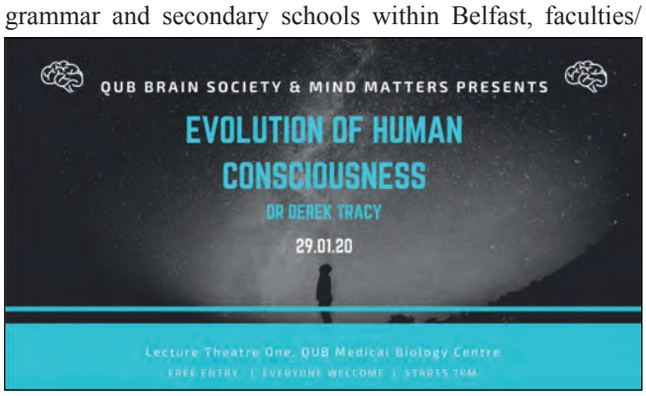

Figure 3 - Advertising poster for the event on Evolution of Human Consciousness

schools within QUB and to contacts in the Ulster University. A number of school students and their teachers came to the events. For example, one school sent 40 of their pupils and a teacher to our first event 'What is the Brain to you?' (See figure 3).

The Benefits of Post-event Feedback

Tickets for our events were sold on Eventbrite, allowing us

to monitor sales and in turn focus our promotional drive. Trends in both years have shown that sales in the second semester are higher than first semester which could be due to increased promotional drive. In the second semesters, more students have had time to visit the Student's Union, hear about student societies through Fresher's Fair and through their fellow students or lecturers. Post-event surveys show the diverse audience members these events have appealed to (See figure 4). We found that social media was the main platform by which people heard about our events. It is crucial for student societies to regularly update the social media

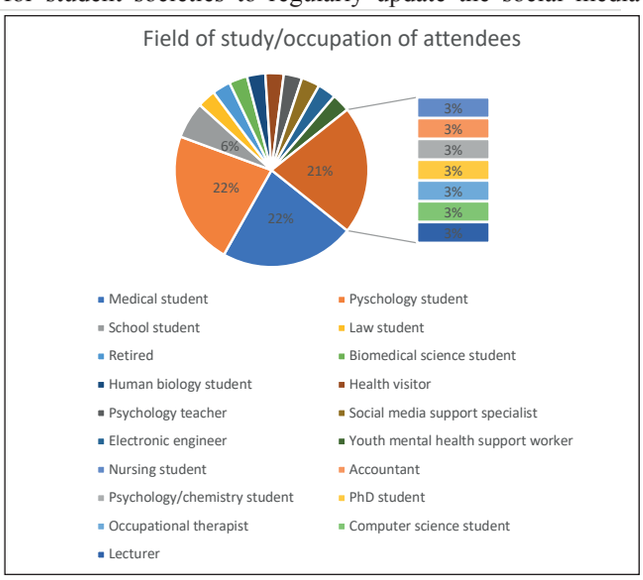

Figure 4 - Pie chart showing the spectrum of disciplines attending our 'What is the Brain to you? event

platforms to attract more attention for the events.

Membership Benefits

Fresher's Fair is held every year and allows student societies to showcase their work to new university students in order to promote their events and membership for their societies. The QUB Brain Society members receive a monthly newsletter which is created by our first year representatives and Vice President. The newsletter covers our upcoming events and interesting facts about the brain and the Brain Society. QUB Brain Society also has links with NANSIG who offer a mentorship programme with neurologists and neurosurgeons in Northern Ireland and we regularly update our members with information about courses or training programmes that NANSIG offer.

Achievements and Future Aspirations

Now in its second year the Brain Society has 10 committee members, 150 subscribers to our monthly newsletter, and had over 1,000 attendances at our various events. These numbers have grown from the previous year and will hopefully continue to grow.

In the first two years of the society's existence we feel that we were able to achieve this through the fourteen interesting events we held. As a result of our efforts in our inaugural year this led to the society being awarded runner-up for the 'Best New Society' in the Student Union awards for 2018-2019 academic year.

Despite the COVID-19 era we now live in, the business of the committee rolls on (See figure 5), and a new committee was selected by an annual general meeting held virtually. This will allow strategic planning for the best possible start to the 2020-21 academic year. While our new elected committee face a few difficulties in organising events with the current

Figure 5 - Brain Society Committee 2019-2020 – Caitlin O'Callaghan, Naairah Khan, Peter Rogan, Nikita Tokarev, Sarah Collis, Maran Fearon, Ger Mullan, Hannah Kerr, Michael McLarnon, Sabina Pogoson and David Lee with Dr Stanley Hawkins at Dr Ropper's event

social distancing measures in place, there is the potential to run sessions by webinar format.

Neurologists' Perspectives

Drs Michael Kinney and Stanley Hawkins share their perspectives on the value that student societies can bring to the local neuroscience community.

"The Brain Society offers a tremendous opportunity to allow additional educational opportunities throughout the entire undergraduate journey. The students are to be admired for their ambitious project, enthusiasm, and high aspirations"

Dr Michael Kinney (Consultant Neurologist/Epileptologist)

"At an early stage in my undergraduate medical career I became interested in the workings of the brain - the delicate organ that makes us unique, conscious, sentient, insightful individuals. Through the Brain Society it has been a great honour to be able to share my enthusiasm with highly motivated intelligent students, to inspire some of them to become the next generation of neuroscientists."

Dr Stanley Hawkins, (Retired Consultant Neurologist)

Moving forward

Looking towards the future of The Brain Society, we hope it continues to provide a platform for students, patients and the wider public to engage informally with neuroscience experts. We hope to continue advocating for the establishment of

a formal interdisciplinary neuroscience centre at QUB, incorporating basic and clinical neuroscience.

We hope that student-led initiatives like these will help tackle neurophobia and help inspire the next generation of neuroscience clinicians and scientists. Neuroscience is one of the last great "undiscovered countries" of the body and is one of the final frontiers which is calling out for a motivated generation of researchers and clinicians.

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Clinical Paper

Abdominal ectopic pregnancy with implantation on the rectum

Graham MJ, Briggs K, McMullan R, Dorman G

Abstract – We report a patient who presented to our unit 26 days following in vitro fertilisation (IVF) and embryo transfer with vaginal staining, diarrhoea and mild crampy abdominal pain. On transvaginal ultrasound the uterus was empty with an extrauterine sac identified containing a yolk sac and a fetal pole with cardiac activity. Diagnostic laparoscopy was undertaken which confirmed an abdominal pregnancy with implantation on the rectum.

BACKGROUND

In this case presentation we discuss the presentation, diagnosis and management of an extremely rare condition. Ectopic pregnancies are relatively common, occurring in 1-2% of all pregnancies (1). The estimated incidence of abdominal pregnancy is 1 per 10000 live births (2.) In Northern Ireland one would expect approximately two cases of abdominal pregnancy each year. The mortality rate has been reported at 5:1000 (2) therefore it is important that clinicians are aware of and consider this rare condition. Proposed aetiology of abdominal pregnancies include implantation of an aborted tubal pregnancy, abdominal fertilisation and implantation and perforation of the uterus and direct implantation during embryo transfer (3,4).

The presentation of abdominal pregnancies can be variable depending on the location of implantation. Previous case reports have described ectopic implantation in the omentum (5), spleen (6) and liver (7). Other reported cases of rectal ectopic pregnancy have presented with anal pain (8) or rectal bleeding (9).

The Royal college of Obstetricians and Gynaecologists (10) have advised the use of the ultrasound criteria described by Gerli et al (11) when diagnosing an abdominal ectopic pregnancy. These include

1) Absence of an intrauterine gestational sac.

2) Absence of both an evident dilated tube and a complex adnexal mass.

3) A gestational cavity surrounded by loops of bowel and separated from them by peritoneum.

4) A wide mobility similar to fluctuation of the sac, particularly evident with pressure of the transvaginal probe toward the posterior cul- de-sac.

Regarding management, The Royal college of Obstetricians and Gynaecologists recommend that while advanced abdominal ectopic pregnancies should be managed by laparotomy, early gestations should be managed by laparoscopy (8). It is also recommended that methotrexate should be given as an adjunct to surgery.

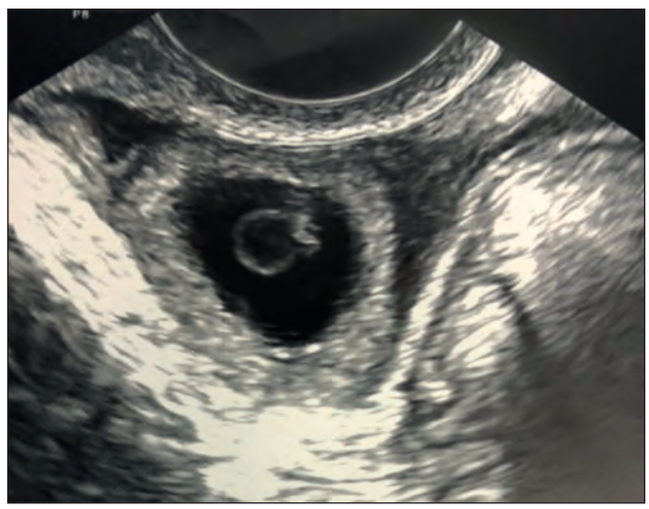

Figure 1, Ultrasound image of abdominal pregnancy. The yolk sac and fetal pole can be seen clearly within the extrauterine gestational sac.

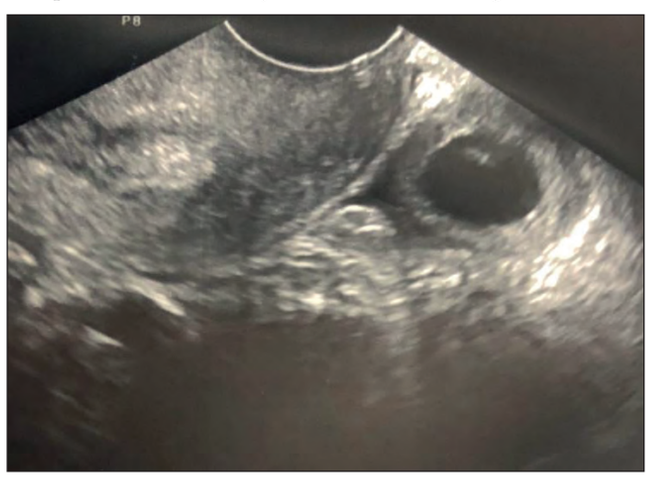

Figure 2, Ultrasound image of abdominal pregnancy between the uterus and rectum

CASE

This 30 year old lady underwent IVF due to primary infertility of unknown aetiology. Hysterosalpingogram had showed patent tubes with ovulation confirmed by a normal day 21 progesterone level. Semen analysis of her partner was normal. Ultrasound pelvis showed a fundal fibroid with no other abnormalities. Following referral to a regional fertility centre she underwent IVF and day 5 single embryo transfer. She presented to our unit 26 days following this with light

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vaginal staining, diarrhoea and mild crampy abdominal pain. On examination her abdomen was soft and not tender on palpation. Serum BHCG levels at this stage were 8273. Transvaginal ultrasound showed an empty uterus with an extra uterine gestational sac. Within the sac was a yolk sac and a fetal pole measuring 5 weeks gestation with cardiac activity present (see figure 1/2)

Due to the presence of an extrauterine pregnancy with fetal cardiac activity a laparoscopy was performed. At laparoscopy the known fundal fibroid was noted and the ovaries and tubes were normal (figure 3). There was no evidence of uterine perforation. On evaluation of the pouch of Douglas an ectopic pregnancy was noted on the rectum (figure 4.) This was in keeping with the previous ultrasound findings. The ectopic tissue was adherent to the rectum and therefore a laparoscopic

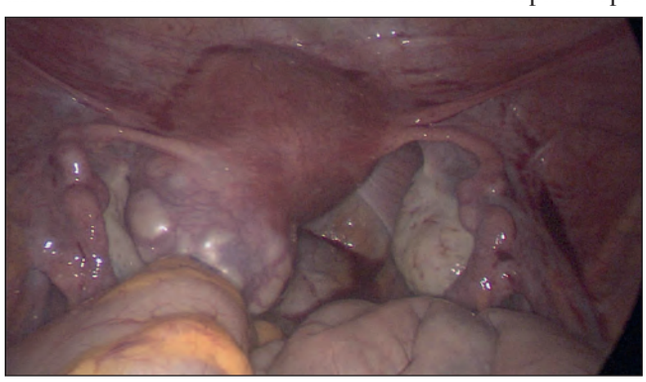

Figure 3, Overview of pelvis at laparoscopy

suction device was used to open the mass bluntly and remove the gestational sac. It was felt that removal of all ectopic tissue would come at a high risk of a rectal injury so this was not attempted.

As some tissue was left in the abdomen she was treated with

Figure 4, abdominal ectopic implanted on the rectum.

intramuscular methotrexate the day following laparoscopy. Her BHCG levels fell from 8273 to 271 one week following methotrexate. Within two weeks they had fallen further to 40 and she was discharged.

DISCUSSION

While an ectopic pregnancy is a relatively common presentation it is usually confined to a fallopian tube. When implantation occurs in the abdominal cavity this can present differently to a tubal ectopic depending on the implantation site.

In this case we have described how a rectal ectopic can present with gastrointestinal symptoms (diarrhoea) alongside more common symptoms such as vaginal bleeding and pain. As complete surgical excision of the pregnancy would have come at a high risk of rectal injury, medical therapy was used as an adjunct in accordance with national guidelines.

While an abdominal ectopic pregnancy is rare it also can be life threatening. It should always be considered when evaluating women with pelvic pain in pregnancy, especially when there are gastrointestinal symptoms. We hope that reporting this case will lead to increased awareness amongst clinicians.

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Medical History

WAR NEUROSURGERY: TRIUMPHS AND TRANSPORTATION

John Hedley-Whyte, M.D., F.A.C.P., F.R.C.A. Debra R. Milamed, M.S.

Key Words: Neurosurgery, Mentors, Air Evacuation, World War I, World War II

INTRODUCTION

In both World War I and World War II approximately seven percent of battle casualties were due to cranial injuries. In1915 Harvey Cushing led a Harvard-financed hospital to Paris. Cushing and Colonel Andrew Fullerton of Queen's University Belfast with advances of much specialist surgery, whole blood and trained nurses nearer to the Front Line halved the mortality in France of the Allies. Hugh Cairns of Adelaide volunteered as a Private. He survived paratyphoid, was returned to Australia but was later able to return to combat in France. Cairns was to train in Neurosurgery at Harvard under Harvey Cushing and then in World War II to emulate his teacher Cushing by also halving combat cranial injury deaths, in comparison to World War I, through advances in Neurosurgery and superb evacuation. Colonel Cecil Calvert of Belfast played a key role.

Figure 1 *Harvey W. Cushing, MD, Yale to Harvard MD, FRCS, FRCP, NAS, FRS (1869-1939); youngest of ten children. His father and grandfather were general practitioners in the U.S. Mid-West. Winner of Pulitzer Prize for History, protégé of Sir William Osler and Father-in-Law to FDR's eldest son James. Oil on canvas, 1908, by Edmund C. Tarbell (1862-1938), 86.36 cm x 111.76 cm. From the collections of the Dittrick Medical History Center, Case Western Reserve University, Cleveland, Ohio, USA, and reproduced with their permission.*

HARVEY CUSHING AND THE FOUNDING OF THE PETER BENT BRIGHAM HOSPITAL

The years before World War I saw medico-political struggles on both sides of the Atlantic. Between 1902 and 1912 the Peter Bent Brigham Trustees had negotiated with President Lowell of Harvard for the establishment of the Peter Bent Brigham Hospital next door to the Harvard Medical School[1]. Mr. Lowell wished Harvey Cushing to be Moseley Professor and first Chief of Surgery at the Peter Bent Brigham Hospital (Fig. 1). Cushing eventually accepted Lowell's offer in 1912 after Harvard's president travelled to Johns Hopkins

Figure 2 *Sir Alfred Keogh, MD, Galway, GCB, GCVO, CH, LLD (1857-1936), oil-on-canvas, by Arthur Hacker, RA (1858-1919), 110 cm x 85 cm. From the collections of the Trustees of the Museum of Military Medicine, Surrey, UK and reproduced with their permission. Appointed Surgeon General in 1901, and Director General of the Royal Army Medical Service until 1910, and 1914-1919. Rector of the Royal Army Military College, Millbank, London, 1910-1922. Keogh established an association for women students and staff at the Imperial Medical College.*

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to discuss the details in person[2]. Early in 1913 Cushing performed the 'opening' surgical operation.[3]

RAMC IN SOUTH AFRICA

Major A.H. Keogh sailed in October 1899 as "the Registrar and Secretary" of the RAMC 3rd General Hospital for South Africa[4] (Fig. 2). Supported financially by the Iveaghs of Guinness fame, staffing consisted of a quintet of RAMC officers, a dozen civil surgeons, a sole Warrant Officer and over a hundred other RAMC men. By the first week of December 1899, the 3rd General had open 620 beds. In the next six months over 3,500 patients were passed through[4]. In the RAMC thereafter, sanitation, hygiene, epidemiology, pure water and vaccines were emphasized and funded by the political power of Richard Burdon Haldane, the first Viscount Haldane, Prime Minister Balfour and Kings Edward VII and George V[4,5,6]. A full establishment of nursing sisters and nurses was funded. Keogh called for specialist doctors and surgeons to join as Territorial Royal Army Medical Corps Officers. No.1 Territorial Army (TA) Hospital was formed at Newcastle-upon-Tyne, and No.2 at Birmingham[4].

With the support of the British Secretary of State for War William St. John Broderick and King Edward VII, the *Lancet* commented "never had the Army Medical Board had so much influence"[4]. Within the 1902-1907 quinquennium Keogh was a Lieutenant General and Director General of the RAMC. Sanitation, hygiene, epidemiology, pure water and vaccines were required[4,5].

WORLD WAR I

By 1910 Lieutenant General Keogh had in preparation for another war arranged for the British Medical Schools and their Teaching Hospitals including Keogh's own Galway

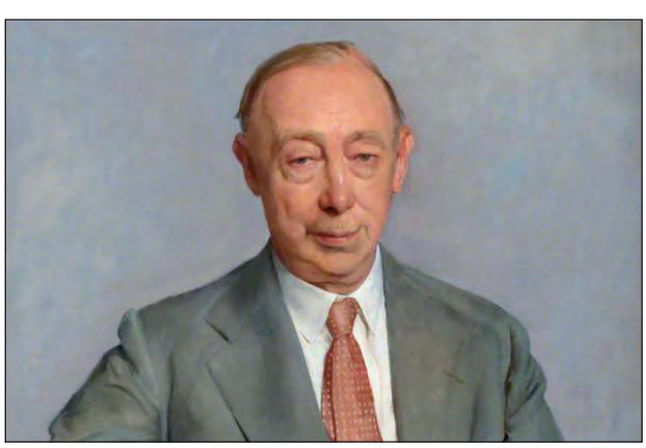

Figure 3 *Sir Geoffrey Jefferson, MD, FRCS, FRCP, FRS (1886-1961), oil on canvas by Sir Gerald Kelly, PRA (1879-1972), 1955-56. 82 cm x 68 cm, RCSSC/P 396. On loan to the Hunterian Museum, Royal College of Surgeons from the Jefferson Family, and reproduced with permission.*

"That they shall become components of the UK Emergency Medical Services [EMS]." He also organized surgical specialization especially in orthopaedics and bacteriology. Early in World War I King George V reappointed Keogh as Director General of Medical Services of the RAMC. In 1915 the leading British Neurosurgeon, Sir Victor Horsley, died of heat stroke[7,8]. Sir Alfred Keogh with tact, persuasion and Royal and Harvey Cushing's help organized Cushing's Neurosurgical Unit and later Sir Geoffrey Jefferson's nearby Neurosurgical Unit at Wimereux near Boulogne[4,5,9]. Another specialized Combat Neurosurgical Unit was established in the

Figure 4 *Sir Hugh William Bell Cairns, DM (1896-1952), by Walter Stoneman. Bromide print, February 1947, image size: 134 mm x 97 mm. ©The National Portrait Gallery, London, image no. NPG x 166314. Reproduced solely for this Medical History.*

Pas de Calais visited by Cushing[9].

Having been returned to Australia, Hugh Cairns was later able to return to combat in France[10]. During World War I, Geoffrey Jefferson (Fig. 3), after extraordinary service in Czarist and Revolutionary Russia, had been given permission and support to form the first British Neurosurgical Unit at Wimereux, near Boulogne on the Channel, alongside Harvey Cushing's Neurosurgical Unit[11]. In 1918 Jefferson had under his own care over 100 neurosurgical case casualties. Gertrude Jefferson, his wife, a Canadian physician, was a protégée of the Oslers. The close friendships of these families and their contacts are the foundations of modern neurosurgery[3,9,10]. Cairns was to train in Neurosurgery at Harvard under Harvey Cushing and then in World War II to further emulate his teacher Cushing by also halving combat cranial injury deaths, in comparison to World War I (Fig. 4)[10].

According to Sir Ian Fraser, "Cecil Calvert from Belfast was second in command to Brigadier Hugh Cairns in the Neurosurgical Unit in St. Hugh's College"[12]. From 1942 to 1945, I[1] met with Colonel Calvert and his wife Eileen at 29 Charlbury Road, Oxford, when we were guests and waiters for the Cairns'.

1 This and other first-person references refer to the first author.

In January 1943 Ian Fraser was flown from Accra to London by the U.S. Army Air Force. In London the RAMC Directorate of Surgery said he was, via Belfast, to go to Oxford to work with Professors Florey and Cairns and Colonel Cecil Calvert, a former Queen's Belfast colleague: "In fact, Calvert was largely in charge of the unit [at Oxford] during Cairns' frequent absences"[12,13]. Cairns' and Cushing's friend Geoffrey Jefferson from Manchester, was responsible for Neurosurgery in the UK Emergency Medical Services[9,12,14]. On 2nd May 1943, Ian Fraser and bacteriologist RAMC Major Scott Thompson and their Medical Research Council Team steamed past Northern Ireland to arrive in Algiers on 12th May. They sailed in the Hospital Ship *Newfoundland,* later sunk off Salerno[12].

Ian Fraser received a DSO for his superb surgical results in the invasion of Sicily. In the Salerno landings he landed from a light RAF plane, but soon contacted diphtheria and was treated successfully by Max Rosenheim[12,15]. Invalided to Cairo, Ian Fraser helped Clifford Naunton Morgan close colostomies[12]. Penicillin was shown to be particularly efficacious in post-combat neurosurgery, but not quite as effective in relation to abdominal surgery, as confirmed by Brigadier Cairns in his observations on the Mediterranean Theatre[16,17].

GEOFFREY JEFFERSON, HARVEY CUSHING AND COLLEAGUES

During most of July 1901 Harvey Cushing had visited the Charles Sherringtons chiefly in Liverpool and in Oxford, and Cushing did the required surgery on cortical localization in chimpanzees, orangutans, monkeys and gorillas[3,9]. Similar visits followed in 1904 and 1909. When Hugh Cairns came up to Oxford in 1919 as a Rhodes Scholar, he took over these duties. In June 1920 Cairns also rescued a punting Lady Sherrington from drowning in the Thames. Lady Sherrington could not swim. Sherrington wrote to Cushing at the Peter Bent Brigham Hospital in Boston and arranged the financing of Cairns' Rockefeller Fellowship for 1926-27[18]. Under Cushing and Gilbert Horrax, later Head of Neurosurgery at the Lahey Clinic[19,20,21], Cairns was Cushing's assistant[22].

Harvey Cushing's daughter Betsey married Eleanor and Franklin Delano Roosevelt's son James on June 4, 1930, two days after his Harvard graduation[3,23]. FDR frequently exchanged letters with Harvey Cushing[23]. According to the Cairns', FDR told Cushing to get Cairns, now the designate Nuffield Professor of Surgery, all the neurosurgical equipment that would be needed for the forthcoming World War II. FDR and Cushing knew from World War I of the specialized steel and other specialized equipment needed[10,24]. In 1935 Hugh Cairns and Cushing resumed their 1926-27 and 1930 collaboration. FDR saw to financing especially from the Rockefeller Foundation. In 1938 Cushing came to Oxford to collect an LLD, and approved of the Neurosurgical British Emergency Medical plans: St. Hugh's College Neurosurgical Hospital at Oxford, Cairns and Calvert, Jefferson at Manchester, Dott at Edinburgh (1923-24 with

TABLE 1. CROSS-CHANNEL CASUALTY AIR EVACUATION D-DAY THROUGH MAY 1945 (Almost all by DC3 Dakotas)[28]

MONTH	EVACUATIONS
June 1944	27,387
July 1944	37,685
Aug. 1944	29,151
Sept. 1944	26,126
Oct. 1944	17,518
Nov. 1944	26,059
Dec. 1944	31,478
Jan. 1945	17,483
Feb. 1945	17,428
March 1945	44,108
April 1945	81,701
May 1945	42,567
TOTAL*	**398,691**

*Approximately 7 percent (27,908) were destined for the UK Neurosurgical Centres (see Table 2)

Harvey Cushing in Boston) and Rowbotham, Mancunian protégé of Jefferson, at Newcastle-upon-Tyne. FDR said 10,000 Dakotas, DC3, C47s and lots of Nightingales would be needed—"build the planes for 'my' allocation, train the Nightingale Anglo-American flight nurses[24]".

FDR spurred on the production of C47s (DC3 Dakotas) to one every 28 minutes, night and day. They were equipped to carry jerry cans of fuel in and the wounded out[24]. Typical landing from unloading to loading wounded was twenty minutes. Concealed air-landing strips could be as short as 50 yards; delivery from the US to France and Italy was by Ascension Island, flying distance 11,600 miles. Control was given in

TABLE 2. DISTRIBUTION OF NEUROSURGICAL CASES EVACUATED TO THE UK, D-DAY THROUGH MAY 1945

HOSPITAL:NEUROSURGEON(S)	NO. CASES (approximate)	REFERENCES
Oxford (St. Hugh's): Cairns, Calvert	13,000	34,35,36,37
Manchester :Jefferson	6,683	9,11
Edinburgh: Dott	3,000	38
Newcastle-upon -Tyne : Rowbotham	125	39
Hackwood Park: Botterell	2,100	40
Americans treated in the UK by Spurling and Sweet at Birmingham and Oxford	3,000	41,42,43,44,45,46,47
Total	**27,908 (see Table 1)**	

1943 to Eisenhower and his deputy Tedder[25]. In France from June 1944 onwards to May 1945, Patton told his 3rd US Army, "We do not worry about our flanks, we go get our fuel and our Nightingales with our wounded often from behind Nazi lines." A verbal correction from the Combined Allied Surgical Consultants Committee ordered that he, Patton, must not refer to "Our Nightingales"[26,27]. Typically one trained Air Nightingale Nurse and one Medical Technician was on each fuel supply DC3[28,29].

AIR EVACUATIONS

On DC3 cross-channel return flights from June 1944 to the end of May 1945, nearly 399,000 patients were evacuated[28,29] (Table 1). Patton's Third Army did have fuel problems in September 1944, but this was corrected well before the left swing to relieve Bastogne in the Battle of the Bulge[30]. The

performance of the Allied Air Evacuation of the wounded under the ultimate control of Professor General Elliott Cutler, Harvey Cushing's successor as Moseley Professor at Harvard, was superb[31,32].

From 6 June to 23 July 1944, approximately 18,415 U.S. Army patients were flown to the U.K. by the U.S. Army Air Force, averaging 418 per day[33].

Approximately seven percent of the casualties evacuated to the United Kingdom by air, or 27,908 patients (Table 1), were flown to the Neurosurgical Centres (Table 2). Almost half, about 13,000, were flown to airfields surrounding Oxford: Abingdon, Brize Norton, and Benson and thus to the care of Colonel Calvert and Brigadier Cairns at St. Hugh's College RAMC Hospital[34,35,36,37]. The others were placed under Jefferson at Manchester[9,11], Dott at Edinburgh (3000 cases)[38], and Rowbotham at Newcastle-upon-Tyne (125 cases)[39]. The Canadians at Hackwood Park, near Basingstoke under Major Harry Botterell received 2,100[40]. A further 3,000 U.S. soldiers and airmen were treated in the U.K. after evacuation from Northwest Europe by Glen Spurling[41,42] and William H. (Bill) Sweet[43,44,45,46,47] at either Birmingham or Oxford . In 1962, I became Bill Sweet's Head of Neurosurgical Anaesthesia at the Massachusetts General Hospital. The aforementioned numeration agrees with Bill Sweet's recollections. I also worked with his successor Nick Zervas[48].

Only seven in-flight patient deaths were reported from January 1944 through September 1945 during air evacuation from Europe[33] (Table 1); perhaps among them was a neurosurgical patient. This stellar record was marred only by reported losses ranging from 95[28] to 101[33] patients, in addition to their medical staff and flight crews, in 3 reported plane crashes and one crash landing[28,33].

PERSONAL NOTE

From the autumn of 1940 until the summer of 1942, I was taught and supervised by Harvard-trained physicians, and by my brother Michael's godfather, later Sir Benjamin Rycroft[15,49,50]. Generally we met in the house my parents had rented from the Toppings which overlooked the Lagan; sometimes at Musgrave Park where my father was Commanding Officer [30,51]. My Harvard "tutors" and I discussed many topics: splitting the atom and the recent work of Lise Meitner (Magnus I. Smedal from MIT)[30,52,53], the antigenicity of bacteria and viruses (Max Rosenheim from Massachusetts General Hospital)[15,54], need for blood transfusion (Colonel Thomas Lanman, Boston Children's Hospital)[32,51,55], tuberculosis (Ted Badger, Boston City Hospital, Thorndike Laboratory)[56,57,58], epidemics and digestive diseases (Richard Warren)[30,59,60], food poisoning (Bert Dunphy)[30,61], and basic endocrinology (Robert Zollinger)[30,62].

With this background and exceptional tutoring my father wrote to the Lynams, father, Hum, and son, Joc, suggesting I should become a pupil at the Dragon School in Oxford, round the corner from 29 Charlbury Road, the large house of Hugh and Barbara Cairns and Dragons Margaret and Elizabeth, their daughters. The Lynams said they were full but the Nuffield Professor of Surgery, Hugh Cairns, claimed

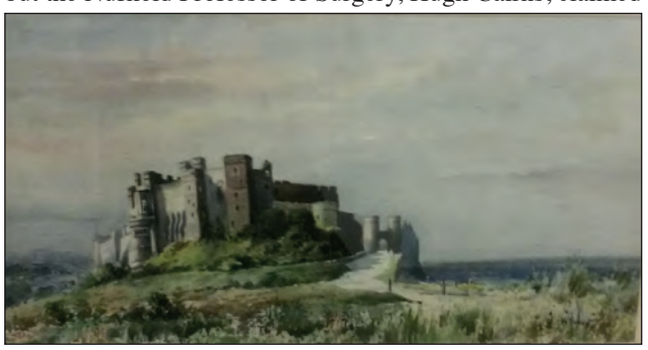

Figure 5 *Bamburgh Castle, Northumberland. Watercolour by William Fergie (1893-1971), 1961, 20.5" x 11.0". Reproduced by permission of owners. Site of pre-Norman fort. For the next 500 years owned by The Crown then gifted to Sir John Forster, and subsequently a hospital in the 18th-19th centuries.*

to have seen me as a baby when the Surgical Travellers[31] visited Newcastle-upon-Tyne and thereafter at Bamburgh, Northumberland. So I was admitted to the Dragon until 1947.

Barbara, later Lady Cairns, had not been able to go to Boston in 1926 and 1927 when her husband Hugh was Harvey Cushing's Assistant at the Peter Bent Brigham Hospital and Harvard. She appeared fascinated by my stories of the Dragon School and Oxford.

I knew that Barbara Cairns had been an open scholar at Girton College, Cambridge University, and that her mother Mary, née Forster Baird[63] had chosen her a boyfriend, Australian physician Rhodes Scholar and Oxford Rowing blue at Balliol.

TABLE 3. WORLD WAR II BRITISH MOBILE NEUROSURGICAL UNITS OVERSEAS (CAIRNS, 1947[36])

UNIT	DATES	THEATRE	ADMISSIONS	OPERATIONS	GUNSHOT HEAD WOUNDS NON-PENETRATING	GUNSHOT HEAD WOUNDS PENETRATING	NOTES
1	June, 1940	France	800	—	—	—	Captured
	Nov. 1941 - Feb. 1942	Western Desert	—	134	15		
	Feb. 1942 - June 1945	Cairo	3,804	—	343 (up to Feb. 1944)	534 (up to Feb. 1944)	
2	March 1942 - June 1945	Poona, Bangalore, Dinapore, Burma (14th Army)	—	—	443 (1944 only)		
3	July 1942 - June 1945	Ranchi, Bareilly, Imphal, Comilla	2,045	1,200	1,100		Including peripheral nerve injuries
4	Dec. 1942 - June 1945	No. Africa, (8th Army) Sicily, Italy	6,063	4,334	3,013	1,336	Forward and Rear Sections
5	Dec. 1942 - June 1945	No. Africa (1st Army), Italy	4,600	—	1,350	889	Only cases primarily operated on in unit
6	June 1944 - June 1945	Normandy to Germany (21 Army Group)	3,100	1,125	989	1,110	Sometimes split into forward and rear sections

Adapted with permission from *The British Journal of Surgery*

Hugh had in 1920 proposed to Barbara on a rock at Holy Island Lindisfarne within binocular sight of our Bamburgh House on the Wynding opposite the Castle[10] (Fig. 5).

During my Dragon education from 1942 to 1947, I also discussed with Barbara Cairns her great-grandfather, John Forster, also known as John Forster Baird's, career as a famous surgeon at the Newcastle Infirmary, later the R.V.I. of which I knew well[64] Barbara told me of Queen Mary casting covetous eyes on the Forster-Baird watercolours of family and North Northumberland. The Forsters had sold Bamburgh Castle and it was now owned by Lord Armstrong (Fig. 5). With Professor Hugh Cairns at the time of El Alamein we discussed Ulsterman General Montgomery and his support for the Cushing-Cairns initiation of Mobile Neurosurgical Units (MSNSUs)[36,37](Table 3). The results from 1942-45 were to us like a long running Test Match. My Uncle Frank Nettleton, my mother's younger brother's crash of his photo-reconnaissance Spitfire at Benson[65] was discussed as was his successful treatment under Colonel Calvert and Brigadier Cairns at St. Hugh's College[36,37], Oxford Neurosurgical Hospital. The Cairns-Calvert duo knew of my treatments in Northern Ireland of my pneumococcal pneumonia and tuberculosis, and of Oxford and Harvard's failure to provide penicillin and streptomycin[15,57]. I knew that Arthur Jefferson had dined with Chain and discussed penicillin with his father Geoffrey Jefferson in 1941[11,17].

From Charlbury Road the only task I was worried about was the wood gathering. I asked my Brigadier father whether in war-time generals were entitled to other people's wood. A month later I was told it was Jowett-Balliol wood and not to worry. Barbara was the late Master's youngest daughter[66]. As a guest to a World War II U.S.-provided Sunday lunch at 29, Charlbury Road I was asked how I got from Newcastle to Bamburgh. I described how, before dawn, we usually hacked two ex-race-horses through Newcastle from our home stables beside the Moor with its Territorial Army Emergency Medical Service Isolation Hospital to Newcastle Central Station and into a horse box which was attached to the Kings Cross to Edinburgh Night Sleeper. Sometimes the Night Express stopped for us at Chathill and we were shunted onto the Local Independent Chathill to Seahouses Railroad and sometimes we were detached further north at Belford. If the tide was out at Seahouses, we rode along the sands to Bamburgh Castle and then past the A.L. Smith-Cairns, now Barbara's St. Aidan's house to 13th century St. Aidan's Church. If we were detached from the night express train at Belford, we rode the northern way past Budle Bay to the lovely stables of St. Aidans. If it was winter we crossed the Bamburgh golf course well-known to Hugh Cairns and where my father was to be Captain. Barbara Cairns said she would look out for us from her Bamburgh House.

After World War II I played cricket for Bamburgh on their pitch opposite St. Aidan's, their house; another cricket boundary was the basalt rock of the Castle. We never did persuade Sir Hugh Cairns to play for Bamburgh. As a useful all-rounder he did play village cricket in the 'South'; typically '30 runs – 2 wickets'. Barbara Cairns died in 1987 in Bamburgh and is buried along with many Bairds and Forsters dating back to the 14th century in this lovely St. Aidan's Church. We took our horses to the stables of 13th Century Saint Aidans Church by train because from 1940 to 1945 petrol was rationed and in very short supply. We used our horses for sheep herding and transport. On the tenth of October 1944, I, on my mare Neuagh, received an award at Hen Hill from Hugh Algernon, 10th Duke of Northumberland (Fig. 6)[67]. Neuagh knew how to herd sheep. On the 10th of October 1944 I was on leave from the Dragon School and the Duke from the Army. He had been left for dead at Marathon. On regaining consciousness it is claimed he ran to Athens before evacuation from Greece with the remainder of the Northumberland Hussars.

Figure 6 *Hugh Algernon Percy KG, GCVO, FRS (1914-1988), 10th Duke of Northumberland, Chancellor of the University of Newcastle-upon-Tyne (1963-1988), Chair, Agricultural Research Council (1958-1968), Medical Research Council (1969-1988). Oil on canvas, 110 cm x 85 cm (43.3" x 33.5"), by Andrew Festing (b.1941). From the collections of Newcastle University, Newcastle-upon- Tyne, accession no. PCF15, and reproduced with permission of the artist.*

As a Councilor of the Northumberland County Council from 1944 until 1955 Hugh Algernon Northumberland took a leading role in support of Rowbotham's Neurosurgical Centre at the Newcastle General Hospital and at the Royal Victoria Infirmary[39,67]. The Neuropathology was strengthened and continued support of the Medical Research Council was correctly foreseen. The Duke, post-World War II, chaired the Agricultural (1958-1968) then the Medical Research Council (1969-1988). Medicine and Agriculture benefited significantly; his FRS was well-earned and appropriate[67,68].

From 1958 until his death in 1988, Northumberland would ask me in conversation, who there were in my view, Barts, Harvard, MIT or Smithsonian experts, in matters he was chairing in the Agricultural or Medical Research Council. Opinions were exchanged in Northumberland, London, or Boston, Massachusetts, always à *deux*. Northumberland was a quick learner and appraiser of cutting-edge science[67]. My reward was that Northumberland proposed me in 1971 for his London Club.

TO BOSTON

At about 10:00 pm on June 15th, 1960, I was ordered by the Barts' butler to the office of the Professor of Surgery, Sir James Paterson-Ross. The Professor I knew had been Assistant to Harvey Cushing at Harvard. Sir James asked that I give his Best Wishes to Pete Churchill[32] whose Harvard Department of Surgery I was joining, also to J.C. White, Head of Neurosurgery at the Massachusetts General Hospital and Paul Dudley White, Eisenhower's cardiologist. Sir James said that I would be working with them; so it came to pass. Sir James knew that my wife Tessa had been appointed intern to Professor Sidney Farber at the Boston Children's where Franc Ingraham was Cushing's successor, both at the Peter Bent Brigham Hospital and the adjacent Children's Hospital Medical Center[69,70].

After my arrival both Professors White and Churchill asked about the management of Hugh Cairns' fatal lymphosarcoma of the caecum. Pete Churchill knew that Sir Clifford Naunton Morgan to whom I had been Senior House Surgeon at Barts had been consulted about Cairns' management in 1951 and 1952[10]. Franc Ingraham, two years younger than Hugh Cairns, had also trained with Cushing and Sherrington[18,71]. In June 1952, Franc Ingraham had facilitated the Cairns' daughter Margaret's swift return to Oxford from the United States, escorted her home, then flown straight back to Boston. Margaret's father, Professor Sir Hugh, died of his post-irradiated cæcal sarcoma on 18 July 1952[10]. Sir Charles Sherrington also died in 1952[71].

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Medical History

David Alexander Draffin: An Irish ENT Surgeon and Inventor

Sevasti Konstantinidou[1], Miane Min Yan Ng[2], Neil McCluney[3]

Key words: Draffin, Draffin rods, Tonsillectomy, History of Medicine, Otolaryngology

ABSTRACT

David Alexander Draffin was an Irish ENT surgeon and inventor of the internationally famous ENT instrument used in tonsillectomy, which carries his name and is called Draffin's rods. His story is not as well-known as his eponymous ENT instrument and this article attempts to shed a light into his life. He studied in Queen's University in Belfast and was a medical officer in World War II. During that time, he demonstrated great courage and spirit. On his return from the war, he worked in many hospitals as an ENT surgeon and published multiple articles. His career was an unconventional one though, since due to multiple extracurricular activities he never became a consultant! He was actually struck off the medical register for drink-driving charges just a little before his early death. His life was evidence of his bravery, innovative spirit and mischief and his legacy shaped the way tonsillectomies are done to this day.

MEDICAL LEGACY

Tonsillectomy is one of the oldest operations performed, dating back at least 2000 years ago. Celsus in Rome described for the first-time tonsillectomy surgeries in the first century B.C.[1] The surgical techniques and the instruments used have changed greatly over the years, but tonsillectomy remains one of the most popular operations. In the United Kingdom, tonsillectomy is the fifth commonest procedure performed across all specialties, with an annual number of 50,846.[2]

The pioneering invention of Draffin rods by the Irish otolaryngologist David Alexander Draffin changed tonsillectomy practice advancing its safety and efficacy. Despite the ongoing debate regarding the best tonsillectomy technique, most of the traditional surgical approaches require the patient to be in the same "Rose position", with the head and neck extended, and the use of a mouthgag, to keep the mouth open. One of the fundamental tonsillectomy instruments used to secure this position is the Draffin bipod. [1] In 1951, Draffin published an article introducing his method to suspend the Boyle-Davis gag used to keep the mouth open during tonsillectomy by utilizing two rods or a bipod. The two rods created a tent-like framework by standing like two poles in the sterile towels in each side of the patient's head and meeting at the ''free end'' of the mouthgag. He explained the advantages of this new device, which included easy and timely application, practical re-adjustment, good ergonomics and safe to use in dental anatomical variations.[3] Before this invention, the Boyle-Davis gag was supported manually by the anaesthetic team. This had obvious disadvantages as it increased significantly the anaesthetic workload and was distracting for the operating surgeon. The anaesthetists had to have impossible multitasking abilities, as they had to secure the mouthgag while monitoring the patient's observations and depth of anaesthesia! For that reason, Draffin dedicated his invention "to the weary hands of cooperative anaesthetists and nurses". Previous attempts to stabilise the Boyle-Davis gag with other methods included complicated and impractical structures, like ropes hanging from the ceiling and supporting bars pressing on patient's chest! Draffin's idea was received with great enthusiasm internationally and was widely adopted. Draffin rods have remained part of the basic equipment for tonsillectomy ever since. [4]

EARLY LIFE AND MEDICAL EDUCATION

Alexander David Draffin was born on the 31st of August in Ballybey, Co Monaghan, Ireland. [5] He came from a large family and his father, a farmer also called Alexander, died aged 90 in 1951. His mother was Sarah Ann Draffin, who died in 1965, aged 85 in the United States of America (USA). [6] He had five brothers and four sisters. The youngest of his siblings, Walter Draffin, died only recently in 2017, in the USA. [7]

Alexander David Draffin attended local school in Co Monaghan. He then commenced his medical degree in 1934 at QUB, graduating in 1939 with Bachelor of Medicine, Bachelor of Surgery, Bachelor of Obstetrics. [5] During his university studies, Draffin was well known for his athletic abilities and was an active member of the Belfast Athletic Club.

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Figure 1. Photo of Draffin rods. Obtained from the surgical equipment used in theatre by our team in November 2019.

SERVICE IN THE ROYAL ARMY MEDICAL CORPS

In December 1939, shortly after his graduation from University, he volunteered for the army and became an emergency commissioned officer in the Royal Army Medical Corps. He was immediately sent to France and Belgium and was the youngest person to serve as a regimental medical officer with the British Expeditionary Force. [8] During his time there, he experienced some of the most gruesome events of the war. He was part of the 2nd Royal Norfolk Regiment, which was involved in the famous war crime committed in La Paradis. In this event, German troops massacred 97 British soldiers and amongst them were 26 of Draffin's fellow officers. Thankfully, he managed to avoid captivity at that time; but his luck did not last for long. He was eventually captured and remained under German imprisonment for most of the war. However, he was troublesome to his captors, even as a prisoner. He was notorious for multiple escape attempts and acts of rebellion. Due to this behaviour, he was transferred to many different camps. Because of that, the question 'Did you meet Draffin in your travels?' became a way to confirm the authenticity of a new prisoner. At one camp he managed to save 90 of his fellow prisoners during one of his escape plans. Unfortunately, he was wounded and captured before he escaped. His constants efforts to escape resulted in multiple terms of solitary confinement and camp transfers, but when these measures failed to faze him, he was transferred to the notorious Colditz Castle. He remained there from August 1943 until September 1944. This castle was well known as a prisoner-of-war camp during World War II for "incorrigible" Allied officers who had numerous previous escape attempts. Some of the most notable of Draffin's fellow prisoners include Sir Douglas Bader and Sir Airey Neave. Draffin continued his escape attempts even while in Colditz Castle, but he never succeeded in escaping from the Germans. He finally managed to escape captivity, only after the Russians had taken over from the Germans. His last escape was as eventful as the rest of his imprisonment. Before he escaped, he saved the six German nurses with a smart move. He asked them to hide in the cellar and he wrote in the door 'Typhus Ward – Keep Out' in German, Russian and English! Because of his distrust to the Russian army, he swam all the way across river Elbe to the American Second Army to ensure his liberation. [4] As recognition for his service in the war he was awarded the King's Badge for Loyal Service. [8]

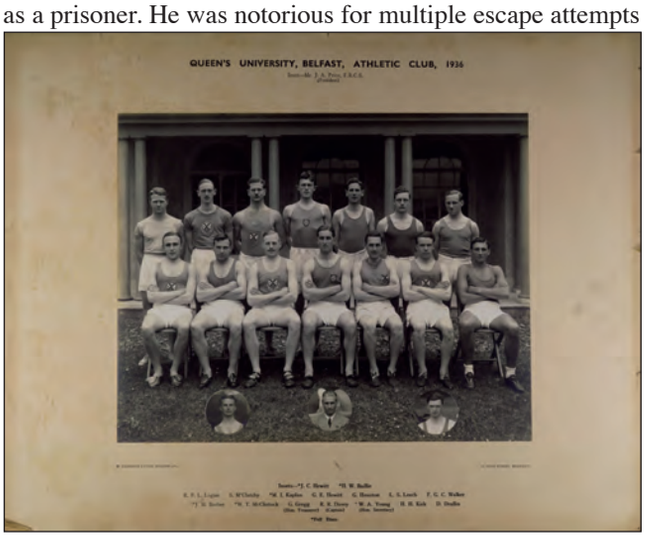

Figure 2. Photo of the Queen's University Belfast Athletic Club in 1936. David Alexander Draffin is the first on the right on the front row. Permission for publication obtained from Queen's University of Belfast Special Collections and Archives.

LIFE AFTER THE ARMY

Its thought that Draffin's traumatic experiences during the war made his transition to civilian life difficult. He married Margaret R Lyle in July 1948, in Newcastle upon Tyne. In the same year he obtained the Diploma of Laryngology and Otology and started working as an otolaryngologist. It seems that he did not settle in one place, but rather moved around. He worked in various hospitals, including the Hospital of St Cross, Manor Hospital, Nuneaton and George Elliot Hospital, and South East Kent Hospital Group. [8] He was also active academically and published several medical articles with international citations. He published about his eponymous invention in 1951 in British Medical Journal. His method was a complete success and became popular practice around the world. He had other articles published in the Journal of Laryngology and Otology (JLO). [9]

Despite his active career in clinical practise and research, he never passed the exams for the Fellowship of the Royal Colleges of Surgeons and therefore he was never officially a consultant. That might be because he was distracted by his several extracurricular activities. He was a very successful businessman and was involved in real estate dealings. He owned a block of flats with significant rent income that allowed him to live a luxurious lifestyle, which included the purchase of two Rolls-Royces. [4]

His lifestyle may have contributed to his demise - he was summoned to appear before the General Medical Council (GMC) following several incidents involving driving under

the influence of alcohol. The first disciplinary committee meeting took place in 1964 and Draffin was given the opportunity to overcome his alcohol problems by postponing judgement for two years. His careless behaviour however continued. He failed to appear at one of the GMC hearings because he claimed that he was too busy reading about the fall of the Roman Empire! Following the final meeting at the beginning of March 1967, Draffin was struck off the medical register. [10–13] Shortly after, on the 30th of March 1967, he was found dead in his flat in West Kensington in London. [4] There are several rumours regarding the cause of his death, some of them claiming mischief was involved. However, the post-mortem that was conducted confirmed that the cause of his death was myocardial infarction. [4]

CONCLUSION

Draffin was a daring and unique ENT surgeon with a fascinating life, who is mostly remembered for his inventions in Otolaryngology. He came from a simple background but went on to lead a colourful and adventurous life. During the war he demonstrated his courage, persistence and altruism by saving almost 100 people and attempting multiple escapes from captivity. After the war, his medical career was unconventional. He was an experienced otolaryngologist, but never actually passed his FRCS exams. He was a skilful surgeon, a practical inventor and his eponymous rods are used until today internationally for tonsillectomy. He was also an accomplished businessman and became financially successful. His carefree lifestyle led to controversial life choices and he died at a young age. However, his legacy lives on through his invention and his name is heard daily in the ENT theatres around the world.

ACKNOWLEDGEMENTS

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Game Changers

HEALTHCARE BEHIND BARS– COMMUNICATION IS THE KEY

Dr RT Kirk, Ms P Yates

Prison Healthcare, South Eastern H&SC Trust, Lagan Valley Hospital, Lisburn.

Over 4000 men and women are committed to prison each year in NI, often with numerous co-morbidities and complex needs. Historically information sharing between community healthcare providers and prison healthcare has been limited, for security and operational reasons. Therefore when a patient arrived in prison no medical record followed and no information was given to the community GP informing them their patient was now in prison.

The South Eastern Trust Prison Healthcare team identified this communication between community providers and prison healthcare as a unique opportunity to improve health, reduce risk for patients and ensure continuity of care is maintained during the transition in and out of custody. From a community perspective the benefits of reducing illicit medication supply are well documented as often medications continued to be dispensed in a patient's absence.

Following collaboration with the Health and Social Care Boards, the Business Services Organisation, Northern Ireland Prison Service and the South Eastern Health and Social Care Trust a letter was composed to send to the GPs of all patients in HMP Maghaberry on their entry into prison. This letter advised GPs that their patient was in prison, to de-authorise any repeat medication and requested a short medical summary of their patient.

In this UK first of its kind project, over 5000 letters have been sent to date with very positive feedback from community GPs. This has now become embedded in our system with huge gains in regard to patient safety and collaborative working. The project was recognised nationally with an RCGP 'Bright Idea Award- High Impact'[1] and has been shared and replicated in the Welsh Prison Service.

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SGLT2 INHIBITORS – SOMETHING IN THE WATER, OR THE HEART OF THE MATTER?

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Sodium-glucose co-transporter 2 inhibitors (SGLT2i) are an established therapy in the treatment of type 2 diabetes mellitus. Meta-analysis has recently shown them to have favourable outcomes in renal and cardiovascular disease.[1]

Significant benefits have been shown in mortality, major adverse cardiovascular events, heart failure, and renal outcomes such as progression of kidney disease and albuminuria. For adverse events, rates of discontinuation are <5%, with diabetic ketoacidosis being the most serious raised risk, albeit with low event rates (<1 per 1000 patient-years). Previously reported increased risks of urinary tract infections, amputation and fractures have not been confirmed in meta-analysis.

This has resulted in guidelines recommending SGTL2i as first line therapy for patients with diabetes and atherosclerotic cardiovascular disease or high/very-high cardiovascular risk factors.[2]

SGLT2i mechanism of action is partly understood, with evident glycosuria and natriuresis, but there is still work to be done in this field. Other proposed mechanisms include vasodilatation, reduced intra-glomerular pressure and increased glucagon levels. The finding that dapagliflozin improved heart failure outcomes in patients without diabetes is fascinating.[3] Additional mechanisms of action are being investigated, as are the effects on other conditions like heart failure with preserved ejection fraction (NCT03619213), and the results are eagerly awaited.

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Abstracts

Junior Members Forum & RBHSC Annual Lecture

16th March 2018 Riddell Hall, Belfast

POSTER PRESENTATIONS

TECHNOLOGY-ASSISTED CLINICAL PRACTICE: ASSESSING VIEWS AND EFFICIENCY OF MOBILE PHONES ON THE WARDS.

Dr P Mallett, APNP C Junk, Dr J Wallace, Dr P Mallett, Dr A Thompson

Aims:
Technology-enhanced learning has transformed many aspects of clinical practice.1 Some healthcare organisations in N.Ireland are reluctant to advocate the staff use of mobile phones due to infection control concerns or reported parental complaints.
Mobile devices provide a multitude of benefits for clinical staff including increased access to useful apps and other validated point-of care tools, which are of high educational value and have been shown to support better clinical decision making and improved patient outcomes.

Methods:
We designed a survey assessing parental and staff perception on the use of mobile phones, using a five point Likert scale. 40 staff and 40 carers participated in the questionnaire. We then created two simulated clinical scenario's assessing administrator and prescriber performance. We assessed length of time to complete task and degree of accuracy, with and without mobile phones.

Results:
38/40 (95%) parents and 39/40 (97%) staff members supported the appropriate use of mobile technology.
For the drug administration scenario (performed by nursing staff), all participants were quicker using mobile phone assistance. The average length of time was 82 seconds quicker.
For the medical prescriber scenario, again all participants were quicker using mobile phons, with an average length of 86 seconds quicker. Accuracy of 100% was maintained in both cohorts in each scenario.

Conclusion:
This survey highlights the strong carer and staff support for healthcare professionals using mobile phones in clinical areas. We have demonstrated an improvement in efficiency of performing clinical tasks with the assistance of mobile phones, ensuring accuracy was maintained.

A FOUNDATION IN ACUTE PAEDIATRICS (FAPS) - TARGETING PAEDIATRIC SPECIALITY RECRUITMENT USING HIGH FIDELITY SIMULATION

Dr P Mallett, APNP C Junk, Dr T Bourke, Dr A Thompson

Background:
Paediatrics, like many specialties in the UK, is experiencing a decline in applications for specialty training.1 Reasons include perceptions of poor flexibility, arduous training programme and lack of adequate career guidance and support.2 Transition between foundation level training and specialty training is an uncertain and stressful time.3 We believe that offering access to high-fidelity simulation course affords a unique opportunity to showcase our specialty, as encouraged by the RCPCH.

Methods:
We designed, delivered and evaluated 'A Foundation in Acute Paediatrics Simulation' (FAPS) course aimed at offering junior doctors an introduction into the management of common paediatric conditions. A highly experienced inter-professional faculty provided an insight into a career in paediatrics and an opportunity for group discussion and tailored personal career advice.

Results:
16 Foundation doctor candidates took part in the pilot FAPS course. Prior to the course 11/16 (69%) candidates were unsure whether they were going to apply for paediatrics. After the course all 11 candidates indicated that that they were more likely to apply [mean score- 2.9 before vs 4.0 after; 1-very unlikely, 3-undecided, 5-
Very likely to apply]. Subsequently, 15/16 candidates (94%) felt more confident in the assessment of the unwell child.

Conclusions:
This is the first known use of high-fidelity simulation to enhance specialty recruitment in N.Ireland. This course provides an opportunity to gain access to motivated junior trainees in a safe, simulated learning environment. This course actively helps in addressing the current plight of low trainee recruitment and retention in Paediatrics and could be easily replicated in other areas.

ORAL PRESENTATIONS

EYES WIDE SHUT: ARE WE MISSING PAEDIATRIC OBESITY IN GENERAL OUTPATIENT CLINICS?

Anne-Marie McClean (presenting author)

Jenny Thompson (F2 Paediatrics) Karen Orr (Paediatric Outpatients Ward Manager) Patricia Anderson (Nursing Support Worker) Tom Waterfield (Paediatric Registrar) Bernadette O'Connor (Consultant Clinical Lead) Mugilan Anandarajan (Consultant Paediatrician and Project Supervisor) Organization: Paediatrics Department, Ulster Hospital, Dundonald, South Eastern Health and Social Care Trust, Belfast, UK

Background and Aims:
Reducing childhood obesity rates will save lives[ii]. Children are only routinely screened for obesity twice (4-5years, 10-11years) through the National Child Measurement Programme (NCMP)[iii]. Additional opportunities to identify overweight/ obese children cannot be missed. This study aims to explore the prevalence and recognition of overweight/obese children in the outpatient population of a district general hospital (DGH).

Methods:
An audit of growth parameters for 87 children (2-16 years) attending paediatric outpatient/ambulatory clinics was performed during one week in September 2017. Retrospective body mass index (BMI) centile plotting enabled identification of overweight (≥ 91st centile) obese (≥ 98th centile) and severely obese (> 99.6th centile) children. Clinic letters were reviewed to check if children were recognised as overweight/obese. Public Health Agency (PHA) collaboration facilitated NCMP data comparison.

Results:
BMI centiles were retrospectively plotted for 75 children (56%-male, 44%-female). 14% were excluded as no heights measured. 28% were overweight/obese comparing similarly to NCMP data: 27% 10-11-year olds in the SEHSCT are overweight/ obese[iv]. Our study had more obese children at 15%. (4% severely obese) compared to NCMP data at 6.6%.

Only 3 patients were diagnosed as obese (all severely obese) during consultations. 86% of overweight/obese children (presenting with constipation, asthma, enuresis etc) went unrecognised.

Conclusions:
Despite a high prevalence of overweight/obese children, our recognition rate is poor at 14%. Telephone scoping exercises indicate this is an issue across all Northern Irish hospitals. Questionnaires show strong support for the introduction of routine BMI plotting and a joint PHA-Paediatric regional training package to improve recognition and response to childhood obesity by paediatric staff.

HATS OFF TO MUM…IS THERE SUFFICIENT EVIDENCE FOR THE USE OF HATS FOR TERM NEONATES WHEN SKIN-TOSKIN CARE IS PRIORITISED?

Dr Anne-Marie McClean, Dr Roisin MacMahon, Dr Michael Coffey, Alison Bartlett, Dr Mugilan Anandarajan

Background and Aims:
The Ulster Hospital Dundonald (UHD) guidelines recommend hats for preterm babies but not term babies (unless deemed necessary by a midwife/doctor or parental choice). This contrasts with regional thermal care neonatal guidelines which recommend hats for all babies in the first six hours of life. This study aims to assess if there is sufficient evidence to recommend hats for babies ≥ 37 weeks gestation.

Methods:
One-hour temperatures were collected from babies born during September 2017 using a "temp ticket" proforma. Delivery method, gestation and thermoregulation practices were documented on the proformas which were later analysed.

Results:
146 (46% of eligible babies) were included. 96% were ≥ 37 weeks gestation. All preterm babies received hats. 34.9% of term babies received hats (parental/midwife choice). 65.1% of term babies did not have hats.

88% of babies had a normal temperature: 89% of babies without hats and 84% of babies with hats had normal temperatures. 79.7% of normothermic babies were skin-to-skin with a nappy and blanket over the top at one hour (63% of these skin-to-skin babies had no hats, 37% had hats).

Conclusions:
Hats did not lead to better temperatures for term babies- in fact more babies without hats had normal temperatures than babies with hats. Most normothermic term babies were skin-to-skin with mum and whether they had a hat or not did not impact their temperature. This shows hats are not needed for well neonates ≥ 37 weeks when skin-to- skin care is prioritised. The regional neonatal thermal care guideline is changing to reflect these findings.

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Abstracts

Junior Members Forum & RBHSC Annual Lecture

22nd February 2019 Riddell Hall, Belfast

POSTER AND ORAL PRESENTATIONS

THE NORTHERN IRELAND CYSTIC FIBROSIS APP – A NEW AND INNOVATIVE RESOURCE FOR PATIENTS AND THEIR FAMILIES

Dr Ben McNaughten, Dr Laura Jenkins, Dr Alastair Reid

Background: Cystic Fibrosis (CF) is a genetic condition affecting approximately 200 children and young people in Northern Ireland. A diagnosis of CF is life-changing for patients and their families. At diagnosis they are provided with a wealth of educational information. This can often be overwhelming at what is already a particularly challenging time. Consequently the CF team were keen to develop a resource which would enable patients and their families to access reliable educational information in their own time which would be of benefit both at the time of diagnosis and as they grew older.

Methods: We decided to create an app which could be downloaded and accessed free of charge. During the design process we consulted with medical professionals, CF specialist nurses, dieticians, physiotherapists, pharmacists, clinical psychologists and social workers in addition to patients and their families.

Results: We created an app containing information about the local adult and paediatric CF services and providing links to useful online resources in addition to material on physiotherapy, dietetics, medications, common infections, evolving research and the transition process. The app was made available to patients in 2018. To date it has been accessed over 3,200 times. Verbal feedback has been very positive. It costs approximately £75 per year to publish online and is updated regularly by members of the multi-disciplinary team.

Conclusions: The app has already proved a useful resource for patients and their families. We are keen to continue to develop this resource by formally evaluating and adjusting the content accordingly.

DOES FLASH GLUCOSE MONITORING IMPROVE PATIENT SATIFACTION & HBA1C IN 12-16 YEAR OLD PATIENTS WITH TYPE 1 DIABETES AND SUBOPTIMAL HBA1C LEVELS

Dr Kathryn Parker, Dr Julia Smyth, Dr Shilpa Shah, Dr Sarinda Millar

Background and Aims: Type 1 diabetes requires significant self-management. Teenagers have motivation but are also vulnerable. The Flash Glucose monitoring system is a device that measures interstitial glucose level by scanning the sensor placed upon the arm.

Does flash glucose monitoring improve the HBA1c and overall satisfaction in 12-16 year old patients with type 1 diabetes with suboptimal levels?

Methods: Flash glucose monitoring was made available to all patients with type 1 diabetes who fulfilled set criteria and after completing a training session.

We included 12-16 year olds with hba1c 69 mmol/mol (8.5%) and above. Demographic details were recorded. We monitored their HbA1c at 3 and 6 months from starting flash glucose monitoring.
We also asked them 2 questions

- Do you feel the flash glucose monitoring system has made it easier for you to manage your diabetes on a day to day basis

- Do you think it will improve your overall HbA1c level?

Results:
24 patients aged 12-16 years had Hba1c above 69mmol/mol

8 were eliminated either due to recent diagnosis of type 1 diabetes (3) or refusal to use Libre (5) therefore N=16.

Median: HbA1c before starting Libre= 78mmol/mol (mean=85), at 3 months 86 mmol/mol (mean=85) and 6 months 73mmol/mol (mean 73) p=0.016 At 3 months all felt Libre made it easier to manage day to day sugar levels

Conclusion: There was a significant fall in Hba1c (P=0.016) 6 months after using Flash Glucose monitoring. Most felt it improved overall satisfaction

THE MIND BUBBLE – A PATIENT EMPOWERMENT TOOL. A QUALITATIVE ANALYSIS OF WHAT YOUNG PEOPLE REALLY WANT TO DISCUSS AT DIABETES CLINICS.

K. Parker, S Shah, S Millar, J Smyth. Paediatric Diabetes SHSCT.

Background and Aims: In the SHSCT diabetes team, our goal is to empower our young people and encourage self-management of their diabetes. A key component of this is to understand the expectations of young people attending our clinics, and therefore provide patient centred consultations. Our aim was to identify each patient's goals and specific

areas for discussion when attending clinic.
Methods: We distributed questionnaires, the in form of a 'mind bubble', to young people over 12 years attending paediatric diabetes clinics in the Southern Trust over a two month period. A 'mind bubble' is a simplified visual questionnaire designed to be user-friendly and engage with young people. Young people were asked 'What would you like to discuss today at your diabetes clinic?' and their responses were then addressed at that attendance.

Results: We received 32 completed 'mind bubbles'. The most common response was for advice on hyper- and hypoglycaemia (44%). 7 responses (22%) were regarding practical advice on holidays and exercise, 6 responses (19%) for specific questions regarding insulin pumps and infusion sets, and 3 (9%) regarding the use of associated computer programmes. 3 responses (9%) asked for education on ketones.

Conclusions: The 'mind bubble' provides a practical way for young people to inform the diabetes team of their expectations for each clinic visit. The wide variety of responses highlights the challenges of engaging with young people with complex, life long conditions, and the need for patient centred care to enable our young people grow in confidence.

Ulster Med J 2020;**89(2):**114-121

Abstracts

Ulster Paediatric society Annual Conference

30th September 2017

TITANIC BUILDING BELFAST

BRINGING NURSING HANDOVER TO THE BEDSIDE- AN INTERVENTION TO IMPROVE COMMUNICATION AND PATIENT SAFETY

J Holland, Dr McClean & Dr Anandarajan

BACKGROUND: Nursing handovers represent the transfer of professional responsibility for patient care between team members. Patient safety depends on clear and accurate handovers. Staff surveys in 2014 identified dissatisfaction with previous handover practice. Verbal handovers occurred away from the patient bedside, without use of standardised communication tools. An opportunity to improve nursing handovers was identified.

AIMS: To achieve 90% compliance of Bedside Nursing Handovers. To improve staff, patient and parent satisfaction. To create a culture of handover practice which prioritises patient safety

METHODS: A literature search was performed to identify best practice. Staff feedback exercises and "brainstorming" allowed evidence based interventions to be tailored to address specific shortcomings.
Plan-Do-Study-Act cycles focused on:
- -Face-to-face education/staff training
- -SBAR communication tool implementation
- -Introduction of written handover proformas
- -Improving start and end times (minimising interruptions)
- -Improving accuracy of patient information transfer
- -Utilisation of the Patient Safety Scan (safety checklist)

-Regular audits monitored compliance. Results were displayed on a noticeboard for staff to identify areas for improvement and celebrate success.

RESULTS: Bedside handovers have increased from 0% to 100%. Parents and patients listen to handovers and have an opportunity to contribute. All handovers utilise SBAR communication and patient safety checks (name-bands, PEWS charts, fluid balances, airway equipment and medications). Staff and parental feedback has demonstrated increased satisfaction and confidence with this safer, holistic, patient-centred handover.

CONCLUSIONS: Nursing bedside handovers have become routine practice in Maynard- Sinclair Ward and staff, patient and parental feedback continues to be extremely positive.

WEIGHT A MINUTE – COMPARISON OF ACTUAL VERSUS ESTIMATED WEIGHT USING APLS FORMULAE IN PATIENTS ATTENDING THE PAEDIATRIC EMERGENCY DEPARTMENT

CR Parris, T Bourke

Background & Aims: In the paediatric patient, weight is required to calculate drug dosages and fluid prescriptions. In some instances, an actual weight measurement is not possible or practical and an estimate must be made. This study aimed to compare the accuracy of weight estimation using the current versus previous APLS formulae in Northern Irish children.

Methods: The actual weight and age of patients was collected from patient records from children attending the RBHSC Paediatric Emergency Department in April 2016 (n=523). The estimated weight using current and previous APLS formulae was calculated for each subject and compared to actual weight using the mean residual sum of squares (RSS). A sub-analysis of age groups was conducted (1-11 months; 1-5 years; 6-12 years; 13+ years).

Results: The Mean RSS across all age groups was 46.75 for the current formulae versus 103.23 for the previous formula. The comparative Mean RSS (current:previous formulae) for specified age groups was as follows: (1-11 months 1.65:4.88 n=82; 1-5 years 10.29:10.29 n=231; 6-12 years 77.85:181.12 n=185 ; 13+ years 301.40:708.13 n=25).

Conclusion: The current APLS formula is overall more accurate than the previous APLS formula at estimating weight in children and across almost all age groups (note: the formulae for 1-5 year olds were equivalent). Weight estimates are less accurate in older children with both calculation methods.

Ulster Med J 2020;**89(2):**114-121

Abstracts

Ulster Paediatric society Annual Conference

28th September 2018

HILTON HOTEL, TEMPLEPATRICK

"WHAT IS KNOWN ABOUT CHILDREN AND YOUNG PEOPLE'S EXPERIENCE OF RECEIVING HEALTHCARE FROM THEIR PRESENT PERSPECTIVE?"

Gail Davison, Richard McCrory, Andrew Thompson, Tim Dornan

Background & Aims: Most studies explore children and young people's (CYP's) experience of healthcare without consulting CYP directly. The aim of this study is to explore "what is known about children and young people's experiences of receiving healthcare from their present perspective?"

Methods: Scoping review methodology was used to address the research question through a phenomenological lens of direct quotation. Basic numerical analysis and qualitative content analysis was completed.

Results: 3095 CYP, aged 0-18 years, participated in the 89 studies included in this literature review at an international level. Studies describing CYPHCEs through direct quotations have increased from 2005. Most studies used semi-structured participatory interviews. CYPHCEs are complex and unique to that individual. Twelve themes emerged. Communication and autonomy were the most common themes. CYP are asking for better communication at an understandable level.

Conclusions: CYP have an increasingly active voice in qualitative healthcare research at an international level. A lack of patient-specific communication, which acknowledges the patient's ability to understand, has a negative impact on CYPHCEs. CYP's participation in their own care affects their experience, however, the level of participation each seeks is varies.

Ulster Med J 2020;**89(2):**114-121

Abstracts

Ulster Paediatric society Annual Conference

13th September 2019

HILTON HOTEL, TEMPLEPATRICK

FOR THE FUTURE: STARTING TO ADDRESS THE GAP IN PAEDIATRIC OBESITY SERVICES

Anne-Marie McClean, Jodie McGoldrick, Joanne Gordon, Arlene Long, Jennifer Gawley, Mugilan Anandarajan, Bernie O'Connor

Background and aims: Fit Families for the Future launched in May 2019 and is presently Northern Ireland's only multidisciplinary service for children (4-16 years) with BMI > 98th centile. Over 12 months we aim to support 48 children to achieve a healthier BMI.

Methods: Children are referred by paediatricians, GPs and school nurses. Each family is invited to clinic for holistic assessment by a paediatrician, physiotherapist, associate psychologist and dietician. Outcome measures include BMI, 6-minute walk test, grip strength, blood pressure testing, dietary history and quality-of-life measures. Parents are encouraged to have their own weight/BMI checked. An individualised family plan is coproduced. Treatments include a series of educational evening classes and/or one-to-one input from dietetics/physiotherapy/health coaching. Outcome measures will be reassessed at 3, 6 and 12 months.

Results: Currently 30 children have attended Fit Families assessment clinics. 29 are in the treatment phase. 1 child discharged as <4 years. 8 children participated in the first 5-week cycle of evening classes. Attendance averaged 73%. 6/8 children have had their BMI reassessed. 60% (4/6) have reduced their BMI including one family who collectively lost >12kg. One child's BMI increased, and another's remained static. Family and staff feedback have been overwhelmingly positive.

Conclusions: In response to feedback we have extended our evening class programme to 6-weeks, introduced text reminders for appointments and strengthened our outreach programme with community organisations including Parkrun and local councils. We are excited to recruit more families, see more results from the programme and develop a viable business case for this gap in paediatric services.

MEDICATION ADMINISTRATION ERRORS IN CHILDREN: MIXED METHODS STUDY OF CRITICAL INCIDENTS

Vincent McLarnon, Richard Conn and Angela Carrington

Background and Aims Medication administration errors (MAE) are a common problem. To address this problem it is important to understand the how and why MAEs occur. The study aims to investigate;

- o Type and characteristics of MAE;
- o Underlying factors that led to these errors.

Methods: A mixed methods study of clinical incident reports related to MAE was undertaken. MAEs involving children 0-16 years, in paediatric medical and surgical wards in Northern Ireland (NI) between 2011- 2015 were included. The characteristics and types of MAE were quantified, then MAE descriptions were thematically analysed t determine the underlying contributing factors which led to error.

Results: In total 369 incident reports of MAEs (including 391 drugs) were analysed. The most common: MAE type was omitted and delayed (n=103; 28%). The most common drug class was antimicrobials (n=93; 24). MAE characteristics include; children 5 years and under (n=178; 48%); insignificant harm (n=257; 70%); Contributing themes were related to management and organisational processes; features of the team, environment, task, and patient; and unsafe acts of staff. Defences were also found but commonly occurred after MAEs reached the patient.

Conclusion: This research has found there are multiple types, characteristics and contributing factors associated with MAE. The findings should be used to target specific error types, drug classes and contributing factors to prevent potential MAEs in future practice.

LAUNDERED LANYARD OR NOT SO MUCH?

Emma McCann, Rachel Philpott , Mugilan Anandarajan

BACKGROUND: White coats to lanyards, did we solve the infection control risk problem? Lanyards serve as a quick method of identifying the position of staff. However, with infection control becoming a prominent clinical priority, we are washing our hands but are we washing our lanyards? By exploring hygiene practices with regards to lanyards we can assess whether there is a need for change in the responsibility we take for what hangs around our neck.

AIM: To assess the lanyard hygiene practices of healthcare professionals within a district general hospital.

METHOD: A mixed-method survey of healthcare staff with dichotomous, nominal and free-text responses which were analysed numerically and thematically.

RESULTS: This questionnaire provided information on potential gaps relating to appropriate lanyard infection control measures. Common themes demonstrated that the majority

of lanyards were not washed nor replaced regularly, despite being worn continuously throughout the day, including travel to and from work. Gaps in staff adherence and understanding of adequate lanyard hygiene were evident.

CONCLUSION: The survey reiterated the need for clear information and guidance with regards to lanyard hygiene practices. The data collected raises awareness of the current discontinuity in attention and supply of adequate information in order to empower staff to take responsibility for their neck-suspended lanyard. The implementation of a lanyard hygiene protocol and consideration of future movement towards rubberised lanyards are practical measures that could improve upon infection control standards within hospitals.

THE PRO-VAC MOVEMENT-A QUALITY IMPROVEMENT & EDUCATIONAL INITIATIVE

A.E. Henry, V. McLarnon, M. Hanna, R. Hearst, S. Shah

Background & Aims: Some people choose not to vaccinate their children resulting at least in part to a rise in the incidence of vaccine preventable disease such as measles globally. Interactions between Health Care Professionals (HCP) and parents help to alleviate vaccination concerns.

- What is the prevalence and cause of vaccine hesitancy or refusal in mothers attending antenatal clinics in a District General Hospital?
- Can targeted intervention strategies such as group educational sessions improve confidence in vaccine safety?
- Can educational sessions delivered to HCP about 'vaccine safety & having conversations with vaccine hesitant families' improve their confidence to undertake these discussions?

Methods:

- 147 consecutive mothers attending antenatal clinics filled questionnaires. Data including prevalence and spectrum of vaccine hesitancy with causation was obtained and analysed.
- Bespoke information sharing sessions on vaccine safety and having conversations with vaccine hesitant parents were delivered by trained HCP to families and HCP respectively.
- Feedback was analysed

Results:

- Majority of mothers had no concerns about vaccinating their baby (86%)with commonest concerns being 'side effects like fever and allergic response' followed by 'link between MMR and autism'
- 2 'Vaccine safety' sessions for families significantly increased their confidence in vaccine safety (p=0.0004)
- 4 'Vaccine safety & having conversation' sessions attended by multidisciplinary HCP significantly increased their confidence in the above area (p=0.001)

Conclusions: Majority of families are confident about the safety and efficiency of vaccines. Education and vaccine safety sessions targeted towards families and HCP both increase the confidence in vaccine safety.

FRAGILE X SYNDROME; A SURPRISINGLY UNCOMMON CAUSE OF INTELLECTUAL DISABILITY

C McKenna, D Beattie, C Gervin, T Dabir

Fragile X Syndrome (FXS) is often described as the most common cause of intellectual disability (ID) in males. Anecdotally, we have noted a low diagnostic yield from FXS testing. FXS is typically caused by a triplet repeat expansion (>200 CGGs) in FMR1. FXS more commonly affects males, however it is estimated that one third of females are symptomatic. Classical features of FXS include ID, autism, behavioural disturbance and dysmorphism. Smaller expansions in FMR1 (pre-mutations) are associated with Fragile XAssociated Tremor/Ataxia Syndrome (FXTAS) and Premature Ovarian Insufficiency (POI).

We retrospectively reviewed the results of FMR1 assays undertaken at the NIRGC between 24/05/12 – 08/07/19. In total, 521 FMR1 assays were performed for a variety of indications (FXS, FXTAS, POI and carrier status). Thirteen full mutations (>200 repeats) and 34 pre-mutations (59-200 repeats) were identified. All but two of those patients with a full mutation had a known family history of FXS. Of those with a full mutation, five were male and eight were female. Five of the females had symptoms of FXS.

Our findings suggest a low diagnostic yield from FMR1 assays, particularly in the absence of a family history. It is also noteworthy that an equal number symptomatic females and males were diagnosed. This may be a reflection of the small sample size and/or ascertainment bias. We propose that FXS testing should not be undertaken as a first line investigation in children with ID, and only sought if there is a high degree of clinical suspicion, or a known family history.

Letters

IATROGENIC PNEUMOTHORAX FOLLOWING PLATE FIXATION OF THE CLAVICLE

Editor,

A 37-year-old right hand dominant male sustained a comminuted, displaced midshaft fracture of his left clavicle as the result of a motorcycle accident. He did not incur any other injuries. After discussing the treatment options, a decision was taken to proceed with open reduction and plate fixation of his left clavicular fracture. The procedure was performed under general anaesthesia in the beach chair position. A direct incision was made over the left clavicle and the fracture was exposed and reduced. The fracture was stabilised using a pre-contoured titanium plate with a combination of non-locking and locking screws. No concerns were reported in the peri-operative period by the anaesthetic team. A routine check x-ray of the left clavicle was obtained the following day which demonstrated an excessively long medial screw (**Figure 1a**) with a left apical pneumothorax confirmed on a chest radiograph (**Figure 1b**). The patient returned to theatre for insertion of a left-sided chest drain and screw exchange. The pneumothorax resolved and the patient's left clavicular fracture proceeded to complete union.

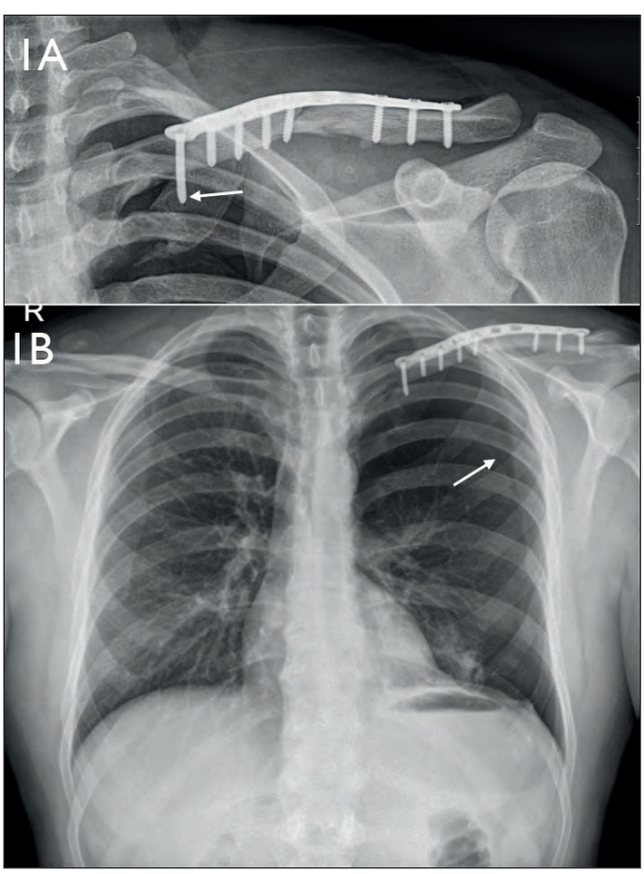

Figure 1a (top): left clavicle check x-ray demonstrating an apical pneumothorax and an excessively long medial screw (white arrow); **Figure 1b** (bottom) demonstrating a left-sided pneumothorax (white arrow pointing to edge of lung).

Fractures of the clavicle are common representing 2.6 to 5% of all fractures and approximately 80% of fractures affect the middle third of the clavicle.[1] The incidence of high-energy fractures with displacement, comminution and shortening is increasing and as a result operative fixation for such injuries is being performed more commonly.[1] Infection, implant failure, non-union, scar-related pain, prominent hardware and refracture are the most commonly reported operative complications.[2]

Plate fixation is the most common method of operative management.[3] The plate is most commonly placed on the superior surface of the clavicle with screws inserted in a cranial-caudal direction potentially placing the lung apex and the neurovascular structures at risk during drilling and screw insertion. The risk however of either an iatrogenic pneumothorax or neurovascular injury is regarded in the literature as a rare occurrence.[3,4] Some centres have recommended obtaining a chest x-ray routinely to exclude pneumothorax following clavicle fixation. Shubert et al.[3] concluded from their study that due to the rarity of iatrogenic pneumothorax, radiation exposure and cost, in combination with the poor sensitivity of chest radiographs to detect pneumothoraces, obtaining a routine chest x-ray without clinical indication may be unnecessary.

Pneumothorax in relation to clavicular fractures is a well-described preoperative complication existing in the literature.[3,5] In our case, the patient had a preoperative chest x-ray which did not demonstrate pulmonary trauma and given the excessive difference in length between the most medial screw and the adjacent screw we conclude that the patient incurred an iatrogenic pneumothorax due to surgical error. We acknowledge that intra-operative screening would have identified the long medial screw but the pneumothorax may not have been appreciated.

We emphasise the importance of careful surgical technique when performing plate fixation of a midshaft clavicular fracture, in particular, ensuring a guard is placed under the clavicle when drilling and close attention to screw length. Furthermore, we recommend careful scrutiny of postoperative clavicle radiographs due to the rare but potential risk of iatrogenic pneumothorax.

Miss Rebecca Waterworth

Mr Neville W Thompson

Department of Trauma and Orthopaedics, Altnagelvin Hospital, Glenshane Road, Londonderry BT47 6SB

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BRASH SYNDROME: AN UNDER RECOGNISED CAUSE OF COMPLETE HEART BLOCK IN THE ELDERLY

Editor,

An 81 year old lady with a background of chronic kidney disease (CKD), hypertension and type two diabetes mellitus presented to Craigavon Area Hospital via ambulance as a stroke lysis call. She was dysarthric and profoundly bradycardic with an unreadable blood pressure. Following administration of 600mcg atropine a blood pressure of 100/60mmHg was obtained. An ECG demonstrated complete heart block (CHB) with a ventricular rate of 29 bpm (Figure 1). A further 1.8mg atropine did not rectify her CHB and ventricular rate remained 40bpm albeit with a satisfactory blood pressure. Dysarthria was felt to be secondary to cerebral hypoperfusion in the context of CHB and her management was deferred to the cardiology team with the assumption that she would require a pacemaker.

An arterial gas sample was taken at this point which demonstrated elevated potassium of 8.3mmol/L. Interestingly, her ECG did not demonstrate dramatically peaked T waves as would be expected with hyperkalaemia and initially this first reading was thought to be erroneous. Repeat sampling

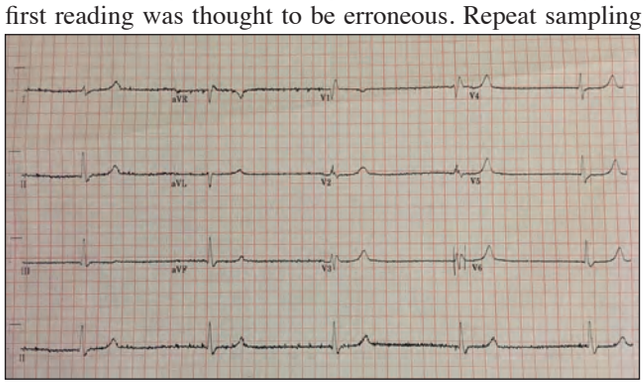

Figure 1 ECG demonstrating ventricular escape rhythm 29bpm without discernible atrial activity. RSR pattern with QRS 140bpm in keeping with RBBB noted in v1-3 with QRS in remaining leads noted to be relatively narrow with mild peaking of T waves noted.

however confirmed hyperkalaemia. Additionally, her formal laboratory biochemistry soon confirmed she was in acute on chronic renal failure with an eGFR of 12mls/min which had deteriorated from a baseline of 30mls/min. The hyperkalaemia remained refractory to conventional medical treatment and haemofiltration was commenced. Upon normalisation of serum potassium, her rhythm reverted to sinus of rate 74bpm (Figure 2). Haemofiltration was weaned over the coming days and a permanent pacemaker was not required.

It emerged she had been taking both atenolol and Ramipril for hypertension and had recently commenced a NSAID for joint pain. This likely precipitated an acute nephrogenic

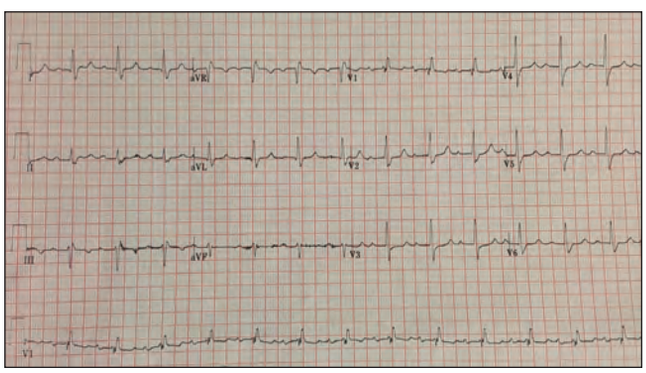

Figure 2 ECG demonstrating restoration of Sinus rhythm with mildly prolonged PR interval of 240ms.

insult resulting in the accumulation of atenolol causing further renal hypoperfusion and hyperkalaemia which, in synergy with B-blockade, precipitated CHB and cerebral hypoperfusion.

This case illustrates the recently coined BRASH syndrome (Bradycardia, Renal failure, AV-node blockers, Shock and Hyperkalaemia). This describes a series of events in a patient with CKD taking AV nodal blockers where an initial insult (such as dehydration or nephrotoxic medication) triggers a cascade of events where AV nodal suppression impairs the normal compensatory response to renal hypoperfusion thus causing renal decompensation resulting in worsening hyperkalaemia. The synergistic effect of hyperkalaemia and B-blockade on AV nodal function causes further decompensation resulting in a pathological downward spiral of events.[1,2]

This is an under-recognised cause of CHB and renal failure which may be refractory to initial conventional treatment measures. ECG changes may not be characteristic of classical hyperkalaemia, occur at lower than expected serum potassium levels and remain refractory to conventional treatment.[3,4] Co-morbid elderly patients on multiple medications are at high risk of developing this syndrome therefore as physicians we must be cognisant of prescribing AV nodal blockers or indeed additional nephrotoxic agents, so as to not incite the pathological cascade of events leading to BRASH syndrome.

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Keywords: *BRASH Syndrome, Hyperkalaemia, complete heart block, pacing, polypharmacy, elderly care medicine, cardiology, nephrology*

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DEGLUTITION SYNCOPE – A CASE REPORT

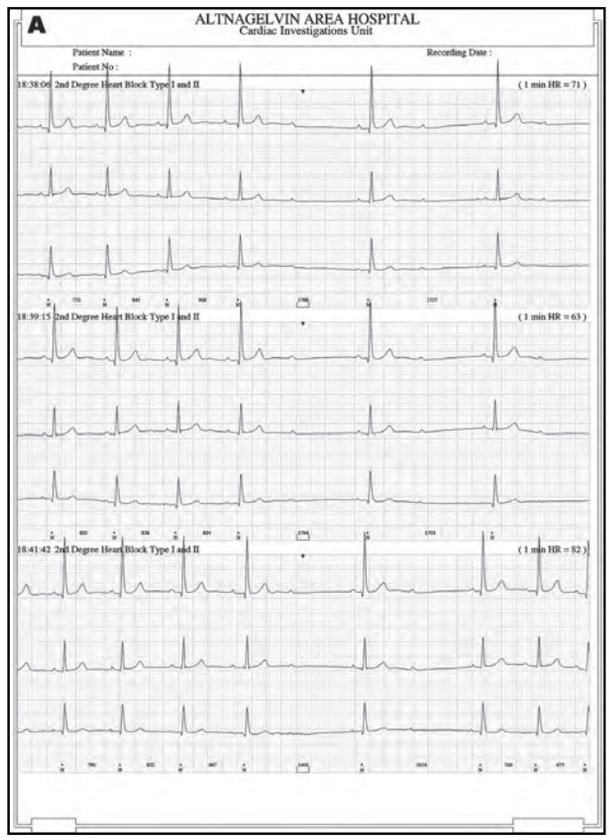
Editor,

A 38-year-old woman was referred to hospital for investigation following a three-year history of lightheadedness, dizziness and poor balance associated with eating. During this period, she had one episode of loss of consciousness. Symptoms were associated with flushing of the face which resolved spontaneously within 15 seconds. She reported that she could have up to fifteen episodes per week. She denied headaches and did not have any autonomic problems with her bladder or bowels. She had no significant past medical history. She did not take any regular medication and had no known allergies.

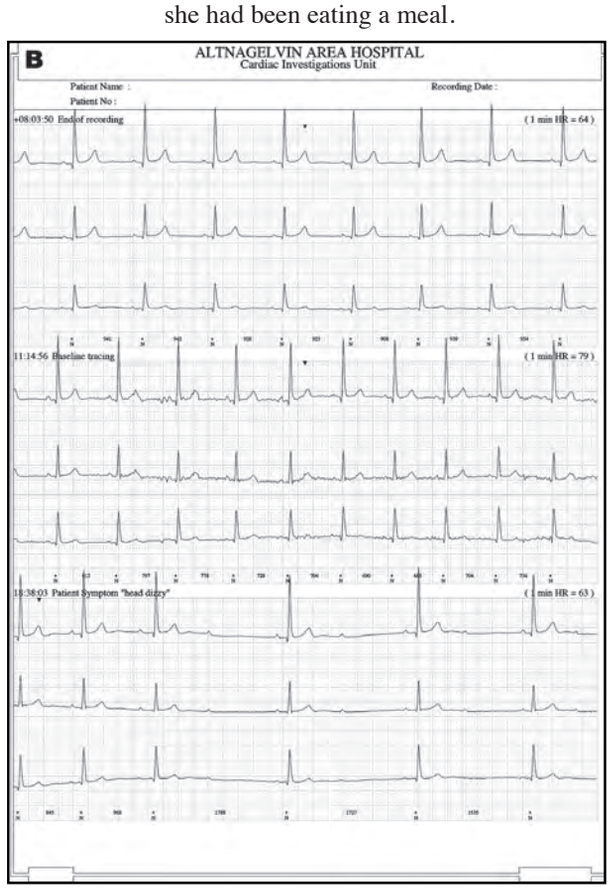
Blood pressure and heart rate were within normal ranges and she had no postural hypotension. A 12-lead ECG showed normal sinus rhythm with QTc interval within normal limits at 400ms.MRI brain and EEG were unremarkable. A 24-hour ambulatory ECG showed episodes of Mobitz Type 2 second degree atrioventricular block of which the patient was symptomatic, all occurring whilst she was eating (Figure 1 (a) and (b)). A diagnosis of swallow or deglutition syncope was made. Permanent pacemaker was implanted with complete resolution of symptoms.

DISCUSSION

Swallow syncope is a rare disorder thought to be due to a vagus nerve-mediated reflex. An increase in afferent



Figures 1 (a) and **(b)** showing 2nd degree heart block. On both occasions, the patient had documented that she had been eating a meal.



vagal activity from the oesophageal plexus to the nucleus solitarius in the medulla is associated with swallowing food. Efferent parasympathetic fibres to trigger peristalsis have a cardioinhibitory effect and lead to bradycardia, hypotension and vasodilatation. Severe cardiac conduction disturbance may cause loss of consciousness [1]. Over one hundred cases have been described in literature[2], despite having been first reported[3] in 1793.

The management of swallow syncope should include the withdrawal of any medication that slows the rate of cardiac conduction or causes vasodepression. Anticholinergic medications such as atropine have been trialed with a view to prevent bradyarrhythmias by inhibiting vagal tone. However, results have been inconsistent, and many drugs have undesirable side effects and are therefore poorly tolerated [2] .

Eighty-five percent of reported cases of swallow syncope had either sinus bradycardia, sinus arrest, SA block or AV block. Implantation of a permanent pacemaker is increasingly used for patients with swallow syncope [4]. Whilst permanent pacemaker implantation does not correct the cause of the condition, it has been demonstrated to be an effective treatment.

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FOLLICULAR LYMPHOMA OF THE RECTUM

Editor,

Non-Hodgkin's lymphoma compromises a diverse group of malignant neoplasms, rarely involving the colorectum. [1, 2] Follicular lymphoma is a common subtype and constitutes 1%–3% of all primary gastrointestinal tract lymphomas. [1, 3] There are very few cases reported of recurrence of follicular lymphoma in the rectum. [4] Rectal follicular lymphoma is difficult to diagnose due to limited available data, low clinical suspicion and non-specific symptoms. It also has variable growth pattern and ill-defined histopathological picture, making it difficult to distinguish from benign proliferative lymphoid lesions. [3]

This 67-year-old lady presented in January 2010 with a right neck mass. Initially she was managed with watchful waiting for putative atypical lymphoproliferative disorder, but in August 2011 histopathology confirmed follicular non-Hodgkin's lymphoma which was treated successfully with chemotherapy. In May 2016 she presented with worsening faecal incontinence and a palpable rectal mass. Clinically,

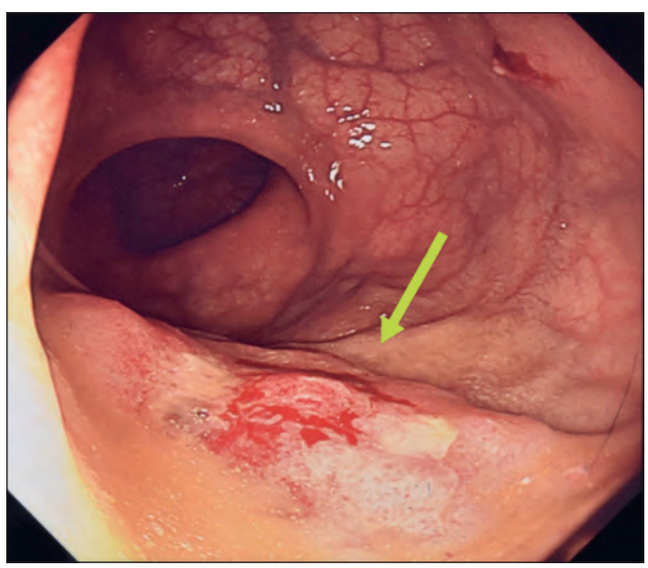

Figure 1 - Endoscopic appearance of low rectal lesion (arrowed)

this appeared to be a low rectal adenocarcinoma. [Figure 1 – Endoscopic appearance of low rectal lesion (arrowed)]. Magnetic resonance imaging (MRI) and computed tomography (CT) confirmed this rectal tumour extending to the anorectal junction with a radiological staging offered at – T3N1Mx. [Figure 2 – MRI view (coronal) demonstrating the low rectal lesion]. The initial biopsy showed a probable high-grade lymphoma, but two subsequent biopsies demonstrated only chronic inflammation. Another biopsy in December 2016 confirmed the presence of a low-grade follicular lymphoma. The patient was clinically stable and given the locality of the disease and the significant risks of chemo/radiotherapy a 'watch and wait' approach was chosen. However, her symptoms progressed and in January 2018 she had low-dose radiotherapy in the pelvis. As of September 2018, the patient has had a relapse confirmed and is under the ongoing care of haematology/oncology.

Gastrointestinal tract follicular lymphomas have usually inert clinical course. Patients can present with various non-

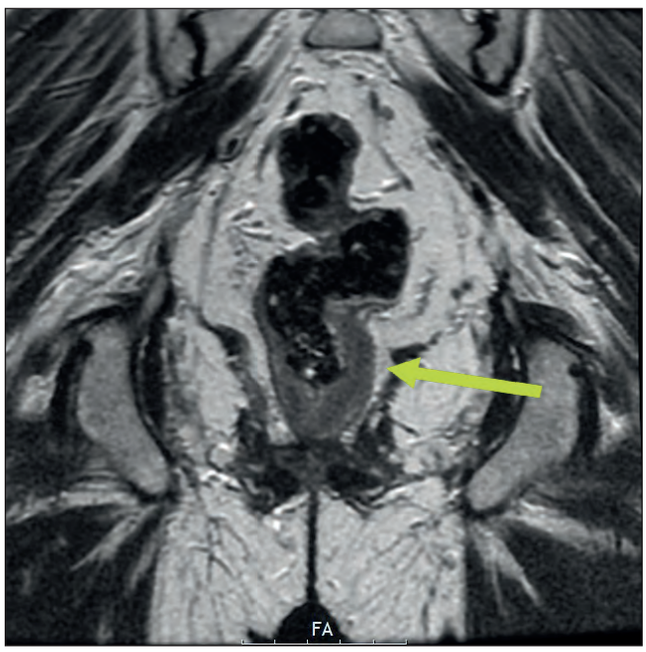

Figure 2 - MRI view (coronal) demonstrating the low rectal lesion

specific symptoms, but faecal incontinence has not been previously reported in the literature.[1 2 5] The histopathological evaluation of colorectal follicular lymphoma can be difficult. It is not uncommon for initial histological misinterpretation and requirement of multiple biopsies before the definite diagnosis. This case emphasises the challenge of accurate histopathological diagnosis. Suitable biopsy samples and immunophenotyping analysis are recommended for accurate interpretation of the pathological diagnosis of follicular lymphoma.[4, 5] The management of gastrointestinal follicular lymphoma is not well established because of its rarity, but multidisciplinary approach should be undertaken. In this patient, after a watchful period, local radiotherapy was implemented with good effect. This appears in accordance to general consensus, as intestinal follicular lymphoma is usually approached as nodal follicular lymphoma and a watch-and-wait strategy or radiation therapy can be applied in case of limited disease.[1]

In conclusion, rectal follicular lymphoma is a rare presentation, but important to consider in the differential diagnosis of rectal lesions. Endoscopists should remain alert whenever they observe ambiguous lesions in the colorectum and consultation with pathologist is advised to ensure appropriate immunostaining. Histopathologists should also maintain high clinical suspicion in differential diagnosis of follicular hyperplasia of mucosa-associated lymphoid tissue.

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TACKLING ANTIMICROBIAL RESISTANCE (AMR) - IN VITRO EFFECT OF SODIUM CHLORIDE ON ANTIBIOTIC SUSCEPTIBILITY IN CLINICAL PSEUDOMONAS AERUGINOSA ISOLATED FROM PATIENTS WITH CYSTIC FIBROSIS (CF)

Editor,

Relatively little is known about the potential interactions of cystic fibrosis (CF) co-therapies on antimicrobial susceptibility in CF respiratory pathogens, particularly inhaled/nebulised interventions, including those aiding sputum clearance, in particular, hypertonic saline (HTS). Whilst such interventions are not designed *per se* as anti-infectives, the effect (if any) of such molecules to CF patients' microbiological status and the potential effect on antibiotic susceptibility merits careful monitoring. Hence, we examined the effect of hypertonic saline on the *in vitro* antibiotic susceptibility to clinical *P. aeruginosa* from adult CF patients.

P. aeruginosa isolates (n=50) from adult CF patients were examined and were obtained from freshly expectorated sputum specimens submitted by adult CF patients, as part of the routine microbiological workup. Antibiotic susceptibility of each isolate was assessed employing standard CLSI disk diffusion assay,[1] against the antibiotics listed in Table 1, in the presence of sodium chloride (0.6M) and without supplementation, where 0.6M NaCl was chosen as a surrogate for NaCl concentration in sputum following HTS treatment. Resulting zone of inhibition were measured (mm) and compared statistically employing a two-tailed paired t-test, where p values <0.05 were considered significant, as shown (Table 1).

There was a significant effect on antibiotic susceptibility when supplemented with NaCl (0.6M). For each class of antibiotic examined, there was a statistically significant increase in zone size, ranging from a 19.3% increase with tobramycin to an 81.8% increase for piperacillin/tazobactam, with a mean increase of 60.1% over all classes of antibiotics examined.

Table 1: *In vitro effect of supplementation with sodium chloride (0.*6M) on antibiotic susceptibility of clinical isolates of *Pseudomonas aeruginosa* isolated from the sputum of patients with cystic fibrosis

	Mean Zone size (mm)			
Name of antibiotic	**Antibiotic alone**	**Antibiotic + 0.6M NaCl**	**Change in zone size (%)**	**P value**
Piperacillin/Tazobactam	20.9	38.0	+81.8	<0.0001
Meropenem	23.6	39.5	+67.4	<0.0001
Tobramycin	15.0	17.9	+19.2	0.02
Ciprofloxacin	17.3	30.0	+73.4	<0.0001
Colistin	13.7	21.7	+58.4	<0.0001

Using CLSI interpretative criteria, these changes in mean zone size would shift intermediate resistant isolates for piperacillin-tazobactam and ciprofloxacin to being sensitive, with the others remaining sensitive, with and without salt supplementation, albeit with increased susceptibilities in the presence of salt.

The mechanisms contributing to enhanced antibiotic susceptibility in the presence of increased saline concentration (0.6M) are not fully understood, but it appears that increased osmotic pressure is responsible for altered MIC value. *P. aeruginosa* cells had been precultured in isotonic conditions and were suddenly exposed to unusual hypertonic conditions, leading to a sudden change in external osmotic pressure. The immediate result of this would have been water efflux and cell dehydration, leading to adversely altered cytoplasmic solute concentration and a disruption in normal cellular physiology. Additionally, such osmotic stress would lead to alterations in physical properties of the cell architecture, including cell volume of the cytoplasm/periplasm, turgor pressure, cell wall strain and cytoplasmic membrane tension.[2]

The increasing burden of AMR amongst CF bacterial pathogens is clinically important, as it limits the efficacy of antibiotics used. Therefore, any positive shift in regaining susceptibility is to be welcomed and exploited, to maintain the effectiveness and value of the current CF antibiotic formulary.

In conclusion, the inclusion of NaCl demonstrated an increase in zone diameters for all antibiotics tested. Our results suggest a potential synergistic effect of NaCl and commonly used anti-pseudomonal antibiotics. Further work is now needed to evaluate the *in vivo* effect of HTS and PA antimicrobial therapy and if the reduced MIC is maintained over time.

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DECLARATION OF INTERESTS

The authors have no interests to declare.

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FIRST CASE OF COVID-19 IN IRELAND

Editor.

Covid-19 is the disease caused by SARS-CoV-2 virus[1]. Some notable members of this family include MERS-CoV and SARS-CoV which were responsible for epidemics in the past[1]. On 11th March 2020, WHO declared Covid-19 to be a pandemic and urged the world to come together in order to slow down further spread of this virus[2].

We present the first case of Covid-19 diagnosed in Ireland. This middle-aged lady travelled to Northern Italy and returned on 17th February 2020. On the same day, she developed general malaise and cough. Symptoms persisted and she developed dyspnoea and fever which prompted her to seek advice from her GP.

Following advice from the Public Health Agency, samples were taken, and on the 26th February, SARS-Cornavirus -2 RNA was detected in a Nasal and Throat Swab (NTS) using previously published real-time PCR assays[3]. Briefly, the screening assay targeted the RNA dependent RNA polymerase (RdRP) gene, with positivity confirmed using assays targeting the envelope (E) and nucleocapsid (N) genes. RNA was extracted with the MagNAPure Compact system (Roche, UK) and real-time PCR for each gene target run as a 25ul reaction (containing 5ul RNA, 12.5ul of 2X Superscript III of step RT-PCR reaction buffer, 0.4uM dNTPs, 3.2mM $MgSO_4$, 1ul of RT/Taq enzyme (Invitrogen, UK) and primer and probe concentrations for the respective assays. PCR cycling conditions using LightCycler 480 II were as follows: 55 °C for 10 min for reverse transcription, 95 °C for 3 min and 45 cycles of 95 °C for 15 s, 58 °C for 30 s. Ct values less than 40 were reported as positive.

On the 27th February, the patient was admitted for clinical observation and containment. She reported the following symptoms during her stay: cough, night sweats, fever, nausea, loose BO, dyspnoea, chest pain, nausea, general malaise and headache. Her vital signs showed low grade pyrexia with a maximum temperature of 38°C. The lowest peripheral oxygen saturation was 92% (on room air). She remained haemodymically stable throughout her stay. Blood investigation showed mild leucopenia at $3.5x10^9$cells/L, lymphopenia at $0.9x10^9$ cells/L, and maximum CRP was 27 mg/L. X-ray demonstrated no evidence of pneumonia. The NTS remained positive until last sampled on the 11/3/2020 (i.e. at least 15 days' duration). She suffered ongoing dyspnoea on minimal exertion. Investigations including D-Dimer, Cardiac Troponin, ECG and CXR demonstrated no acute abnormality.

This lady had a mild clinical episode of Covid-19. Young et al reports prolonged viral shedding in nasopharyngeal samples up to 24 days[4]. As this pandemic unfolds, admission will be reserved for confirmed and suspected cases with symptoms and signs of severe disease.

Written informed consent was obtained from the patient for publication of this case report.

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MYELOLIPOMA IN THE KIDNEY TRANSPLANT: A UNIQUE ENTITY TO BE ACKNOWLEDGED

Editor,

Kidney transplantation is the best treatment option for end stage renal disease and the impact of cancer affecting the transplanted graft is higher when compared to the general population. It significantly affects the patient quality of life, meaning return to dialysis, along with worse life expectancy[1]. It is therefore envisaged to be able to discern between benign lesion treatable conservatively or with surveillance and those requiring graft nephrectomy[2]. In particular, misdiagnosis of rare entities such as myelolipoma, could represent a challenge requiring dedicate expertise.

Myelolipoma is often incidentally discovered, with no laboratory alterations. Less than 10 cases have been reported in the native kidney as well as in the surrounding tissue[3]. There is no association with gender and tends to be more common in the seventh decade of life, with the first case described in 1905 by Gierke in the adrenal[4], its preferential site. On imaging, it tends to show as a solid mass with fat density attenuation and no contrast-enhancement.

At our Institution, we have treated the only myelolipoma involving a transplanted kidney. This was in a 48 years old male with persistent high C-reactive protein levels,

despite no infection source identifiable. His past medical history included Bardet–Biedl syndrome, blindness and kidney failure secondary to reflux nephropathy, for which he underwent deceased donor kidney transplantation 20 years before that worked for 18 years. The failed transplant was left in situ for the remaining two years, on immunosuppression consisting of cyclosporine and prednisolone. At this time, he experienced repeated hospital admission with raised inflammatory markers and fever. On imaging concerns were raised about liposarcoma around his left sided renal transplant (Figure 1). Decision was made to proceed with graft nephrectomy and excision of the retroperitoneal mass

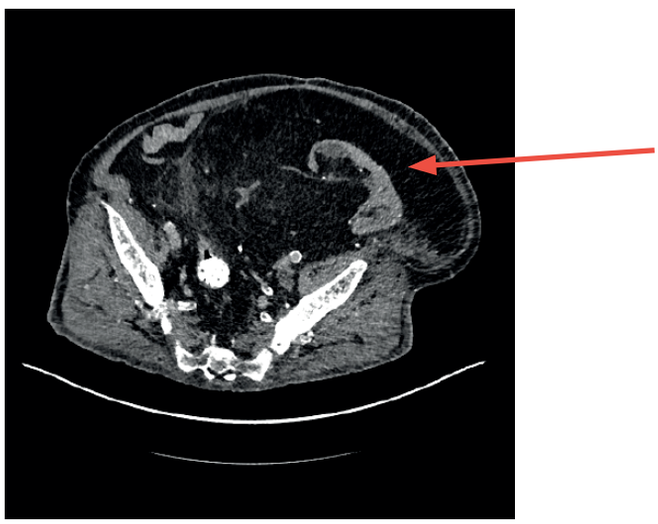

Figure 1 - Suspected malignant lesion surrounding the left sided kidney transplant (arrow)

(Figure 2). The operation required also ileofemoral arterial bypass and ileofemoral venous bypass in order to achieve radical oncology. Post-operative course was characterised by deep vein thrombosis, for which he was therapeutically treated with enoxaparin. The patient was discharged on 12 days after surgery, with current follow up of 1 month.

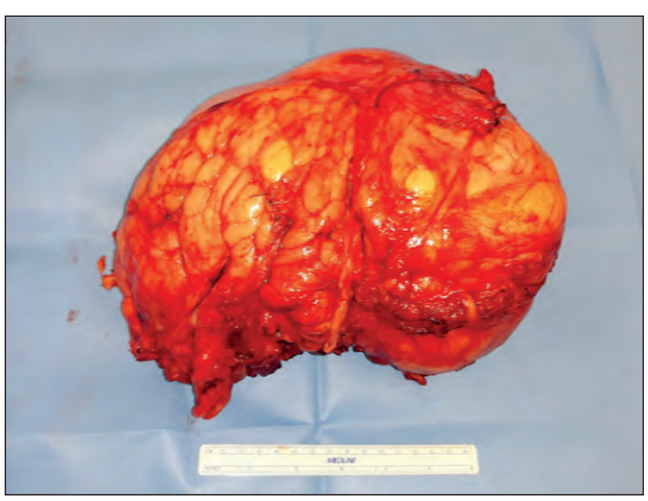

Figure 2 - Specimen.

In view of this unicity, the majority of clinicians would be unfamiliar with the features and management of myelolipoma in the kidney graft, and indeed even our first diagnosis was of a malignant lesion leading us to pursue a more aggressive treatment, with major vascular reconstruction. The patient was already on dialysis, but more debate regarding the most effective treatment would rise for working grafts. Retrospectively, more awareness of this rare disease, with attention to its radiological features and consideration of risk factors such as endocrine (Bardet–Biedl syndrome) and hematopoietic disorders (long effects of immunosuppression) might have been considered and possibly modified the intended radical oncology.

In conclusion, treatment options of rare benign diseases such as myelolipoma have to be tailored to patient needs, with a conservative management preferable for small, asymptomatic lesions or working grafts and partial/radical nephrectomy in enlarging masses. Embolization is rarely effective, as often the only vascularity present is small and peripheral.

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THE MICROBIOLOGY OF THE *CAMÁN*

Editor,

Camogie is a popular sport amongst women and involves an estimated 100,000 players, administrators, referees and coaches through 573 clubs across Ireland, as well as clubs in Europe, Australia and North America (www.camogie.ie). Fifteen-a-side camogie is a stickhandling, high velocity, multidirectional field sport,[1] played with a hurl or *camán*, which is usually crafted from ash (*Fraxinus excelsior*) plants. The hurl is not allowed to be greater than 13cm in width at its base, thus combined with the high velocity nature of the game, sports injuries in camogie have been reported, which have mainly consisted of hand, facial and laceration injuries.[2] Given the history and potential for lacerations and open wounds from hurl-related injuries, we wished to examine the microbiological flora of these, with particular attention to the types of bacteria that may be potentially introduced from the hurl into an open wound, from a laceration-related injury.

Hurls (n=24) were sampled anonymously from active amateur camogie players in the Ulster provincial game during active training sessions. A 2cm x 2cm area of each hurl was swabbed using a sterile pre-moistened transport swab (Sterilin, UK) and was examined microbiologically by inoculating the swab onto Standard Plate Count agar (Oxoid CM0463, Basingstoke, UK), followed by incubation at 37°C for 48h, as previously described.[3] Resulting colonies, which were phenotypical different, were purified and identified using matrix-assisted laser desorption/ionization – time-of-flight (MALDI-TOF) mass spectrometry technology. The taxonomy of bacteria identified is shown in Table 1.

Seven bacterial species were identified from the surface of the hurls, including four Gram-positive bacteria and three Gram-negative bacteria, from six taxonomic genera. The natural niche of these bacteria is the environment, including soil, so it is most likley that the wooden hurls became contaminated when they were in contact with the soil on the grass pitch. Whilst some of the bacterial species isolated have previously shown some degree of pathogenecity in infection and therefore may be considered as opportunistic pathogens, they are not normally considered to be an infection risk to immunocompetent hosts, such as healthy camogie players.

Laceration injuries in camogie which are inflicted from a hurl should seek medical advice and appropriate wound management. GPs and Accident & Emergency clinicians should be aware of the spectrum of endogenous organisms from the player's skin, as well as those detailed above originating from the hurl, in any related wound complication from such injuries. Additionally, whilst our study did not isolate any *Clostridium tetani* organisms, given the origin of the organisms we identified as being from soil, camogie players should ensure that they are have a complete and up-to-date tetanus vaccination record and should seek re-vaccination in accordance with the Green Book,[4] where there is an incomplete vaccination history or where defecits exist.

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Conflicts of interest None

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DEATH FROM DIABETES IN IRELAND/HISTORY

Editor,

In your journal in 1987 Crawford reported on the history of deaths from diabetes in Ireland.[1] His report showed that in the second half of the nineteenth century death rates associated with diabetes rose exponentially and he hypothesized that this was due to increases in the intake of carbohydrate and fat. For the last thirty years I have always opened my lectures on type 2 diabetes with this report. However, due to recent information from epidemiological studies of the consequences of famines, I believe that the original interpretation of this study is incorrect.

China's Great Famine (1959-1961) showed that adults born between 1960 and 1961 had a 23% increased risk of developing diabetes and if born in a particularly affected area

there was a 40% increase. This suggests that fetal exposure during the famine increased the risk of diabetes in adulthood.[2]

In the Ukraine Famine, individuals born between 1930 and 1939 had in 2001 an increased risk of developing diabetes. The prevalence of diabetes increased by 47% in those born in regions with severe famine compared with those born in areas where a famine did not occur.[3]

The Dutch Winter Famine occurred during the final six months of the second World War. 702 subjects born in Amsterdam between November 1, 1943 and February 20, 1947 were shown at age 50 to be more likely to have glucose intolerance and insulin resistance.[4]

The Irish Potato Famine began in 1845 and ended in 1852. From Crawford's paper it can be seen that the greatest increase in death from diabetes occurred between 1880 and 1911 when those born during the famine would be between 30 and 60 years old.

The reason that starvation in utero is associated with a higher risk of type 2 diabetes in later life is that the fetus prepares for its likely adult environment which is not encountered (thrifty phenotype). These epigenetic changes are due to increased gene activity and expression rather than by starvation induced changes in the DNA sequence.[5]

Therefore, after 33 years, I believe it is time to reinterpret Crawford's data and conclude that the large increases in death from diabetes during nineteenth century in Ireland was due to the in utero effects of starvation during the Irish Potato Famine and not due to increases in the intake of fat and sugar.

The author has no conflicts of interest.

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SEPTIC CAVERNOUS SINUS THROMBOSIS; A RARE CAUSE OF UNILATERAL EXOPHTHALMOS

Editor

We wish to present an interesting case of Septic Cavernous sinus thrombosis (CST), which is fatal yet infrequent condition associated with high mortality and debilitating morbidity.[1] A 28-year-old man presented with cold like symptoms for 7 days which progressed into worsening headache, fever and nausea. His past medical history was unremarkable with no recent travel history. His examination revealed temperature of 38.1 ^{0}C and facial puffiness with no other systemic findings. His investigations only showed raised C-reactive protein 288 mg/L and white cell count 15.0 x 10^{9}/L. In light of headache and visual symptoms he had Computerized tomography scan (CT) Head done without contrast which only revealed sphenoid & posterior ethmoid sinusitis. He remained febrile for four days despite being on broad spectrum antibiotics, and on day 5 he developed double vision, Cranial nerve VI palsy and unilateral exophthalmos, confirmed by formal ophthalmological/orthoptic assessment with no papilledema or any retinal disease. Repeat CT imaging of head/orbits failed to identify any cause of unilateral exophthalmos. Both initial blood cultures from the admission of day grew Proteus mirabilis sensitive to pipercillin/tazobactam while subsequent multiple blood cultures did not grew any organisms. A CT Head venogram was performed which confirmed a filling defect consistent with CST and inflammatory changes in sphenoid & ethmoid sinuses (figure 1 and 2). Other investigations such as chest X-ray, viral serology, abdominal ultrasound, echocardiogram, lumbar puncture, urine and stool cultures were all negative for any alternate source of infection.

He was initially treated with ceftriaxone/amoxicillin for

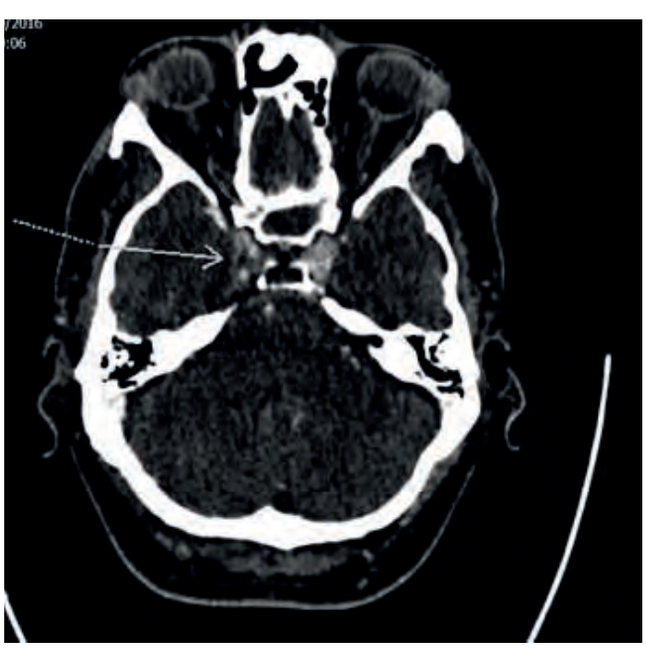

Figure 1 CT Venogram with arrow showing the cavernous sinus thrombosis on the right

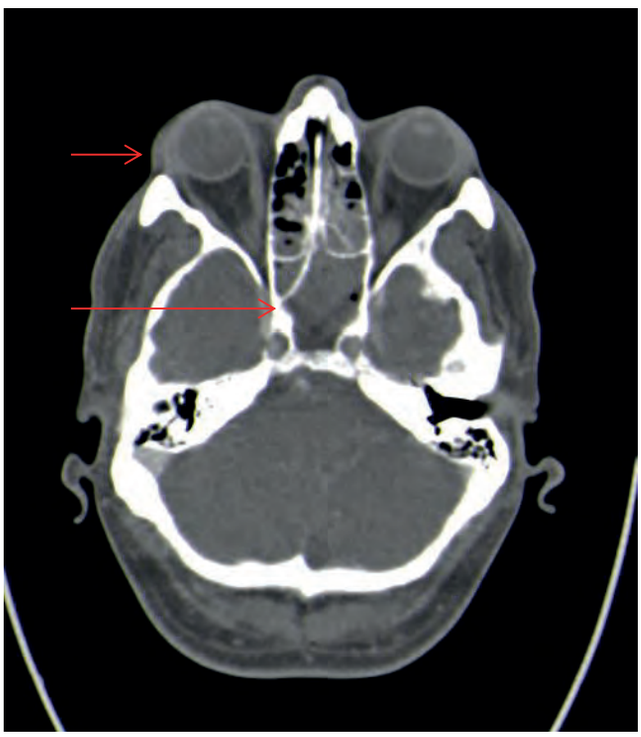

Figure 2 CT Venogram showing exophthalmos on the right (short arrow) and sphenoid sinusitis (long arrow)

3 days for possible meningitis which was later switched to piperacillin/tazobactam as per sensitivity on the blood cultures. After no response clinically and confirmation of septic CST, he was started on therapeutic dose of low molecular weight heparin alongside intravenous Meropenem and Metronidazole (combination therapy) on day 6, to effectively cover a wide number of potential organisms including Proteus mirabilis. He underwent urgent functional endoscopic sinus surgery (FESS) and stopped spiking temperature 24 hours later. Nasal swab culture during FESS grew mixed faecal flora of indeterminate significance. He was discharged home on day 16 to complete antibiotics and anticoagulation for another 4 weeks. On review after 8 weeks he had complete resolution of his symptoms with normal MRI venogram.

CST of septic origin is associated with significantly high mortality (23%) despite advances in medical care.[2] Retrospective studies on anticoagulation in septic CST have shown some benefit in reducing mortality and morbidity such as blindness, opthalmoplegia, seizures and stroke; hence experts suggest anticoagulation for a minimum of 4 weeks.[3]

The authors' main purpose of this letter is to raise awareness around diagnosis of this condition as septic CST can only be identified with high index of suspicion, requires early imaging with correct modality (either CT or MRI Venogram) and prompt initiation of antibiotics as well as surgical intervention and potential anticoagulation, all of which are paramount to preventing long-term complications and mortality.

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