ISSN 0041-6193

THE ULSTER MEDICAL JOURNAL

Volume 85 (3) September 2016

The Ulster Medical Journal

The journal of the Ulster Medical Society. First published in 1932.

Successor to the Transactions of the Ulster Medical Society (1862-1929), and the
Transactions of the Belfast Clinical and Pathological Society (1854-1860)

Honorary Editor:
John Purvis *(Londonderry, UK)*
editor@ums.ac.uk

Honorary Assistant Editors:
Roy AJ Spence *(Belfast, UK),*

Section Editors:

Curiositas
Dr Gerry Gormley

Gamechangers
Dr Nicholas Cromie

Continuing Medical Education
Dr Gerry Hanna

Editorial Board:

Timothy Beringer *(Belfast, UK)*
Ian Bickle *(Brunei)*
Barry Clements *(Belfast, UK)*
Dr Janitha Costa *(Belfast, UK)*
Nicholas Cromie *(Belfast, UK)*
Peter Crookes *(California, USA)*
David J Eedy *(Craigavon, UK)*
Gerry Gormley *(Belfast, UK)*
Paul Hamilton *(Belfast, UK)*
Gerry Hanna *(Belfast, UK)*
John Hedley-Whyte *(Boston, USA)*
Joe Houghton *(Belfast, UK)*
Claire T Lundy *(Belfast, UK)*
Andrew McIvor *(Hamilton, Ontario)*
Gail McLachlan *(Junior Medical Representative)*
A Peter Maxwell *(Belfast, UK)*
David Mills *(Belfast, UK)*
John E Moore *(Belfast, UK)*
Anthony O'Neill *(Belfast, UK)*
Peter Stanton *(Hobart, Tasmania)*

Honorary Treasurer: Fiona J Stewart **Sub Editor:** Mary Crickard

Editorial Assistant: Kathy Clarke **Book Reviews Editor:** Roy AJ Spence

Statement: The Ulster Medical Journal is an international general medical journal with contributions on all areas of medical and surgical specialties relevant to a general medical readership. It retains a focus on material relevant to the health of the Northern Ireland population.

Disclaimer: The Ulster Medical Journal is owned and published by The Ulster Medical Society, itself founded in 1862 by the amalgamation of the Belfast Medical Society (founded 1806) and the Belfast Clinical and Pathological Society (founded 1853). The owner grants editorial freedom to the Editor of the Ulster Medical Journal. The Ulster Medical Journal follows guidelines on editorial independence produced by the World Association of Medical Editors, and the code of good practice of the Committee On Publication Ethics.

Copyright: © 2012 Ulster Medical Society. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise without the prior permission of the Ulster Medical Society.

The journal is published in January, May and September, by the Ulster Medical Society, and typeset and printed in the UK by Dorman and Sons Ltd, Belfast. See inside back pages for institutional and personal subscriptions.

Contact Details: All enquiries on submissions, subscriptions, permissions and advertising to the Editorial Office, The Ulster Medical Journal, Whitla Medical Building, 97 Lisburn Road, Belfast BT9 7BL. United Kingdom.
T/ F: +44 (0) 28 9097 5780 **E:** umj@qub.ac.uk **W:** http://www.ums.ac.uk/journal.html

C O P E COMMITTEE ON PUBLICATION ETHICS

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics.

Ulster Med J 2016;**85(3):**151-152

Editorial

Clinical Reasoning: The Analysis of Medical Decision Making.

Summer, 1982, The Ulster Hospital Dundonald. On a distant radio, Tears for Fears are seeking Pale Shelter. My group of 6 second year medical students are on a pick-up round with Dr Ken Nelson, Consultant Endocrinologist.

The next patient is a 68-year-old lady who has been admitted with increasing fatigue and weight gain. We ask a few questions – she is slow to reply and her voice is gravelly. Dr Nelson shows us the blood results -only basic results – this is 1982 and sophisticated tests will take some time to come back from the lab. He asks for a diagnosis. Various suggestions are made by the group: anaemia (she looks pale), diabetes (weight has increased), smoking (hoarseness) and Cushing's disease (impaired mental processes).

Dr Nelson is starting to look impatient – "it's fairly obvious" he says. Someone tentatively suggests hypothyroidism – "Yes, of course!" is the response.

Exposure to hundreds of similar cases in the past meant that Dr Nelson was able to use a fast, pattern recognising, intuitive way of thinking that can reach conclusions with just a few data points – *Type 1 thinking*, whereas we medical students plodded step-wise through a slow, logical but high effort approach – *Type 2 thinking*. [1]

Psychologists believe there is a very strong human trait to make consistent stories out of everything around us– a *narrative engine*. We like our world to make sense. If some of the information isn't there, we start to fill in the gaps. The only problem is, if our store of background knowledge and experience is lacking, then our story may not reflect reality. It also takes more mental effort to work things out from first principles and many of us are somewhat cognitively lazy. [1,2]

Pat Croskerry, an expert in Clinical Reasoning, talks about skilled clinicians having a bank of *illness scripts* where the clinical presentation is mentally compared with the script and if the pattern fits, a spot diagnosis (*Type 1 thinking*) can be made. If the pattern is not recognised or the patient doesn't respond to treatment, then it's back to plodding through differential diagnoses or finding a different script for comparison. [3]

Difficulties can arise if our spot diagnosis is wrong and we don't notice or respond to clues that something isn't right – we may develop an *anchor bias* – an unwillingness to consider other possibilities.

The narrative engine can suffer from other cognitive biases [4] including:

Confirmation Bias

Agreeing with evidence that supports our diagnosis (script) and ignoring data that refutes it.

Premature Closure

Facts are not checked and new data is not considered.

Search satisficing (a combination of satisfy and suffice)

Having found one diagnosis, we fail to look for a second – e.g., a small deep stab wound in the back as well as an obvious gunshot wound in the front.

Posterior Probability Bias

The diagnosis on the last 3 admissions may not be the right diagnosis this time.

Outcome Bias

A desire for a favourable outcome, e.g., blaming sepsis on pneumonia rather than an IV line infection.

We can also be strongly influenced by what Croskerry calls the *cognitive miser function*. [5] It sometimes takes a lot of cerebral effort to stop "*diagnostic momentum*" at an early stage:

2000 hrs: Patient states epigastric pain is similar to that during MI 20 years ago – admit cardiology as possible acute coronary syndrome.

2010 hrs: Commence loading doses of Aspirin 300mg plus Ticagrelor 180mg for ACS.

0130 hrs: Brisk haematemesis! Urgent call to hospital GI bleeding team.

0150 hrs: OGD shows duodenal ulcer.

Did the patient mean it was the same character of pain or the same intensity of pain? Would a more systematic consideration of causes of epigastric pain (*Type 2* thinking) led to a safer outcome?

At this stage, no-one knows if critical analysis of medical decision making will lead to a long term improvement in patient safety. Some units are starting to incorporate such analysis into morbidity and mortality meeting data. The concept is certainly interesting and I think we will hear more about "Clinical Reasoning" in the future.

John Purvis, Hon. Editor

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

REFERENCES/BIBLIOGRAPHY

1. Kahneman D. *Thinking, Fast and Slow*. Penguin, 2012.
2. Hughes M, Nimmo G. Models of clinical reasoning. In: Cooper N, Frain J (eds), *ABC of Clinical Reasoning*. Wiley-Blackwell, Oxford, 2016.
3. Croskerry P. A universal model of diagnostic reasoning. *Acad Med* 2009; **84**: 1-7.
4. Croskerry P. Bias. A normal operating characteristic of the diagnosing brain. *Diagnosis* 2014: **1**: 23-7
5. Croskerry P. Clinical decision making. In: Barach P, JacobsL, Lipshultz SE, Laussen P (eds), *Paediatric and Congenital Cardiac Care: Vol 2: Quality Improvement and Patient Safety*. Springer-Verlag, London, 2015; pp. 397-409.

Ulster Medical Society Programme 2016 - 2017

President: Prof Patrick J Morrison CBE MD DSc. **Theme:** Medical Myths and legends

AUTUMN SEMESTER				
Date	**Meeting**	**Speaker**	**Title**	**Location**
Thursday 6th October 2016	**Presidential Address**	**Prof Patrick Morrison** CBE MD DSc FRCP FRCPI FFPHMI FRCPCH Consultant in Genetic Medicine	**Medical myths and legends***	8.00pm North Lecture Theatre MBC G07NT
Thursday 20th October 2016	**Joint meeting with NIMDTA & QUB. Research for Trainees - Opportunities, Presentations & Prizes**	**Prof Stephen Gordon** MD FRCP FRCP(Edin) Director Malawi-Liverpool-Wellcome Trust Clinical Research Programme	**Research is Global**	9.00am - 4.00pm Postgraduate Lecture Theatre BCH (Buffet from 12.00)
Thursday 10th November 2016	**Joint Meeting with the Ulster Society for the History of Medicine The Gary Love Lecture**	**Dr Brian Barton** MA PhD Historian and Author	**Medical aspects of the Belfast Blitz***	8.00pm Whitla Medical Building SR5 & SR6
Thursday 24th November 2016	**Joint Meeting with Belfast City Hospital Medical Staff. The 2016 BCH Lecture**	**Dr Fred MacSorley** MBE MB BCh FRCGP DipIMC(RCSEd) General Practitioner	**Medicine between, in and frequently over the hedges. 30 years of pre-hospital care in N. Ireland**	5.30pm Postgraduate Lecture Theatre BCH (Buffet from 5.00pm)
Thursday 1st December 2016	**Sir Thomas & Lady Edith Dixon Lecture**	**Prof Alexander McCall-Smith** CBE LLB PhD DLitt FRSE FRCP (Edin) FSL Author; Emeritus Professor of Medical Law, University of Edinburgh	**The Real Things that Happen to Fictional Characters***	8.00pm North Lecture Theatre MBC G07NT
Wednesday 7th December 2016+	**Desmond Whyte Lecture**	**Dr Fiona Stewart** MBE FRCP FRCPCH Consultant in Genetic Medicine	**Sweeping up the leaves – new approaches to old diseases**	6.00pm Centre for Medical and Dental Education and Training, Altnagelvin Hospital. (Buffet from 5.30pm)

SPRING SEMESTER				
Date	**Meeting**	**Speaker**	**Title**	**Location**
Thursday 12th January 2017	**Joint Meeting with the Ulster Obstetrical and Gynaecological Society**	**Dr Catherine Calderwood** MA FRCOG FRCP(Edin) Chief Medical Officer, Scotland	**Realistic Medicine**	8.00pm Whitla Medical Building SR5 & SR6
Tuesday 17th January 2017+	**Joint Meeting with the Ulster Medico-Legal Society**	**Dr Christopher Bass** MA MD FRCPsych Consultant Liaison Psychiatrist Oxford	**Somatoform and factitious disorders involving the limbs***	6.30pm Larmour Lecture Theatre QUB. Dinner Great Hall QUB 7.30pm
Thursday 16th February 2017	**Ulster Medical Society**	**Prof Dan Bradley** BA PhD FTCD MRIA Professor of Population Genetics, Trinity College Dublin	**Ancient Irish Genomics & Human origins on the Island***	8.00pm Whitla Medical Building SR5 & SR6
Thursday 23rd February 2017	**The Robert Campbell Oration**	**Dr Deirdre Donnelly** MD MRCPCH Consultant in Genetic Medicine	**From St Valentine to Easter Island – Neurocutaneous disorders through time**	8.00pm Whitla Medical Building SR5 & SR6
Thursday 9th March 2017	**Joint Meeting with Belfast City Hospital Medical Staff. The 2017 BCH Lecture**	**Prof Sir John Burn** MD FRCP FRCPE FRCPCH FRCOG FMedSci Professor of Clinical Genetics, Newcastle University, Chair QuantuMDx Ltd	**The rise and fall of Genomic Medicine**	5.30pm Postgraduate Lecture Theatre BCH (Buffet 5.00pm)
Friday 24th March 2017	**Annual Presidential Dinner**	**Dr Éamon Phoenix** BA MA PhD PGCE	**Voices 16: Northern Narratives of the 1916 Rising and the Somme**	7.15 for 8pm Canada Room, Great Hall QUB
Thursday 11th May 2017	**Annual General Meeting**			5.00pm Ulster Medical Society Council Room, Whitla Medical Building

*Suitable for a non-medical audience +Note different day of the week

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Ulster Med J 2016;**85(3):**153-157

Medicine Outside the Comfort Zone

Helping create "Wellness Warriors": Primary Care for remote Alaska Native Communities

Sarah Dobbs

Accepted: 22nd June 2016
Provenance: Internally peer-reviewed

It was not clear if the young patient had been taking his diabetes medication, but as his blood sugar deteriorated and he became confused, we were not sure what was going on. With flights dependent on good weather and only scheduled back to the mainland three times a week, the "ordinary" suddenly escalated to high priority; should we or shouldn't we request a full medivac ?

There are two words that I never appreciated before coming to Alaska — ''remote" and "wilderness." The main population centre, Anchorage, is rather deceptive. It appears to be just another American city, with its Walmarts, McDonalds, strip malls and grid of straight roads. Yet, it is a little island of the familiar, surrounded by an unimaginably vast wilderness where, as Alaskans like to remind you, man is not the top predator.

Fig 1. Small plane travel forms the "life-line" for many outlying communities

The 49th U.S. state is famous for its bears, and is often referred to as the "Last Frontier." Its huge area (about seven times the size of the UK) is sparsely populated with only around 700,000 people, just under half of whom live in Anchorage. There are no connecting roads to the western part of the state, and only one leading north, so access to the interior majority of the state is typically by small bush plane.

Around 150,000 Alaska Native people belonging to separate ethnic groups with different languages and traditions have lived across the region for millennia. Many still follow subsistence lifestyles fine-tuned to their particular environments. There are many diverse cultures: Inupiat, St. Lawrence Island Yupik, Yup'ik/Cup'ik, Aleut/Alutiiq, Athabascan, Tlingit, Haida and Tsimshian. With English being a second language for some Alaska Native Elders, it is sometimes difficult to believe that this is indeed part of the USA.

Alaska has only been "westernised" for the last hundred years or so, and some of the population live in "villages" widely dispersed across the state. Life can be tough. More and more villages are gaining access to running water and sewerage systems, but often there is little food in the stores and what is available can be very expensive.

Within Anchorage, the ethnic mix is one of the greatest in the whole of the USA. Many people relocated to Alaska to work in the oil industry, which was also lucrative to the state and generated large financial reserves. Up until recently, the state has been replete with money and was a popular relocation destination with no state income tax or sales tax. However, the recent decline in global oil prices has had a negative impact.

I came to Anchorage with my geologist husband. I had previously worked in Houston, Texas, where I had completed all the requirements to work in the USA. After working as a General Practitioner partner and trainer in Surrey for about 10 years, this was a last chance to do something different. General practice had become routine. I knew and respected the local consultants. Emergency medicine was almost irrelevant with the local hospital just three minutes from the surgery. Additionally, I was becoming frustrated by endless paperwork and targets, but I knew that I was not ready to

General Practitioner Southcentral Foundation, Anchorage, Alaska, USA
E-mail: sarahdobbs@mac.com
Correspondence to Sarah Dobbs

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

retire. Alaska seemed to be the perfect location where we could both work, but I was not sure I wanted to work in the private sector.

Anchorage is filled with modern medical facilities, most of which are privately owned and staffed by independent groups of doctors all working in their own office complexes. Care is expensive for patients even with health insurance. "Obama Care" has certainly not decreased premiums and last year, even with the best medical insurance, my family spent about $15,000 on health care.

Despite the emphasis on "for profit" health care, there are facilities which are partially supported by the federal government: The Veterans Administration, and the Alaska Native Medical Center, which includes a 150-bed hospital, a full range of medical specialties, and the primary care centre where I work, which is run by Southcentral Foundation (SCF), a tribal organisation.

Fig 2. Southcentral Foundation, Anchorage clinic

At SCF, we are grouped into clinics, and within the clinic are further divided into 4 person units. The unit I work with includes a "scheduler" who makes appointments, a medical assistant who brings patients into the consultation room, measures vital signs and does routine screening questionnaires and most wonderful of all, the "Nurse Case Manager" who is central to care co-ordination, chronic disease management, triage of patients and giving patients information about their laboratory results and medical conditions.

Also a behaviour health counsellor, dietician and pharmacist are within the clinic and are available to participate in clinical care. Complementary medicine and physiotherapy are in the next building. The hospital is on the same campus and shares the same electronic medical record so we always know what is happening with patients.

SCF has achieved international recognition for its "*Nuka*" health care system. (*Nuka* is a native concept meaning strong, giant living things). SCF's Nuka System of Care puts the *"client-provider relationship at the forefront. Instead of being objects with which medical services are provided, beneficiaries have become the essential partner; metaphorically, the managing director of a series of processes focused on attaining wellness rather than just treating illness. Patients have transformed into customer-owners"* [1] .

Fig 3. Comprehensive treatment includes traditional native practices

Throughout the year, people visit from around the world to view this award-winning health care system. The Kings Fund recently published a study on the system [2]. Through federal funding and occupational health insurance, SCF manages to provide accessible health care for the Alaska Native Community.

TRADITIONAL HEALING

Traditional healing practices are also included alongside day-to-day westernised medicine. They are provided in an outpatient setting in conjunction with the other services offered at SCF.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Tribal doctors assist people of all ages with practices such as: healing hands, culturally-sensitive supportive counseling, cleansing, Healing Touch, talking circles, prayer, songs, dances and consultations with Elders. In addition, there is an Alaska Native Traditional Healing Garden. These plants are native to Alaska, and are cherished for their nutritional and medicinal value.

Alaska Native people have gone through tremendous cultural changes in recent times and in common with other indigenous cultures, suffer from high rates of alcohol and drug abuse as well as domestic violence. Before SCF partnered with the Native Community to transform health care, the Alaska Native population had a health care system with long waiting lists, low satisfaction for both employees and patients, high staff turnover, and poor health outcomes. Direct involvement of the community has certainly improved things.

One of SCF's approaches to address the problems of domestic violence, abuse, and neglect is a program called the ***Family Wellness Warriors Initiative*** (FWWI). *"Its purpose is to equip organizations families and individuals to effectively address the spiritual, emotional, mental, and physical effects of domestic violence, abuse, and neglect. It is our desire to encourage wellness in each of these areas in the individual, the family, the community, and the world in which we live"* [3].

Benefits of participating in FWWI include*: "eliminating the shame and guilt of people harmed by domestic violence, child sexual abuse and child neglect; re-establishing the roles of parents as protectors of families; making one's own story coherent; and using spiritual beliefs to re-establish moral and ethical direction. Participants who attend trainings demonstrate a greater sense of family satisfaction, less stress and conflict within the family"* [3,4].

MY ROLE

In addition to working in the main facility in Anchorage, I help provide services to two island villages in the Bering Sea. These windswept, volcanic islands are about 750 miles away from Anchorage and the nearest hospital and 350 miles from the mainland. I act as a consultant to the permanent staff on a daily basis and make a field visit to each of the islands twice a year.

Nothing excites me more than catching a plane to work. However, I am always filled with nervous anticipation as I wait at the gate for the PenAir flight to the Pribilof Islands of St. Paul and St. George. Although St. George has a resident population of only about 70, and St. Paul around 400, the waiting room is usually filled with an incredible mix of people: fishermen wearing wellington boots, hunters in camouflage gear, locals returning home and the occasional "birder" tourist usually with binoculars around their neck. Most will be going to the bigger island of St. Paul.

It is never certain whether the plane is actually going to fly. Once I waited all day at the airport on a weather hold, only to be told after seven hours that the flight had been cancelled. My food box had to be unloaded and the frozen food unpacked, in the hope that you may have better luck on the next flight. If you do make it out, there is always a sigh of relief when the captain announces that all the luggage has made the flight as well.

The islands are somewhat similar to the Galapagos being located beside upwelling, nutrient-rich cold water currents. These support dense populations of sea birds and marine mammals. They used to be home to the world's largest northern fur seal population.

Fig 4. Male Northern Fur Seal and harem

Fur seals were hunted for their pelts until 1986 when the plants were closed down leaving some inhabitants without work. Leaving the islands would mean that they would be leaving their Aleut language, family and way of life behind. People have tried to adapt, but change is hard. There is no agriculture, the fishing is usually based out of Seattle and tourism is scarce due to the remoteness of the location.

Arriving at St. George's airport is an experience. Fog tends to circulate the high cliffs, and if it is too dense, the pilot may just turn around and head the four hours back to Anchorage. On occasion, the plane has not been able to land for about three weeks. When luck is on my side and I do arrive, I am always greeted by name, and may be the only person getting off the 20-seat plane. St. George's airport terminal is not much more than a portacabin. An unpaved road heads back to "town," a tiny community challenged by many things.

Fig 5. St. George Island community

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Satellite dishes bring American television into homes together with the hopes, expectations and aspirations of any other American town. Many people drive a four-wheeler despite fuel being expensive on the islands. The local "canteen" is in the city hall and has basic supplies. Shelves are often empty when the plane has not made it in. Fruit and vegetables are conspicuous by their absence. The Anchorage based dietician is always urging that these should be part of their diet, but availability and cost can be prohibitive.

When I arrive with a mixture of fresh fruit, vegetables and baked goods, the latter attracts the most attention. I am reminded that health delivery needs to be culturally appropriate and although these islands are American, their background is dependent on what the sea around can offer: seal meat, fish, gull eggs and sea urchins.

The health facilities are modern and well-staffed. The larger island (St. Paul) has two permanent nurse practitioners or physician assistants, while the smaller island St. George has one. The clinics are well stocked. Basic X-rays can be done; full blood count and finger blood glucose can always be measured and sometime electrolytes. Medications are sourced from the "Pick Point" which is rather like a vending machine. Medicines are ordered through the medical record. The order is relayed to Anchorage for pharmacist review and approval, and then sent back to the island when a label is automatically printed and the medication "dropped," a system called telepharmacy.

Fig 6. Pick Point medicine vending machine

Regular flights bring medicines to re-stock the Pick Point machine. Sometimes these do not arrive, either due to bad weather or insufficient space on the plane. However, stocks of emergency drugs are available, but opiates are kept to a minimum to prevent diversion.

I have been more challenged working on these islands than I have ever been in my life. Life threatening conditions are still a four-hour flight away from specialist care once the "medivac" air ambulance plane reaches the islands. In the meantime, the patient has to be stabilised. Each emergency evacuation costs about $80,000, and just to get a second opinion requires patients to be sent on a scheduled flight to Anchorage, which costs $1,000. While most of the islands inhabitants are Aleut people who are covered by treaty agreements through the Indian Health Service funding (eligible for care at SCF's Nuka System of Care), there are a few non-Native people who are covered through the Community Health Center grant or have to pay their own way.

Despite these issues, day-to-day clinics do not seem that different from working in the NHS. The electronic medical records are linked through to Anchorage and the main hospital. Recent improvements in internet connectivity have enabled video conferencing and tele-medicine link-ups with the team in Anchorage. When this works, it is truly impressive, but there can still be internet blackouts. It is very frustrating when the system goes down part way through detailed data entry into a remote system.

Fig 7. Telemedicine systems for transmission of patient data to Anchorage hospital

There has been a recent outbreak of tuberculosis. We have had to test everyone on the islands. The state has been involved with teams of staff going out to screen, rescreen and determine the type of TB. We had one young adult who was diagnosed while they were away from home. The patient was unable to fly back home and had to stay in his hotel room for a month with his meals and medications left on his doorstep until his sputum sample came back clear.

On another occasion, a patient had been seizing for nearly two

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

hours despite treatment with maximal doses of lorazepeam, diazepam and phenobarbitone. We were running out of medication. Our supplies had been diminished, as the mail had not made it in. I mentally play through the list of all the terrible things that could happen including brain death and stoke. Advice has been given over the phone. The air ambulance has been called, but it is still hours away. Are there any treatable causes? Has one forgotten anything? Textbooks are pretty useless: admit to intensive care, intubate, call the anaesthetist on call etc. Medical school and junior hospital jobs seem like a long way away and not very useful. Most relevant was a wilderness first aid course I did aimed at outdoor enthusiasts. You do what you can and look at the vitals - heart rate, respiration and mental status. This medicine is far more challenging than anything I have ever done in my life.

Then a young previously healthy patient, presented with the "worst headache of their life" which was waking them nightly. High blood pressure was newly diagnosed and uncontrolled at 205/110 despite repeated readings. They had unilateral blurred vision and photophobia. Advice is reassuring for the patient, but there is still the anxiety that this might be an intracranial tumour or malignant hypertension. When should I arrange for an urgent transfer? The weather is closing in. The wind has increased to 40 mph with a forecast of stronger to follow; the local high cliffs are no longer visible.

During my time in Alaska, I have had more moments of self-doubt than ever before. I find the tools I learned in my NHS appraisal feedback very useful. I think of my "Puns and Dens." I work through Significant Event analysis with the team. I read the small print of the textbooks. I think of all the obscure diagnoses.

It is difficult not to think about the ethics surrounding care for people living in such remote places with serious medical conditions. What can be done if someone is unlikely to survive a relatively trivial emergency? Should we live so far from modern medical care?

This is a country that provides some of the best health care in the world for the insured. Here, I am working with insured people, but care that is provided in more densely populated areas simply cannot be matched due to access, distance and the elements.

As I walk along the cliffs admiring the rare seabirds, the red-footed kittiwakes, I remember that these are the reasons people live far from cities and medical facilities. There is a richness and abundance of life that is immediate and vibrant in a way that cities can never offer. For most individuals, there is also family, heritage, and the deep sense of belonging to a place. Yes, it does come with trade-offs and one of those is the lack of immediate access to some dimensions of modern medicine…. But what IS offered on site and through telemedicine is actually pretty remarkable. It is a privilege to be allowed to walk with this community on their medical and health journey….and when I feel like I have reached the limits of what I can offer as a doctor nearly 1,000 miles away….and I wish for more….I work to remember that there are choices with consequences to living here – with both wonderful and, at times, challenging implications.

REFERENCES

1. Rasmuson Foundation. http://www.rasmuson.org/news/world-class-health-care-innovation-in-ak/ Accessed 13/07/2016
2. The Kings Fund. Intentional whole health system redesign. http://www.kingsfund.org.uk/publications/commissioned/intentional-whole-health-system-redesign-nuka-southcentral Accessed 13/07/2016
3. Family Wellness Warriors Initiative http://www.fwwi.org/ Accessed 13/07/2016
4. Gottlieb K and Tierney M. Healthcare at Its Best: Southcentral Foundation's Core Concepts Training. *The SoL Journal*; **13(2):** 35-43. https://www.southcentralfoundation.com/wp-content/uploads/2015/11/Reflections-SoL-Journal-13.2.pdf Accessed 13/07/2016

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Ulster Med J 2016;**85(3):**158-163

Review

Mortality Among Children And Young People Who Survive Cancer In Northern Ireland

Donnelly DW, Gavin AT.

Accepted: 2nd May 2016
Provenance: externally peer-reviewed.

Abstract Whilst survival rates for childhood cancers are excellent, it is known that these patients have an increased risk of death from disease recurrence and other causes. We investigate patterns, trends and survival of cancers in children and young adults in N. Ireland.

Materials and Methods 21 years (1993-2013) of cancer incidence data including non-malignant brain tumours from the N. Ireland Cancer Registry for persons aged 0-24 years was analysed using Joinpoint regresssion for trend and the Kaplan Meier method for survival analysis up to end 2013 with excess mortality calculated at one and five years after first cancer diagnosis using standardised mortality ratios.

Results 2633 children and young people were diagnosed with cancer, 1386 (52.6%) male and 1247 female with 1139 (43.3%) aged 0-14. While trends increased over time they did not reach statistical significance except in the 15-24 age group for males and females combined. The most common cancers for age 0-14 were brain, eye and central nervous system and leukaemia with skin (including non-melanoma skin) the most common in the 15-24 age group. 59 patients (2.2%) had a record of a second cancer. Survival was high at 90.7% after 1 year, better among females and similar for older and younger groups. Although mortality in children is low overall, there was an excess mortality 24.7% (22-27.5) p<0.001 at one year and 7.3% (5.5-9.2) p<0.001 for those who survived 5 years. Excluding the primary cancer there was an excess mortality for one year survivors, with deaths twice that of the background level (SMR= 2.2 (1.3-3.0)p=0.005 and although one and a half times background levels at 5 years, the excess mortality was not significant 1.5 (0.6-2.3 p=0.269).

Conclusion Whilst survival from childhood cancers is excellent, this work in common with larger studies, highlights the need for ongoing monitoring of cancer survivors. Preventable skin cancer was identified as a problem in young adults.

INTRODUCTION

Children who have had cancer now have an excellent chance of surviving their disease with 80% of patients alive 5 years from diagnosis[1]. However previous studies have shown these patients are at a higher risk of death from other causes in later life, primarily as a result of recurrence or continuation of their cancer, but also due to the side effects of treatment leading to second cancers and cardiac disease[2,3].

We investigate long term mortality among childhood cancer survivors, and also include young people (aged 15-24) diagnosed with cancer or benign / uncertain brain tumours in N. Ireland between 1993 and 2013.

METHODS

Data on all patients diagnosed with either a malignant cancer or a non-invasive brain tumour when aged 0-24 during 1993-2013 were extracted from the Northern Ireland Cancer Registry (NICR). Information on each patient's sex, age, date of diagnosis and cancer type was included with the latter classified into ten main groups based upon their ICD10 code[4].

Follow up of these patients in order to determine their status up to 31/12/2013 was conducted by electronically matching the extracted data on children and young people to the NICR to identify second malignancies, the medical card register from the HSC Business Services Organisation (BSO) to identify those who emigrated (5%) and deaths information from the General Register Office (GRO[5]).

Cause of death was classified into the same groups as the cancer diagnosis plus a further five categories relating to non-cancer causes of death (Circulatory, Respiratory, External, Congenital Malformation and other). For deaths prior to 2001 cause of death was coded using the ICD9 classification[6].

In a small number of cases where death was recorded and a cause of death could not be identified (30 patients) a manual exercise was conducted in an attempt to obtain this information through physical examination of BSO and GRO records (as opposed to electronic matching). However the cause of death for 14 patients could not be identified. These

N. Ireland Cancer Registry, Queen's University Belfast
E-mail: A.Gavin@qub.ac.uk
Correspondence to Dr Anna Gavin.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

patients were thus assigned a cause of death to be same as their first cancer (total Deaths 215).

TREND ANALYSIS

The trends in age-standardised cancer incidence rates were investigated over the twenty-one year period using the JoinPoint program[7,8] to provide a summary measure for the trend in the form of the annual percentage change (APC) in the age-standardised rate. If a significant change in direction is identified then the trend is broken up into different segments based upon the points where the trend changes and APCs are then presented for each segment.

SURVIVAL

Observed survival was calculated using the Kaplan-Meier method for patients diagnosed in 1993-2008 with estimates for survival up to 20 years. The proportion of patients who survive a specified amount of time after the point that they are diagnosed with cancer was calculated regardless of the cause of death. This calculation results in a lower estimate of survival than net or relative survival, both of which take account of general background mortality.

Excess mortality from all causes was calculated for children diagnosed during 1993-2012 who survived at least one-year from diagnosis of their first cancer and for those diagnosed during 1993-2008 who survived at least five-years from diagnosis of their first cancer.

Using standardized mortality ratios (SMRs- defined as the ratio of the observed number of deaths within the cancer survivor population to the expected number of deaths that would occur within the general population), the expected number of deaths was calculated by first determining the total number of person-years (the cumulative survival time in years) by sex, five-year age group and year of diagnosis and then multiplying this by the mortality rate in the general population for that sex, age and year combination.

Cancer mortality rates for cancer patients were separated into those who died from their first cancer including a recurrence) and those who died of a second different cancer, with the later forming the basis of a comparison with the general population.

RESULTS

Between 1993-2013 there were 2,633 persons (aged 0 to 24) diagnosed with cancer (including non-invasive brain tumours) in Northern Ireland, an average of 125 people per year. Of these 1,386 (52.6%) were male while 1,247 were

TABLE 1:

Children and young people (aged 0-24) diagnosed with cancer during 1993-2013 by sex, age and first cancer type diagnosed

Cancer type (ICD10)	Ages 0-24			Ages 0-14			Ages 15-24		
	Both sexes	Male	Female	Both sexes	Male	Female	Both sexes	Male	Female
All cancers	2,633	1,386	1,247	1,139	644	495	1,494	742	752
Bone C40-C41	105	67	38	44	26	18	61	41	20
Brain, eye & CNS *	611	326	285	364	197	167	247	129	118
Breast C50	11	0	11	0	0	0	11	0	11
Digestive organs C15-C26	63	31	32	27	14	13	36	17	19
Female genital C51-C58	107	-	107	6	-	6	101	-	101
Leukaemia C91-C95	454	262	192	334	196	138	120	66	54
Lip, oral cavity & pharynx C00-C14	36	20	16	10	4	6	26	16	10
Lymphoma C81-C86	350	199	151	107	77	30	243	122	121
Male genital C60-C63	186	186	-	9	9	-	177	177	-
Mesothelial & soft tissue C45-C49	99	63	36	55	33	22	44	30	14
Respiratory organs C30-C39	32	19	13	11	6	5	21	13	8
Skin C43-C44	319	100	219	26	8	18	293	92	201
Thyroid & other endocrine C73-C75	116	38	78	49	24	25	67	14	53
Urinary C64-C68	86	48	38	71	42	29	15	6	9
Other - all others in range C00-C97	58	27	31	26	8	18	32	19	13

*C69-C72, D32, D33.0-33.4, D35.2-35.4,D42,D43.0-43.4,D44.3-44.5

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Table 2:

Observed survival from cancer among children and young people (aged 0-24) by sex and age: Patients diagnosed 1993-2008, followed up to end of 2013

Sex	Survival time	Ages 0-24		Ages 0-14		Ages 15-24	
		Observed survival (95% CI)		Observed survival (95% CI)		Observed survival (95% CI)	
Male	3 months	96.4%	(95.1%, 97.4%)	96.3%	(94.1%, 97.6%)	96.6%	(94.7%, 97.8%)
	6 months	94.2%	(92.6%, 95.5%)	93.3%	(90.7%, 95.2%)	95.0%	(92.9%, 96.5%)
	1 year	89.3%	(87.3%, 91.1%)	88.7%	(85.6%, 91.3%)	89.8%	(87.0%, 92.1%)
	5 years	75.8%	(73.1%, 78.3%)	74.3%	(70.1%, 78.0%)	77.1%	(73.4%, 80.4%)
	10 years	72.8%	(69.9%, 75.4%)	71.8%	(67.4%, 75.6%)	73.6%	(69.6%, 77.1%)
	15 years	72.2%	(69.2%, 74.9%)	70.9%	(66.5%, 74.9%)	73.3%	(69.3%, 76.9%)
	20 years	70.6%	(67.2%, 73.6%)	70.3%	(65.6%, 74.4%)	70.8%	(65.8%, 75.1%)
Female	3 months	98.1%	(97.0%, 98.8%)	97.5%	(95.3%, 98.7%)	98.4%	(97.0%, 99.2%)
	6 months	96.2%	(94.8%, 97.3%)	95.1%	(92.3%, 96.9%)	97.0%	(95.2%, 98.1%)
	1 year	92.2%	(90.3%, 93.7%)	90.2%	(86.7%, 92.8%)	93.5%	(91.1%, 95.2%)
	5 years	83.2%	(80.6%, 85.4%)	80.9%	(76.5%, 84.6%)	84.6%	(81.4%, 87.4%)
	10 years	80.7%	(78.0%, 83.1%)	78.7%	(74.1%, 82.6%)	82.0%	(78.5%, 85.0%)
	15 years	79.5%	(76.6%, 82.1%)	77.8%	(73.1%, 81.8%)	80.6%	(76.9%, 83.8%)
	20 years	79.2%	(76.2%, 81.8%)	77.0%	(72.0%, 81.2%)	80.6%	(76.9%, 83.8%)
Both sexes	3 months	97.2%	(96.4%, 97.9%)	96.8%	(95.4%, 97.8%)	97.5%	(96.4%, 98.3%)
	6 months	95.2%	(94.1%, 96.0%)	94.1%	(92.3%, 95.5%)	96.0%	(94.7%, 97.0%)
	1 year	90.7%	(89.3%, 91.9%)	89.4%	(87.1%, 91.3%)	91.6%	(89.9%, 93.1%)
	5 years	79.3%	(77.4%, 81.0%)	77.2%	(74.2%, 79.8%)	80.9%	(78.5%, 83.1%)
	10 years	76.5%	(74.5%, 78.3%)	74.8%	(71.7%, 77.6%)	77.8%	(75.2%, 80.2%)
	15 years	75.6%	(73.6%, 77.5%)	73.9%	(70.7%, 76.8%)	76.9%	(74.2%, 79.4%)
	20 years	74.7%	(72.5%, 76.7%)	73.2%	(69.9%, 76.2%)	75.8%	(72.8%, 78.5%)

Note: Data for more than 5 years are estimates as full 20 year follow up is only available for earlier diagnosis years
CI: Confidence interval

female. Of these patients 1,139 (43.3%) were aged 0-14 with the remainder (1,494 patients) aged 15-24.

Among the children and young people diagnosed with cancer, 59 patients (2.2%) had two or more cancers recorded during 1993-2013, with 18 of these cancers occurring after the age of 24. In total, 2,676 tumours were diagnosed among children and young people during 1993-2013.

There were differences between the two age groups studied. Among children aged 0-14, brain (including eye and CNS) cancer, and leukaemia were the two most common cancers. They collectively made up almost two thirds of all cancers diagnosed representing 32% and 29% of cancers respectively. The distribution of cancer type was similar for boys and girls, with very few gender specific cancers diagnosed in this age group.

Among young people (aged 15-24) skin cancer was the most common cancer making up one fifth (19.6%) of cases. This was followed by brain, eye and other CNS tumours (16.5%) and lymphoma (16.3%). Leukaemia was less frequent in this age group than among children making up 8.0% of all cancers. The distribution of cancers by type differed between males and females. Among females skin cancer was the most common (26.7%) while male genital cancer (specifically testicular cancer which made up 99% of this group) was the most common among males (23.9%). Brain, eye and CNS tumours and lymphoma were also common for both sexes; however 13.4% of female cases were gynaecological cancers, while skin cancer was the fourth most common male cancer (12.4% of cancers). (Table 1)

TRENDS

During 2009-2013 there were 134 children and young people diagnosed with cancer each year for the first time, a slight increase of 9% on the 123 per year diagnosed during 1994-1998. During this period, the number of cases increased by an average of 0.6% per year. The increase was slightly greater

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

among males than females (10% vs. 7%) with an increase from 64 to 71 male patients per year and an increase from 59 to 64 female patients per year; however the changes by sex were not statistically significant.

Among children aged 0-14 there was little change in the average number of patients diagnosed each year with 58 patients diagnosed each year from 1994-1998 (33 male, 25 female) and 60 patients from 2009-2013 (34 male, 26 female). While there was little change overall, the number of cases declined between 1994 and 2004, and increased annually by 2.9% per year between 2004 and 2013.

Among young people (aged 15-24) there were 75 patients diagnosed with cancer each year for the first time during 2009-2013, an increase of 15% on the 65 per year diagnosed during 1994-1998. The increase was slightly greater among males than females (23% vs. 8%) with an increase from 30 to 37 male patients per year and an increase from 35 to 38 female patients per year. While the annual percentage change in the number of cases was not significant for each sex, for both sexes combined the number of cases increased by 0.9% per year.

ONE YEAR SURVIVORS

There were 2,284 patients aged 0-24 at diagnosis who survived at least one year from a cancer diagnosis in 1993-2012. Of these 972 (42.6%) were aged 0-14 at diagnosis, while 1,312 were diagnosed aged 15-24. There were slightly more male than female survivors (1,190 vs. 1,094) among those diagnosed at age 0-24, however this difference was mostly a result of a greater number of male survivors diagnosed at age 0-14 than in older ages (545 vs. 427).

The most common primary cancers among these survivors were brain, eye and CNS tumours (22.5%), followed by leukaemia (16.4%), lymphoma (13.9%) and skin cancer (13.2%). Among those diagnosed at age 0-14 brain, eye and CNS cancer (31.0%) and leukaemia (29.4%) made up two thirds of survivors. Among those diagnosed at age 15-24 however, skin cancer was the most common (21.4%) followed by lymphoma (16.5%), brain, eye and CNS tumours (16.2%) and male genital cancer (16.5%).

FIVE YEAR SURVIVORS

There were 1,527 patients aged 0-24 at diagnosis who survived at least five years from a cancer diagnosis in 1993-2008. Of these 647 (42.4%) were aged 0-14 at diagnosis, while 880 were diagnosed as young adults aged 15-24.The most common cancers among these survivors were similar to those who survived one year from diagnosis

SURVIVAL

Survival from cancer among children and young people was generally good with 90.7% of patients diagnosed in 1993-2008 alive one year from diagnosis, while after five years, 79.3% of patients were still alive (Table 2). Ten-year survival is estimated to be 76.5% and twenty-year survival to be 74.7%.

Survival among females was higher than among males. Five years survival among females was 83.2% compared to 75.8% among males – the difference in one year survival was similar. By twenty years from diagnosis the difference had increased to 79.2% for females compared to 70.6% for males. Part of the reason for this difference may be a result of the different cancer types experienced by each sex with more bone (five-year survival 67.9%) and less skin (five-year survival 96.7%) or thyroid and endocrine (five-year survival 84.8%) in males than females.

There was very little difference in survival between the 0-14 and 15-24 age groups with one-year survival at 89.4% and 91.6%, five-year survival at 77.2% and 80.9% and twenty-year survival estimates at 73.2% and 75.8% respectively.

Five-year observed survival for study patients diagnosed in 1993-2008 was 74.7% for brain, eye and other CNS cancer (including non-invasive tumours), 70.4% for leukaemia and 86.8% for lymphoma.

For leukaemia survival was much better among those aged 0-14 than those aged 15-24 due to a much higher proportion of acute lymphocytic leukaemia (ALL) in this age group (78.7% of leukaemia's in the 0-14 age group vs. 50.0% in the 15-24 age group) which has better survival than other leukaemia types. (Table 3)

EXCESS MORTALITY

Among children and young people who survived at least one year, deaths from all causes were 25 times (SMR=24.7 (95% CI 22-27.5,) P<0.001) higher than the number found in a similar cohort of children and young people in the general population. However this includes the cancer the survivor was originally diagnosed with. Excluding this cause, the one-year survivors were over twice as likely to die from additional causes (SMR = 2.2,(95%CI 1.3-3..0) p=0.005) than in the general population. This risk was slightly greater for females, SMR 3.3(1.5-5.0) P=0.012 than males SMR= 1.6 (0.8-2.5)p=0.142 with the increased risk not reaching statistical significant for males.

Among children and young people who survived at least five years, deaths from all causes were seven times higher than the number found in a similar cohort of children and young people in the general population (SMR = 7.3,(5.5-9.2) p<0.001). This includes the cancer the survivor was diagnosed with, thus even after five years some patients died from a continuation of their original cancer or from recurrences of this cancer. This risk was higher among females than males (10 times greater vs. 6 times greater). Excluding the primary cancer as a cause, the excess deaths in five-year survivors, although three times greater than the mortality rate in the general population (SMR= 3.2 (95% CI 0.4, 6.1p= 0.122,) did not reach statistical significance.

DISCUSSION

In Northern Ireland, approximately 125 children and young people aged 0-24 are diagnosed with cancer for the first time

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

TABLE. 3:

Observed survival from cancer among children and young people (aged 0-24) by type and age: Patients diagnosed 1993-2008, followed up to end of 2013

(A) AGES 0-24

Survival time	Observed survival (95% CI)							
	Bone		Skin		Mesothelial & soft tissue		Female genital	
3 months	98.7%	(90.9%, 99.8%)	99.6%	(97.1%, 99.9%)	93.6%	(85.3%, 97.3%)	98.8%	(91.8%, 99.8%)
6 months	98.7%	(90.9%, 99.8%)	99.2%	(96.8%, 99.8%)	89.7%	(80.5%, 94.7%)	96.4%	(89.2%, 98.8%)
1 year	97.3%	(89.8%, 99.3%)	97.9%	(95.1%, 99.1%)	80.8%	(70.1%, 87.9%)	92.7%	(84.6%, 96.7%)
5 years	67.9%	(56.0%, 77.2%)	96.7%	(93.5%, 98.3%)	55.1%	(43.4%, 65.3%)	86.5%	(77.0%, 92.3%)
10 years	56.8%	(44.3%, 67.5%)	94.8%	(90.9%, 97.0%)	53.4%	(41.7%, 63.8%)	83.8%	(73.7%, 90.3%)
15 years	56.8%	(44.3%, 67.5%)	94.8%	(90.9%, 97.0%)	53.4%	(41.7%, 63.8%)	83.8%	(73.7%, 90.3%)
20 years	56.8%	(44.3%, 67.5%)	94.8%	(90.9%, 97.0%)	49.6%	(36.5%, 61.4%)	83.8%	(73.7%, 90.3%)

Survival time	Observed survival (95% CI)					
	Male genital		Urinary		Brain, eye & CNS	
3 months	99.3%	(95.1%, 99.9%)	99.3%	(95.1%, 99.9%)	95.8%	(93.5%, 97.3%)
6 months	97.9%	(93.6%, 99.3%)	97.9%	(93.6%, 99.3%)	92.8%	(90.1%, 94.8%)
1 year	96.5%	(91.8%, 98.5%)	96.5%	(91.8%, 98.5%)	86.9%	(83.5%, 89.6%)
5 years	92.3%	(86.5%, 95.7%)	92.3%	(86.5%, 95.7%)	74.7%	(70.5%, 78.4%)
10 years	92.3%	(86.5%, 95.7%)	92.3%	(86.5%, 95.7%)	70.3%	(65.9%, 74.3%)
15 years	91.1%	(84.7%, 94.9%)	91.1%	(84.7%, 94.9%)	70.3%	(65.9%, 74.3%)
20 years	88.2%	(78.3%, 93.7%)	88.2%	(78.3%, 93.7%)	69.6%	(64.9%, 73.8%)

AGES 0-14

Survival time	Observed survival (95% CI)					
	Brain, eye and CNS		**Lymphoma**		**Leukaemia**	
3 months	95.5%	(92.3%, 97.3%)	100.0%		96.9%	(93.8%, 98.4%)
6 months	90.6%	(86.6%, 93.4%)	98.8%	(91.8%, 99.8%)	95.3%	(91.9%, 97.3%)
1 year	84.0%	(79.2%, 87.7%)	96.4%	(89.2%, 98.8%)	91.4%	(87.2%, 94.2%)
5 years	71.4%	(65.7%, 76.2%)	90.4%	(81.7%, 95.1%)	80.0%	(74.5%, 84.4%)
10 years	68.7%	(62.9%, 73.8%)	90.4%	(81.7%, 95.1%)	78.6%	(73.0%, 83.2%)
15 years	68.7%	(62.9%, 73.8%)	90.4%	(81.7%, 95.1%)	77.2%	(71.2%, 82.0%)
20 years	67.5%	(61.2%, 73.0%)	90.4%	(81.7%, 95.1%)	77.2%	(71.2%, 82.0%)

(B) AGES 15-24

Survival time	Observed survival (95% CI)					
	Skin		Female genital		Male genital	
3 months	99.6%	(96.9%, 99.9%)	98.7%	(91.4%, 99.8%)	99.3%	(94.9%, 99.9%)
6 months	99.1%	(96.5%, 99.8%)	96.2%	(88.7%, 98.8%)	97.8%	(93.4%, 99.3%)
1 year	97.8%	(94.8%, 99.1%)	92.4%	(83.8%, 96.5%)	96.4%	(91.5%, 98.5%)
5 years	96.5%	(93.0%, 98.2%)	85.8%	(75.8%, 91.9%)	92.0%	(86.0%, 95.5%)
10 years	94.9%	(91.0%, 97.2%)	84.3%	(74.0%, 90.8%)	92.0%	(86.0%, 95.5%)
15 years	94.9%	(91.0%, 97.2%)	84.3%	(74.0%, 90.8%)	90.8%	(84.1%, 94.7%)
20 years	94.9%	(91.0%, 97.2%)	84.3%	(74.0%, 90.8%)	87.6%	(77.2%, 93.5%)

Survival time	Observed survival (95% CI)					
	Brain, eye and CNS		**Lymphoma**		**Leukaemia**	
3 months	96.2%	(92.3%, 98.2%)	98.4%	(95.1%, 99.5%)	92.6%	(85.2%, 96.4%)
6 months	96.2%	(92.3%, 98.2%)	97.3%	(93.7%, 98.9%)	86.3%	(77.5%, 91.8%)
1 year	91.4%	(86.3%, 94.6%)	93.5%	(88.9%, 96.3%)	75.6%	(65.6%, 83.1%)
5 years	79.9%	(73.3%, 85.0%)	85.3%	(79.2%, 89.6%)	44.1%	(33.9%, 53.9%)
10 years	72.7%	(65.4%, 78.7%)	83.0%	(76.7%, 87.7%)	41.5%	(31.3%, 51.4%)
15 years	72.7%	(65.4%, 78.7%)	80.7%	(73.6%, 86.0%)	41.5%	(31.3%, 51.4%)
20 years	72.7%	(65.4%, 78.7%)	80.7%	(73.6%, 86.0%)	41.5%	(31.3%, 51.4%)

Note: Data for more than 5 years are estimates as full 20 year follow up is only available for earlier diagnosis years

CI: Confidence interval, CNS: Central Nervous System
Brain, eye and CNS includes non-invasive brain tumours

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

each year. Long term survival for these people is generally good, with four out of five patients still alive 5 years from their diagnosis. In concordance with other studies[2,3] we found that deaths as a result of a continuation of the patient's cancer continue to occur after the five-year point and that patients who are free from their first cancers are at an elevated risk of death from second cancers and from other causes. While 59 young people had a record of a second cancer, we were unable to verify whether the second cancer was a consequence of the first. We do know however from registry records that they were two separate cancers.

Compared to other studies[2,3], this study has the disadvantage of being based upon a relatively small number of patients, thereby reducing our ability to investigate some causes of death in particular, respiratory disease and infections. In addition, follow up time was limited to 20 years after diagnosis, with only several hundred patients having that length of follow up time. As a result, the full risk of some conditions, such as circulatory disease, cannot be assessed as the maximum age attained by patients is late thirties and early forties which is before the risk of death from heart disease, stroke and respiratory ailments becomes fully apparent.

The 5% of patients who have emigrated were considered lost to follow up in all survival and excess mortality analysis. These patients were censored at the date they left Northern Ireland and it is thus assumed that if these patients had stayed in Northern Ireland they would not have altered the conclusions drawn from the current analysis. It is difficult to assess the validity of this assumption. In addition, there will undoubtedly be patients in the data who have left Northern Ireland but whose status is unknown to NICR. These patients would appear to survive indefinitely and may artificially increase the long term survival estimates by a small margin.

The number of patients without a cause of death assigned (14 patients) is small. While the assumption that these patients all die from their first cancer is reasonable, it is possible that the absence of information on these patients may influence the conclusions about some of the less frequent causes if in fact, any of these patients did die from the less common causes of death.

Skin cancer accounted for 20% of the cancers diagnosed in those aged 15-24. Exposure to UV radiation is a known carcinogen and skin cancer risks can be modified by taking care in the sun especially in childhood. Skin cancer is recognised as a growing problem in N. Ireland where malignant melanoma and squamous cell skin cancer numbers have doubled in the past 20 years[1]. Further efforts in prevention are recommended.

This study identifies that excess mortality continues five years after diagnosis. This finding highlights the need for ongoing monitoring of young cancer survivors in later life, in particular with regards to potential side effects and long term health implications of treatments such as radiotherapy and chemotherapy. This need is widely recognised throughout Europe with strategic plans[9] introduced which recommend particular consideration to monitoring of follow up conditions.

Despite the difficulties and limitations of this study we have highlighted some of the more serious longer term consequences of cancer among children and young people so that appropriate action can be taken to address this ongoing concern. We plan to repeat this work in later years when we have more data accumulated and recommend the gathering of general health data on childhood cancer survivors in a routine manner. Also, efforts to reduce skin cancer in the Northern Ireland population should continue.

The full analysis will be available on the N. Ireland Cancer Registry website www.qub.ac.uk/nicr

ACKNOWLEDGMENT

The N. Ireland cancer registry is funded by the Public Health Agency for N. Ireland. This work came about following a collaboration with Macmillan Cancer Support

REFERENCES

1. Ranaghan L, Gavin A, 2012. Monitoring the care of leukaemia and lymphoma patients in Northern Ireland diagnosed in 2008. Belfast: N. Ireland Cancer Registry, Queen's University; 2012. Available online from: https://www.qub.ac.uk/research-centres/nicr/FileStore/PDF/NIrelandReports/Filetoupload,532257,en.pdf. Last accessed July 2016.
2. Mertens AC, Liu Q, Neglia JP, Wasilewski K, Leisenring W, Armstrong GT, *et al*. Cause specific late mortality among 5-year survivors of childhood cancer: the Childhood Cancer Survivor Study. *J Natl Cancer Inst. 2008; 100(19):1368-79*.
3. Reulen RC, Winter DL, Frobisher C, Lancashire ER, Stiller CA, Jenney ME, *et al*. Long-term cause-specific mortality among survivors of childhood cancer. *JAMA. 2010;304(2):172-9*
4. World Health Organisation. ICD10 International Classification of Diseases 10th revision. Geneva: WHO; 1997. Available online from: http://www.who.int/classifications/icd/ICD10Volume2_en_2010.pdf
5. Northern Ireland Statistics and Research Agency. Registrar General Northern Ireland Annual Report 2013. Belfast: NISRA; 2014. Available online from: *www.nisra.gov.uk/demography/default.asp57.htm* Last accessed July 2016.
6. World Health Organisation. ICD9 International Classification of Diseases. 9th ed. Geneva: WHO; 1978
7. Kim HJ, Fay MP, Feuer EJ, Midthune, DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med*. 2000; 19(3): 335-51.
8. U.S. Institute of Health, National Cancer Institute, Cancer control and population Sciences. Joinpoint Trend Analysis Software. Available online from: *http://srab.cancer.gov/joinpoint/* Last accessed July 2016.
9. European Society for Paediatric Oncology. The SIOPE strategic plan. A European Cancer Plan for Children and Adolescents. Brussels: SIOP Europe, the European Society for Paediatric Oncology; 2015.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Ulster Med J 2016;**85(3):**164-173

Grand Rounds

Pruritus: an overview. What drives people to scratch an itch?

Michael Joseph Lavery[1], Michael Owen Kinney[2], Hideki Mochizuki[1], John Craig[2], Gil Yosipovitch[1]

Accepted: 6th June 2016
Provenance: externally peer-reviewed.

ABSTRACT

Pruritus is a common complaint associated with many conditions. It negatively impacts sleep, quality of life, and mortality. Itch is transmitted along both histaminergic and non-histaminergic pathways with a complex interplay between keratinocytes, immune cells and cutaneous neurons. Individuals who present with pruritus should undergo a thorough assessment, especially those over 65 years old, to exclude underlying malignancy. Treatment no longer consists of antihistamines alone. Physicians now have an array of therapies in their armamentarium, to help alleviate this distressing symptom.

Keywords: Pruritus, histaminergic, non-histaminergic, unmyelinated C-nerve fibers, immune cells, keratinocytes, neurobiology, neuropathic, malignancy

INTRODUCTION

Pruritus is a common complaint with many aetiologies. It is defined as a sensation that drives the urge to scratch.[1] It can be acute (less than 6 weeks) or chronic (greater than 6 weeks). Pruritus severely impacts upon quality of life affecting activities of daily living and sleep.[2] It is important when assessing patients to take a detailed history, perform a focused physical examination, form a structured differential diagnosis and request appropriate investigations.

CASE REPORT

A 45-year-old woman presents to clinic with generalised itch, which has been present for 1 year but has increased in severity over the last few weeks. It is worse at night. On questioning, she states that while she is itchy everywhere it is worse on the palms and soles. She also complains of fatigue and nausea. Family have commented that recently her skin has turned yellow. She has a past history of hypothyroidism, controlled with thyroxine and she has not been started on any new medications.

On general inspection there is evidence of jaundice and scleral icterus. On full skin examination there are excoriations and lichenification, pronounced on her hands and feet. There is no evidence of a primary skin rash and she is clinically euthyroid.

What is the diagnosis and what would be the management plan for this patient? (*Answer at the end of this review*)

PATHOPHYSIOLOGY

Pruritus originates in the epidermis and dermo-epidermal junction. There is a complex interplay between activated unmyelinated C nerve fibers, immune cells and keratinocytes. There is release of several pruritogens, including proteases, cytokines, prostaglandins, neuropeptides, nerve growth factor and histamine. There is also activation of several pruritic receptors including protease-activated receptors and ion channel receptors. (TRPV1, TRPV3, TRPA1, TRPM8) Opioids and the different receptors are known to be involved in pruritus. Activation of the μ opioid receptor (e.g with morphine) causes pruritus. Conversely, antagonism of the κ-opioid receptor is pruritogenic.

The pruritic nerve impulse is propagated along C nerve fibers to the dorsal root ganglion at the spinal cord. Here the nerve impulse crosses to the contralateral spinothalamic tract, where the impulse then ascends to the laminar nuclei of the thalamus.[3,4] It is interesting to note that the histamine dependent and histamine independent pathways have separate projections in the spinothalamic tracts. Scratching activity has been shown to inhibit activation of spinothalamic tract neuronal activity in primate models and experimental evidence suggests that scratching activates inhibitory interneurons to release glycine and gamma-aminobutyric acid (GABA) and inhibit itch neurons.[5,6]

NEUROBIOLOGY OF ITCH

From the thalamus, the pruritic nerve impulse is transmitted to different regions of the brain. Functional neuroimaging studies have identified many different subcortical and cortical areas involved in itch.[7-10] These areas relate to the sensory perception of itch, evaluation of the sensation, motivation, attention, emotion, and motor functions, such as motor planning.[7-9]

[1.] Department of Dermatology/Temple Itch Center, Lewis Katz School of Medicine, Temple University, 3322 North Broad Street – Suite 212, Philadelphia, PA 19140, USA [2.] Department of Neurosciences, Royal Victoria Hospital, 274 Grosvenor Road, Belfast, BT12 6BA

gil.yosipovitch@tuhs.temple.edu.

Correspondence to Gil Yosipovitch

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

In addition, the precuneus, involved in memory, visual-spatial awareness and consciousness, is activated after acute itch stimulation.[11] In contrast, no activation of the precuneus was identified, after application of an acute painful stimulus.[12]

Once scratching begins, imaging shows activation of the reward system due to the feeling of pleasure.[10]

In one study, the cerebellum, which is involved in the coordination of motor-related activity, showed no activation during both itch-induced scratching and scratching alone, in chronic itch subjects; however in healthy subjects, cerebellar activation was observed.[9] This suggests decreased control of motor-related activity in patients suffering from chronic pruritus.

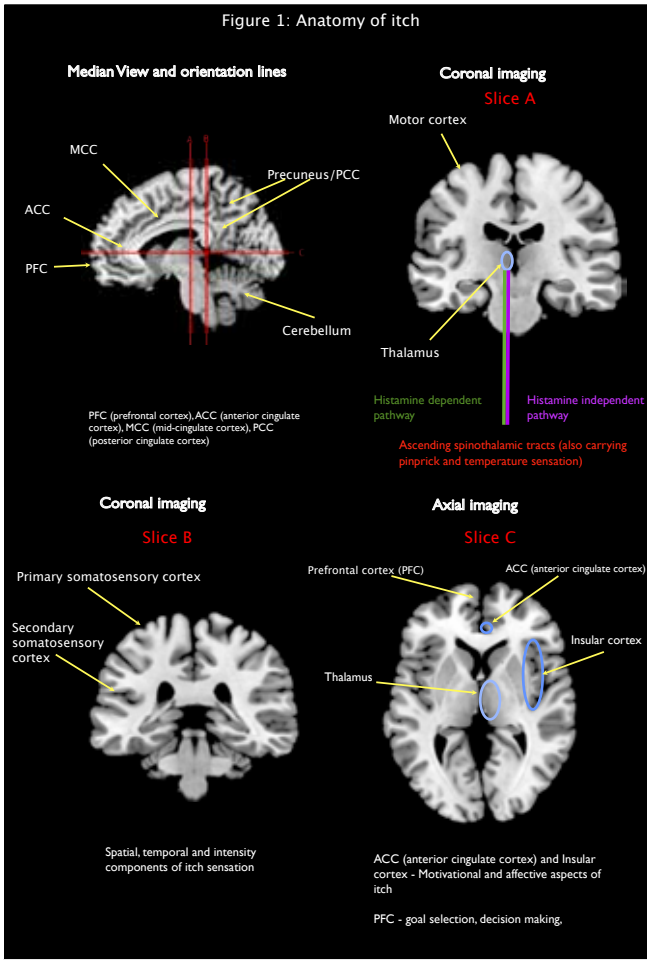


Fig 1. highlights these activated brain regions.

This pattern of neuronal network activation is different from that of pain perception, although there is significant overlap. Early studies have shown that when patients experience itch, activation of the ipsilateral motor areas, which plan the scratching response, occurs. (e.g, allowing the right hand to scratch the left forearm) This is in contrast to a painful stimulus where there is activation of the contralateral motor areas, in order to withdraw the limb from the painful stimulus.[8]

Two mechanisms have been postulated that contribute to chronic itch, namely peripheral and central sensitisation.[7] In peripheral sensitisation there is a reduced threshold at which itch sensation is perceived along with a higher basal activity of pruritogenic receptors and nerve fibres. Central sensitisation results from the effects of neural plasticity, whereby non-itch stimuli exacerbate and are perceived as an itch sensation.

There is also a complex interplay between itch and sleep mechanisms.[2] Pruritus may be experienced throughout the sleep cycle, with a predilection for the lightest stages. There is a complex interaction between circadian factors, and inflammatory mediators as well as psychological factors that can exacerbate nocturnal itch. This is a neglected area, which has already been shown to have a huge impact on mortality in patients with hemodialysis dependent renal failure.[13]

CAUSES

A myriad of conditions can cause chronic pruritus. Table 1 outlines a short list of different dermatologic and non-dermatologic causes.[14-16]

DERMATOLOGICAL DISORDERS:

Numerous dermatological disorders are associated with chronic itch. Some important examples are provided below.

ATOPIC DERMATITIS

Pruritus is the hallmark of atopic dermatitis (AD) and has a significant impact on sleep and quality of life.[2,17] Atopic dermatitis is an immune-mediated inflammatory skin disease with damage to the skin barrier. Epidermal barrier dysfunction has been associated with both decreased expression of filaggrin (an important protein involved in epidermal structure) and a reduced amount of epidermal lipids such as ceramides, aiding the entry of different pruritogens.[18] Repetitive scratching may also disrupt the epidermal barrier, and further contribute to the resultant immune response. Activation of T-lymphocytes results in the release of several cytokines, such as the Th2 cytokines IL-31, IL-4 and IL-13. Targeting these cytokines is revolutionising the treatment of atopic dermatitis.[19] Alloknesis, a phenomenon in which a normally innocuous stimulus induces itch, such as changes in temperature or contact with clothing, is a prominent feature in atopic eczema.

Finally, patients with atopic dermatitis have an altered microbiome favouring growth of staphylococcus aureus. These organisms release molecules which further contribute to the resultant inflammation and pruritus.[(20)]

There are many cutaneous findings in patients with AD – e.g. predominant flexural cutaneous involvement, hyperlinearity of the skin on the palms and soles and Dennie-Morgan folds (creases on the skin below the eyelashes).[21] In addition, an infra-auricular fissure (fissure present on the posterior aspect of the ear lobe) may be present, the severity of which correlates with AD severity.[22]

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Table 1:

Common causes of pruritus.

Common causes of itch	
Dermatological	**Non-dermatological**
Atopic dermatitis	Cholestasis • Intra-hepatic • Extra-hepatic • Drug-induced
Seborrheic dermatitis	Kidney • End-stage renal disease
Contact dermatitis	Neurological • CNS • Multiple sclerosis • Brain neoplasm • Cerebrovascular accident
	• PNS • Brachio-radial pruritus • Notalgia paresthetica • Post-herpetic neuralgia • Small fiber neuropathy
Psoriasis	Hematopoietic disease • Lymphoma • Multiple myeloma • Myeloproliferative disorders (e.g polycythemia vera, essential thrombocytosis, 1° myelofibrosis) • Iron-deficiency anemia • Myelodysplastic disorders
Urticaria	Endocrine • Thyroid disease • Diabetes mellitus; diabetic neuropathy • Anorexia nervosa • Parathyroid disease
Infestations • Scabies • Bed bugs • Pediculosis • Pinworms	Connective tissue disorders • Dermatomyositis • Scleroderma • Sjögrens syndrome
Dermatophytosis • Tinea corporis • Tinea cruris • Tinea pedis	Psychological • Depression • Delusion of parasitosis • Obsessive compulsive disorder • Stress • Fibromyalgia
Bullous disorders • Bullous pemphigoid • Dermatitis herpetiformis • Pregnancy associated • Drug eruption	Medications (some examples) • Opioids • Anti-hypertensives (ACE inhibitors, ARB's, beta-adrenergic blockers, diuretics, calcium channel blockers) • Antibiotics • Biguanides; Sulphonylurea derivatives • Chloroquine • Hydroxyethyl starch (artificial colloid intravenous fluid) • Statins
Lichen planus; lichen sclerosus	Neoplasia/Paraneoplastic phenomenon
Lichen simplex chronicus	HIV
Cutaneous T-cell lymphoma	Advanced age (senile)
Xerosis	Pregnancy associated cutaneous disorders
Stasis dermatitis (venous eczema)	Post transplant
Mastocytosis (cutaneous & systemic)	Hypereosinophilic syndrome

Abbreviations: CNS = central nervous system. PNS = peripheral nervous system. ACE = angiotensin converting enzyme. ARB = angiotensin II receptor blocker (antagonist). HIV = human immunodeficiency virus

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

TABLE 2:

Examples of topical therapies to treat chronic pruritus

Topical Medications	Mode of action	Dose
Emollients	Improve barrier function	Apply as needed
Oat meal extracts	Anti-inflammatory Anti-oxidant	Apply as needed
Corticosteroid	Anti-inflammatory	As prescribed Short-term use advocated
Tacrolimus Pimecrolimus	Calcineurin inhibitor	0.03%; 0.1% ointment 1% cream
Menthol	TRPM8 agonist	1-2% cream
Capsaicin	TRPV1 agonist Reduces Substance P release from C-nerve fibers	0.025% - 0.1% Transdermal patch 8%
Pramoxine (with hydrocortisone)	Ion channel blocker (anti-inflammatory)	1% cream (2.5%)
Strontium 4%	Calcimimetic	4% hydrogel
Ketamine/Amitriptyline/ Lidocaine	Ion channel blocker	Ketamine 5-10%, Amitriptyline 2-5% Lidocaine 2.5-5% Apply during pruritic episode
Doxepin	H1 and H2 antagonist Tricyclic antidepressant	5% cream

Abbreviation: TRPM8 = Transient receptor potential subfamily M member 8. TRPV1 – Transient receptor potential subfamily V member 1. H1 = histamine 1. H2= histamine 2

PSORIASIS

Psoriasis is a chronic immune-mediated inflammatory disorder, occurring in genetically predisposed individuals, with different environmental factors attributed to the disease and its flares. (e.g infections, medications, stress) Pruritus is reported in approximately 60-90% of psoriatic patients[23, 24] and has only recently been recognized as a major symptom in this chronic disease that affects 2-3% of the population.[25] In psoriasis, a dysregulated immune system is related to the overproduction of pro-inflammatory cytokines, including TNF-α, IL-12, IL-17, IL-23, which have a pruritic effect. In addition, the neural system is activated, with release of multiple substances, (in particular nerve growth factor (NGF) and Substance P), along with abnormal psoriatic skin innervation, imbalance in kappa- and mu-opioid pathways and increased levels of gamma-aminobutyric acid (GABA) and its receptor (GABAA).[24] These have all been shown to contribute to pruritus in psoriatic patients.

INFESTATIONS

Patients suffering from scabies infestation often complain of severe (predominantly nocturnal) itch. The pruritus occurs through the release of proteases excreted in the mite's faeces. The release of pruritic cytokines, from the activation of T-helper 2 lymphocytes, is also attributed to the pruritus in scabies, pediculosis (lice) and pinworm infestations. The movement of enterobius vermicularis (the causative agent in pinworm infestations) on the skin, as well as the release of eggs, commonly causes intense peri-anal pruritus. Subsequent scratching deposits these eggs under the fingernails and the pinworm may therefore re-enter the oral cavity and gastrointestinal tract, if patients exhibit poor hand hygiene.[26,27] Finally bed bugs are attracted to carbon dioxide and heat, and commonly feed on humans while they are sleeping at night.[28]

ADVANCED AGE PRURITUS

Pruritus is a common symptom in the elderly. A detailed history, examination and appropriate investigations must be performed, but often, no cause is identified. Patients exhibit xerosis (dry skin) with epidermal barrier dysfunction (with increased trans-epidermal water loss), alterations in pH, release of molecules (e.g proteases) and decreased estrogen levels. In addition there is immunosenescence (dampening of the immune system during the aging process) and neural degeneration comprising neuropathic itch (e.g. post herpetic neuralgia) and nerve compression (radiculopathy)[29]

CHRONIC URTICARIA

Urticaria is a disorder associated with mast cell degranulation releasing substances including histamine, leukotrienes and prostaglandins. It has a prevalence of 0.5-1%.[30] Clinically, this manifests with wheals, angioedema or both, and usually lasts less than 24 hours. Urticaria is divided into acute (duration

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

<6 weeks) or chronic (duration >6 weeks). New classification subdivides chronic urticaria into chronic inducible urticaria (CINDU) and chronic spontaneous urticaria (CSU).[31] There are many different triggers for CINDU including cold, sunlight, contact and aqueous. In many cases, a specific cause may not be identified.

The arms, back and legs are commonly affected. The accompanying pruritus is described as stinging, tickling or burning.[32]

Second generation, non-sedating antihistamines are currently recommended as first-line therapy for chronic urticaria.[33] . Other treatments include doxepin, leukotriene antagonists, histamine-2 antagonists, ciclosporin and mycophenolate mofetil. Omalizumab, a monoclonal antibody that targets and neutralizes free IgE, is a useful alternative antipruritic medication in unresponsive patients.[34] Its use is restricted to physicians with experience in prescribing this medication.

NON-DERMATOLOGICAL DISORDERS

CHOLESTATIC ITCH

Cholestatic pruritus may be subdivided into intra-hepatic, (e.g chronic hepatitis, carcinoma, primary biliary cirrhosis, intrahepatic cholestasis of pregnancy, Alagille syndrome) extra-hepatic (e.g cholelithiasis/choledocholithiasis, primary sclerosing cholangitis, bile duct stricture, cholangiocarcinoma, pancreatic carcinoma) and drug-induced. (e.g macrolides, chlorpromazine)[35] Patients classically complain of itch affecting the palms and soles of the feet.

The exact pathophysiology is not fully known, however cholestatic pruritus has been associated with accumulation of bile salts, bile acids as well as increased levels of bilirubin and endogenous opioids. Elevated levels of a phospholipid (lysophosphatidic acid) and autotaxin, the enzyme that forms LPA, have been found in this cohort. Autotaxin has been shown to be a biomarker for cholestatic pruritus.[36]

Therapies such as bile acid sequestrants, mu-opioid antagonists, sertraline and rifampicin have been shown to improve cholestatic pruritus.[36,37]

CKD ASSOCIATED PRURITUS

End stage renal disease patients, particularly those requiring haemodialysis, may suffer from chronic pruritus. The Dialysis Outcomes and Practice Patterns study (DOPPS) showed an increased mortality risk of 17% among 18,801 pruritic haemodialysis patients. This was in part attributed to a decreased quality of sleep.[13] Around 50-90% of patients on dialysis suffer from pruritus.[38] The pathophysiology is uncertain. There are several hypotheses, including abnormal calcium, phosphate and parathyroid levels, an imbalance among opioids, central neuropathy and a pro-inflammatory state.[39] Pruritus is usually only observed in patients with chronic (rarely acute) kidney disease.[40]

Itching commonly involves the back, but the head, neck and torso may also be affected.[4,40-42] Treatment involves adequate skin hydration and optimization of renal status. Antihistamines tend not to be effective. Gabapentin has been shown to improve CKD itch,[43] but care should be taken in monitoring renal function. Nalfurafine, a kappa opioid agonist, has also shown to improve CKD pruritus but is currently unlicensed for this indication.[19,44] Ultraviolet light therapy is another modality that may be employed. [39] Other opioid therapies are undergoing trials for this condition.[45-47]

HAEMATOLOGICAL

Itch may be a prominent feature in haematological disorders e.g Hodgkin's lymphoma, chronic lymphocytic leukemia, multiple myeloma, cutaneous T-cell lymphoma (CTCL) and polycythemia vera. Pruritus is present in around 19% of patients with Hodgkin's lymphoma[48] and approximately 15% of patients with non-Hodgkin's lymphoma.[49] The pruritus in Hodgkin's lymphoma is usually associated with disease activity.[14] IL-31 has been shown to be significantly increased in the epidermis and dermis of patients with CTCL.[50] There have been reports of patients who have chronic pruritus with no cutaneous manifestations, but with underlying mycosis fungoides.[51-53] This highlights the necessity to constantly review the diagnosis in patients with chronic pruritus. Finally, while water may also aggravate pruritus in patients with urticaria, aquagenic pruritus warrants investigation for evidence of polycythemia vera.

NEUROPATHIC ITCH

Neurological disorders may also display pruritus. Neuropathic itch has been defined as "an itch initiated or caused by a primary lesion or dysfunction at any point along the afferent pathway of the nervous system."[54] Brachioradial pruritus (BRP) usually presents with itch affecting dermatomes C4-C7. Compression of nerve fibers from cervical disc degeneration, spinal stenosis or malignancy may be the underlying cause. Notalgia paresthetica is another form of radiculopathy that may present with unilateral localized pruritus in the mid back, following a T2-T6 distribution. It may be associated with a sensory neuropathy and burning pain.[54]

Post-herpetic neuralgia can cause significant pruritus in up to 48% of patients. The itch commonly involves the face and neck.[55,56]

Topical capsaicin, which decreases Substance P release from C-nerve fibers, and GABAergic medications, may help.[57]

Central nervous system (CNS) disorders causing itch are usually due to brainstem or subcortical lesions.[7] Unilateral itch has been reported following cerebral infarction, as well as in patients with a cortical stroke.[7] Pruritus associated with multiple sclerosis is rare, occurring in only 4.5% of patients.[58]

INVESTIGATIONS

If pruritus is acute (< 6 weeks) one should determine if any new medications have been prescribed and check for any associated rash – e.g. urticaria causes itch and an erythematous rash but generally does not persist for >24 hours.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

If the pruritus is chronic (> 6 weeks), then a comprehensive review is required. In the elderly, it is important to consider underlying malignancy. The presence of a rash may be pivotal in determining the diagnosis; however not every patient will have a rash and often there may just be excoriations or lichenification. Figure 2 outlines a flowchart for the management of patients who present with chronic pruritus.

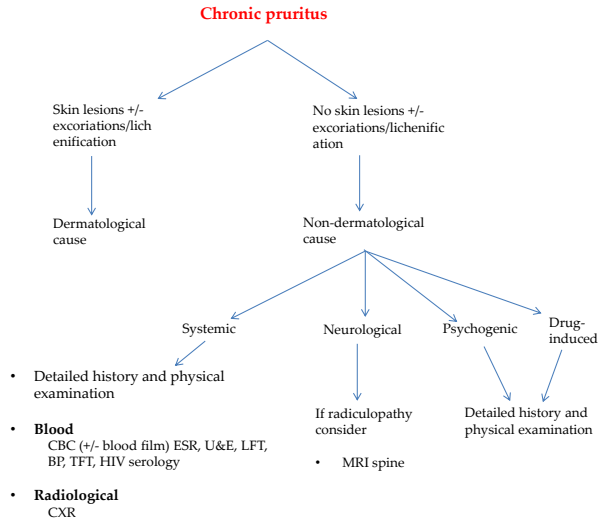


Fig 2. Chronic pruritus algorithm

TREATMENT

Before commencing treatment, it is important to determine if the patient has acute or chronic pruritus, and then investigate for the cause and evidence of any underlying malignancy; however, while results are awaited, therapy may be initiated.

Treatment can be divided into topical or oral therapy. Antihistamines are generally not effective in chronic pruritus. Topical therapies such as moisturizers, low pH cleansers, short-term use of topical corticosteroids, menthol, capsaicin, strontium and topical anesthetic agents may be employed. Oral medications, such as low dose mirtazapine and gabaergic agents (gabapentin, pregabalin) have been shown to be beneficial. Therapies to treat the underlying condition are also important.

Major pharmacological treatment modalities, both topical and systemic, are discussed below and summarized in Table 3 and 4.

Topical

An array of medications is available to treat pruritus. Basic skin care management cannot be over-emphasised. Simple treatment with moisturisers can have a huge impact upon the intensity of pruritus by improving skin barrier dysfunction and reducing the entry of pruritogens. Patients should use moisturisers liberally. For convenience, creams are usually applied during the day and greasier ointments at night. If patients are required to apply topical steroid creams, these should be applied before moisturisers. Wet pyjama therapy, whereby the patient applies a topical moisturiser with a corticosteroid and then dons 'wet' pyjamas (pyjamas that have been rinsed in water and then wrung out) has been shown to improve pruritus.[59] Explanation of the efficacy of

TABLE 3:

Examples of systemic therapies to treat chronic pruritus

Systemic medications	**Mode of action**	**Dose**
Sedating antihistamines e.g. • Chlorphenamine • Diphenhydramine • Hydroxyzine	H1 antagonist	• 4-16 mg • 25-200 mg • 25-100 mg
Non-sedating antihistamines e.g. • Cetirizine • Fexofenadine • Levocetirizine • Loratadine	H1 antagonist	• 10-20 mg • 180-360 mg • 5-10 mg • 10-20 mg
Mirtazapine	SNRI, SSRI	• 7.5-15 mg
Gabapentin Pregabalin	Modulate GABA	• 300-3600 mg • 150-450 mg
Opioids • Naltrexone	• **μ-opioid receptor antagonist**	• 25–50 mg
• Butorphanol • Nalfurafine	• **κ-opioid receptor agonist**	• 1–4 mg • 2.5-5 μg

Abbreviations: H1 = histamine 1. SNRI = serotonin noradrenaline re-uptake inhibitor. SSRI = selective serotonin re-uptake inhibitor. GABA = gamma-aminobutyric acid

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

this treatment is recommended due to the lack of willingness to adopt this approach.

It now recognized that high skin pH results in the release of proteases and activation of proteinase activating receptors. (PAR-2) This leads to inflammation, an impaired skin barrier and decreased stratum corneum cohesion. As such, syndet (synthetic detergent) products, which have a lower pH, (4.5-6.0) should be favored.[60,61]

Ion channels, such as TRPV1 and TRPM8 are known to be involved in the pathophysiology of chronic pruritus. Capsaicin, an ingredient of hot chili peppers, initially activates but over time desensitizes TRPV1 ion channels.[62] It may be used to treat patients with notalgia paresthetica, CKD and prurigo nodularis.[63,64] The burning sensation that may occur after application of capsaicin may be reduced with pre-treatment with local anaesthetic cream.[65] An 8% patch has also shown efficacy in patients with neuropathic pruritus.[62,66] Menthol, a TRPM8 agonist, evokes a cooling sensation and promotes repair of the skin barrier. [19] It may reduce pruritus in conditions such as lichen sclerosus and lichen amyloidosis.[67]

Other topical agents that are useful in reducing pruritus include pramoxine, strontrium and the compounded formulation of ketamine, amitriptyline and lidocaine. Pramoxine is a local anesthetic agent that reduces neuropathic, anogenital and CKD-associated pruritus.[68,69] It may also be combined with corticosteroids to reduce both inflammation and pruritus. Topical strontium 4% hydrogel (a calcimimetic) has been shown to reduce both histaminergic and non-histaminergic induced pruritus.[70,71]

The compounded formulation of ketamine, amitriptyline and lidocaine, (KAL) in various dosing percentages, has been successfully used to treat localised neuropathic itch. (unpublished data, Yosipovitch)

Finally Crisaborole (a topical phosphodiesterase-4 inhibitor) has shown promise in early trials by reducing pruritus associated with AD.[72]

Oral

Traditionally, antihistamines have been used to treat pruritus. These can be helpful in treating urticaria, cutaneous mastocytosis and drug-induced pruritus.[15] Antihistamines work by antagonizing the histamine-1 receptor and can have indirect effects on the TRPV1 ion channel.[16] They can be divided into sedating (e.g chlorphenamine, diphenhydramine, hydroxyzine) and non-sedating (e.g cetirizine, levocetirizine, fexofenadine). Sedating antihistamines cause drowsiness and as such are generally taken at night. These medications can still exert adverse daytime effects and may lead to daytime somnolence and increased risk of accidents. Improvement of nocturnal pruritus is likely due to this sedating effect. Guidelines recommend use of non-sedating antihistamines if these agents are to be employed to treat pruritus associated with urticaria.[33] There is a lack of data however on the efficacy of antihistamines to treat chronic pruritus. Given that the histaminergic pathway is not the main pathway involved in chronic pruritus, novel therapies have been sought.

Gabaergics, such as gabapentin and pregabalin, which are structural analogs of gamma-aminobutyric acid, have shown efficacy in treating pruritus in CKD patients[43] as well as in patients with neuropathic itch. [3] They may also be effective in other causes of chronic pruritus. Side-effects include drowsiness, increased appetite, and lower limb edema.

Mirtazapine has been shown to improve nocturnal pruritus. It is an antagonist of alpha-2 noradrenergic receptors, as well as H1, 5HT-2 and 5HT-3 cutaneous receptors. It has been used successfully to treat pruritus associated with malignant cholestasis, uremia, lymphoma, atopic dermatitis, urticaria and carcinoma en cuirasse.[73-75] Mirtazapine has a favorable safety profile. Side-effects include drowsiness, increased appetite and dry mouth. While patients may be hesitant to commence this medication due to fear of weight gain and drowsiness, these side-effects are also associated with sedating anti-histamines.

As noted above, there is a complex interaction between pain and itch – e.g. when patients scratch an itch it initially incites a pleasurable sensation. Medications, such as morphine, a μ-opioid receptor agonist, are known to cause pruritus. Conversely κ-opioid receptor antagonists will cause pruritus. It is therefore intuitive to prescribe patients either antagonists or agonists of the μ-/κ-opioid receptor, respectively. Naltrexone, a μ-opioid receptor antagonist, has been shown to reduce cholestatic pruritus and refractory itch in burn patients.[76,77] Its efficacy in CKD-associated pruritus has not always been reproduced.[78,79] Nalfurafine, a selective κ-opioid receptor agonist, has been shown to reduce CKD itch, however it is currently not licensed in the USA or Europe.[44] Butorphanol, a partial μ receptor antagonist and κ receptor agonist, has been used for intractable chronic pruritus.[80] It is an intranasal spray with 1 puff representing 1mg. Up to 4mg may be used over 24 hours if necessary. A recent study revealed that butorphanol deactivates areas of the brain that were initially activated during itch processing.[81]

Other

Immunosuppressants such as methotrexate, cyclosporine, azathioprine, mycophenolate mofetil have been used for inflammatory pruritic skin diseases.[82-84]

Novel medications that target specific pruritic cytokines and neurotrophins, are undergoing clinical trials, with promising results. Dupilumab, a monoclonal antibody that targets IL-4 and IL-13 has been shown to reduce pruritus in patients with moderate to severe atopic dermatitis. It has been assigned breakthrough status by the FDA.[85] Monoclonal antibodies targeting the pruritic IL-31 cytokine have shown quantitative reduction in pruritus in early trials.[19] Ustekinumab (IL-12 and IL-23 receptor antagonist) is currently licensed for use in psoriasis and psoriatic arthritis and has been shown to improve psoriatic pruritus. It is currently undergoing

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

clinical trial evaluation in patients with atopic dermatitis.[86] Secukinumab and Ixekizumab (targeting IL-17A) have shown significant anti-pruritic effect in psoriatic patients.[87,88] The oral phosphodiesterase-4 inhibitor, apremilast, has also shown an anti-pruritic effect in psoriasis.[89]

Non-pharmacological therapy

Non-pharmacological management of pruritus may also be employed. Psychological interventions such as progressive muscle relaxation and habit-reversal therapy may improve chronic pruritus.[90] We have found at our institution (MJL, GY) that progressive muscle relaxation, subjectively improves pruritus.

Diet is a major concern for patients with chronic pruritus, especially those suffering with atopic dermatitis. While these patients often have associated food allergies, strict dietary practice is not advocated.[18] The American Academy of Dermatology has recently produced guidelines on the management of atopic dermatitis, including dietary recommendations.[91] These include avoidance of foods that cause a true IgE-mediated allergy; however it does not recommend eliminating foods, based on allergy tests alone.

CONCLUSION

Research has increased our understanding of the pathophysiology of pruritus. It is imperative that physicians investigate for underlying systemic disease and malignancy, especially in the elderly.

There is now awareness of the different brain pathways that are activated and further research into how this knowledge can be incorporated into treatments is warranted.

In addition, knowledge of the different pathways (histamine and non-histamine) and mediators involved in itch has changed the pharmacological management of pruritus. Histamine is no longer the only known mediator associated with pruritus, and therefore antihistamines used alone, may not be effective. Novel targeted therapies which not only reduce the severity of the disease, but also reduce pruritus have ushered in a new era. The aim of treatment for both patients and physicians is to reduce itch intensity. Completely curing the pruritus is unlikely and patients should recognise this.

Conflicts of interest: MJL, MOK, JC declare no conflict of interest. HM is principal investigator for the National Eczema Association. GY is consultant, principle investigator or scientific advisory board member for TREVI, Tioga, Hoffmann-LaRoche, Creabilis, Chugai, Pfizer, Anacor, Celgene, Eli Lily, Johnson & Johnson, Cara, Allergan, GSK-Stiefel and LEO Foundation.

Case report answer

The patient requires immediate investigation for symptoms of chronic pruritus. Given the description of her itch and evidence of jaundice on examination, cholestatic pruritus is high on the list of differential diagnoses. Initial investigation should include a full blood count with differential, erythrocyte sedimentation rate, liver function tests, urea and electrolytes and thyroid function tests. Radiological investigation should be requested following results of these tests or if there is clinical concern regarding underlying malignancy. As this patient is suffering from chronic pruritus, antihistamine therapy is unlikely to be helpful. Bile acid resins, (e.g cholestyramine) mirtazapine and sertraline may reduce the pruritus, however treatment of the underlying condition is important. A therapeutic ladder for the treatment of pruritus in chronic liver disease (as well as in end stage renal disease and lymphoma) has been proposed. [35]

REFERENCES:

1. Stander S, Weisshaar E, Mettang T, Szepietowski JC, Carstens E, Ikoma A, *et al*. Clinical classification of itch: a position paper of the International Forum for the Study of Itch. *Acta Derm Venereol*. 2007;**87(4)**:291-4.
2. Lavery MJ, Stull C, Kinney MO, Yosipovitch G. Nocturnal Pruritus: The battle for a peaceful night's sleep. *Int J Mol Sci*. 2016;**17(3)**:pii E425.
3. Yosipovitch G, Bernhard JD. Clinical practice. Chronic pruritus. *N Engl J Med*. 2013 25;**368(17)**:1625-34.
4. Tarikci N, Kocaturk E, Gungor S, Topal IO, Can PU, Singer R. Pruritus in systemic diseases: a review of etiological factors and new treatment modalities. *ScientificWorldJournal*. 2015;**2015**:803752.
5. Davidson S, Zhang X, Khasabov SG, Moser HR, Honda CN, Simone DA, *et al*. Pruriceptive spinothalamic tract neurons: physiological properties and projection targets in the primate. *J Neurophysiol*. 2012;**108(6)**:1711-23.
6. Akiyama T, Iodi Carstens M, Carstens E. Transmitters and pathways mediating inhibition of spinal itch-signaling neurons by scratching and other counterstimuli. *PLoS One*. 2011;**6(7)**:e22665.
7. Dhand A, Aminoff MJ. The neurology of itch. *Brain*. 2014;**137(Pt 2)**:313-322.
8. Ikoma A, Steinhoff M, Stander S, Yosipovitch G, Schmelz M. The neurobiology of itch. *Nat Rev Neurosci*. 2006;**7(7)**:535-47.
9. Mochizuki H, Papoiu AD, Nattkemper LA, Lin AC, Kraft RA, Coghill RC, *et al*. Scratching induces overactivity in motor-related regions and reward system in chronic itch patients. J Invest Dermatol. 2015;**135(11)**:2814-23.
10. Mochizuki H, Papoiu ADP, Yosipovitch G. Brain processing of itch and scratching. In: Carstens E, Akiyama T, editors. Itch: mechanisms and treatment. Boca Raton (FL): Taylor & Francis Group; 2014. p. 391-408.
11. Papoiu AD, Coghill RC, Kraft RA, Wang H, Yosipovitch G. A tale of two itches. Common features and notable differences in brain activation evoked by cowhage and histamine induced itch. Neuroimage 2012 Feb 15;**59(4)**:3611-3623.
12. Apkarian AV, Bushnell MC, Treede RD, Zubieta JK. Human brain mechanisms of pain perception and regulation in health and disease. Eur J Pain 2005 Aug;**9(4)**:463-484.
13. Pisoni RL, Wikstrom B, Elder SJ, Akizawa T, Asano Y, Keen ML, et al. Pruritus in haemodialysis patients: International results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Nephrol Dial Transplant 2006 Dec;**21(12)**:3495-3505.
14. Yosipovitch G. Pruritus. In: Callen J, Jorizzo J, Zone J, Piette W, Rosenbach M, Vleugels R, editors. Dermatological signs of systemic disease. 5th ed. Amsterdam: Elsevier; 2016. p. 99-103.
15. Reich A, Stander S, Szepietowski JC. Drug-induced pruritus: a review. *Acta Derm Venereol*. 2009;**89(3)**:236-244.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

16. Kremer AE, Feramisco J, Reeh PW, Beuers U, Oude Elferink RP. Receptors, cells and circuits involved in pruritus of systemic disorders. *Biochim Biophys Acta*. 2014;**1842(7)**:869-892.

17. Mollanazar NK, Smith PK, Yosipovitch G. Mediators of chronic pruritus in atopic dermatitis: getting the itch out? *Clin Rev Allergy Immunol*. 2015; May:1-30.

18. Silverberg NB, Lee-Wong M, Yosipovitch G. Diet and atopic dermatitis. Cutis 2016 Mar;**97(3)**:227-232.

19. Stull C, Lavery MJ, Yosipovitch G. Advances in therapeutic strategies for the treatment of pruritus. *Expert Opin Pharmacother.* 2016;**17(5)**:671-87.

20. Weidinger S, Novak N. Atopic dermatitis. *Lancet.* 2016;387(10023):1109-22.

21. Blanc S, Bourrier T, Albertini M, Chiaverini C, Giovannini-Chami L. Dennie-Morgan fold plus dark circles: suspect atopy at first sight. *J Pediatr.* 2015;**166(6)**:1541.

22. Kwatra SG, Tey HL, Ali SM, Dabade T, Chan YH, Yosipovitch G. The infra-auricular fissure: a bedside marker of disease severity in patients with atopic dermatitis. *J Am Acad Dermatol*. 2012;**66(6)**:1009-10.

23. Yosipovitch G, Goon A, Wee J, Chan YH, Goh CL. The prevalence and clinical characteristics of pruritus among patients with extensive psoriasis. *Br J Dermatol*. 2000;**143(5)**:969-73.

24. Szepietowski JC, Reich A. Pruritus in psoriasis: an update. *Eur J Pain*. 2016;**20(1)**:41-6.

25. Roblin D, Wickramasinghe R, Yosipovitch G. Pruritus severity in patients with psoriasis is not correlated with psoriasis disease severity. *J Am Acad Dermatol*. 2014;**70(2)**:390-1.

26. Raju K, Verappa S, Venkataramappa SM. Enterobius vermicularis infestation masquerading as cervical carcinoma: A cytological diagnosis. *J Nat Sci Biol Med*. 2015;**6(2)**:476-9.

27. Patsantara GG, Piperaki ET, Tzoumaka-Bakoula C, Kanariou MG. Immune responses in children infected with the pinworm Enterobius vermicularis in central Greece. *J Helminthol*. 2016;**90(3)**:337-41.

28. Lavery MJ, Parish LC. Bed bugs revisited. *Skinmed*. 2011;**9(1)**:6-8.

29. Valdes-Rodriguez R, Stull C, Yosipovitch G. Chronic pruritus in the elderly: pathophysiology, diagnosis and management. *Drugs Aging*. 2015;**32(3)**:201-15.

30. Maurer M, Weller K, Bindslev-Jensen C, Gimenez-Arnau A, Bousquet PJ, Bousquet J, et al. Unmet clinical needs in chronic spontaneous urticaria. A GA(2)LEN task force report. *Allergy*. 2011;**66(3)**:317-30.

31. Moolani Y, Lynde C, Sussman G. Advances in understanding and managing chronic urticaria. *F1000Res*. 2016; 5:pii F1000 Faculty Rev-177.

32. Yosipovitch G, Ansari N, Goon A, Chan YH, Goh CL. Clinical characteristics of pruritus in chronic idiopathic urticaria. *Br J Dermatol*. 2002;**147(1)**:32-6.

33. Zuberbier T, Aberer W, Asero R, Bindslev-Jensen C, Brzoza Z, Canonica GW, *et al*. The EAACI/GA(2) LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update. *Allergy*. 2014;**69(7)**:868-87.

34. Kaplan A, Ledford D, Ashby M, Canvin J, Zazzali JL, Conner E, *et al*. Omalizumab in patients with symptomatic chronic idiopathic/spontaneous urticaria despite standard combination therapy. *J Allergy Clin Immunol*. 2013;**132(1)**:101-9.

35. Wang H, Yosipovitch G. New insights into the pathophysiology and treatment of chronic itch in patients with end-stage renal disease, chronic liver disease, and lymphoma. *Int J Dermatol*. 2010;**49(1)**:1-11.

36. Kremer AE, van Dijk R, Leckie P, Schaap FG, Kuiper EM, Mettang T, *et al*. Serum autotaxin is increased in pruritus of cholestasis, but not of other origin, and responds to therapeutic interventions. *Hepatology*. 2012;**56(4)**:1391-400.

37. Kremer AE, Bolier R, van Dijk R, Oude Elferink RP, Beuers U. Advances in pathogenesis and management of pruritus in cholestasis. *Dig Dis*. 2014;**32(5)**:637-45.

38. Narita I, Iguchi S, Omori K, Gejyo F. Uremic pruritus in chronic hemodialysis patients. *J Nephrol*. 2008;**21(2)**:161-5.

39. Combs SA, Teixeira JP, Germain MJ. Pruritus in kidney disease. *Semin Nephrol*. 2015;**35(4)**:383-91.

40. Patel TS, Freedman BI, Yosipovitch G. An update on pruritus associated with CKD. *Am J Kidney Dis*. 2007;**50(1)**:11-20.

41. Yosipovitch G, Zucker I, Boner G, Gafter U, Shapira Y, David M. A questionnaire for the assessment of pruritus: validation in uremic patients. *Acta Derm Venereol*. 2001;**81(2)**:108-11.

42. Zucker I, Yosipovitch G, David M, Gafter U, Boner G. Prevalence and characterization of uremic pruritus in patients undergoing hemodialysis: uremic pruritus is still a major problem for patients with end-stage renal disease. *J Am Acad Dermatol*. 2003;**49(5)**:842-6.

43. Nofal E, Farag F, Nofal A, Eldesouky F, Alkot R, Abdelkhalik Z. Gabapentin: a promising therapy for uremic pruritus in hemodialysis patients: a randomized-controlled trial and review of literature. *J Dermatolog Treat*. 2016 Apr 4;1-5.

44. Inui S. Nalfurafine hydrochloride to treat pruritus: a review. *Clin Cosmet Investig Dermatol.* 2015;**8**:249-55.

45. Chalmers D. Cara therapeutics announces positive results from phase 2 trial in uremic pruritus (NASDAQ:CARA). Stamford, Connecticut: Cara Therapeutics; 2015. Available online from: http://ir.caratherapeutics.com/releasedetail.cfm?releaseid=923457. Last accessed July 2016.

46. U.S. National Institutes of Health. Clinicaltrials.gov. Study of Nalbuphine HCL ER tablets in hemodialysis patients with uremic pruritus. Bethesda: National Institutes of Health; 2016. Available online from: https://clinicaltrials.gov/ct2/show/NCT02143648?term=nalbuphine+pruritus&rank=1. Last accessed July 2016.

47. U.S. National Institutes of Health. Clinicaltrials.gov. Study of Nalbuphine HCL ER tablets in patients with prurigo nodularis. Bethesda: National Institutes of Health; 2016. Available online from: https://clinicaltrials.gov/ct2/show/NCT02174419?term=nalbuphine+pruritus&rank=5. Last accessed July 2016.

48. Rubenstein M, Duvic M. Cutaneous manifestations of Hodgkin's disease. *Int J Dermatol*. 2006;**45(3)**:251-6.

49. Kumar SS, Kuruvilla M, Pai GS, Dinesh M. Cutaneous manifestations of non-Hodgkin's lymphoma. *Ind J Dermatol Venereol Leprol*. 2003;**69(1)**:12-15.

50. Nattkemper LA, Martinez-Escala ME, Gelman AB, Singer EM, Rook AH, Guitart J, *et al*. Cutaneous T-Cell lymphoma and pruritus: the expression of IL-31 and its receptors in the skin. *Acta Derm Venereol*. 2016 Mar 22.

51. Deen K, O'Brien B, Wu J. Invisible mycosis fungoides: not to be missed in chronic pruritus. *Dermatol Ther (Heidelb)*. 2015;**5(3)**:213-6.

52. Pujol RM, Gallardo F, Llistosella E, Blanco A, Bernado L, Bordes R, *et al*. Invisible mycosis fungoides: a diagnostic challenge. *J Am Acad Dermatol*. 2000;**42(2 Pt 2)**:324-8.

53. Dereure O, Guilhou JJ. Invisible mycosis fungoides: a new case. *J Am Acad Dermatol*. 2001;**45(2)**:318-9.

54. Berny-Moreno J, Szepietowski JC. Neuropathic itch caused by nerve root compression: brachioradial pruritus and notalgia paresthetica. *Serb J Dermatol Venereol*. 2009;2:68-72.

55. Oaklander AL, Cohen SP, Raju SV. Intractable postherpetic itch and cutaneous deafferentation after facial shingles. *Pain*. 2002;**96(1-2)**:9-12.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

56. Yosipovitch G, Samuel LS. Neuropathic and psychogenic itch. *Dermatol Ther.* 2008;**21(1)**:32-41.

57. Twycross R, Greaves MW, Handwerker H, Jones EA, Libretto SE, Szepietowski JC, *et al*. Itch: scratching more than the surface. *QJM*. 2003;**96(1)**:7-26.

58. Elsone L, Townsend T, Mutch K, Das K, Boggild M, Nurmikko T, *et al*. Neuropathic pruritus (itch) in neuromyelitis optica. *Mult Scler.* 2013;**19(4)**:475-9.

59. Dabade TS, Davis DM, Wetter DA, Hand JL, McEvoy MT, Pittelkow MR, *et al*. Wet dressing therapy in conjunction with topical corticosteroids is effective for rapid control of severe pediatric atopic dermatitis: experience with 218 patients over 30 years at Mayo Clinic. *J Am Acad Dermatol*. 2012;**67(1)**:100-6.

60. Ali SM, Yosipovitch G. Skin pH: from basic science to basic skin care. *Acta Derm Venereol*. 2013;**93(3)**:261-7.

61. Mukhopadhyay P. Cleansers and their role in various dermatological disorders. *Indian J Dermatol*. 2011;**56(1)**:2-6.

62. Zeidler C, Luling H, Dieckhofer A, Osada N, Schedel F, Steinke S, et al. Capsaicin 8% cutaneous patch: a promising treatment for brachioradial pruritus? *Br J Dermatol*. 2015;**172(6)**:1669-71.

63. Patel T, Yosipovitch G. Therapy of pruritus. *Expert Opin Pharmacother.* 2010;**11(10)**:1673-82.

64. Wallengren J, Klinker M. Successful treatment of notalgia paresthetica with topical capsaicin: vehicle-controlled, double-blind, crossover study. J Am Acad Dermatol 1995;**32(2 Pt 1)**:287-9.

65. Yosipovitch G, Maibach HI, Rowbotham MC. Effect of EMLA pre-treatment on capsaicin-induced burning and hyperalgesia. *Acta Derm Venereol*. 1999;**79(2)**:118-21.

66. Misery L, Erfan N, Castela E, Brenaut E, Lanteri-Minet M, Lacour JP, *et al*. Successful treatment of refractory neuropathic pruritus with capsaicin 8% patch: a bicentric retrospective study with long-term follow-up. *Acta Derm Venereol*. 2015;**95(7)**:864-5.

67. Valdes-Rodriguez R, Kaushik SB, Yosipovitch G. Transient receptor potential channels and dermatological disorders. *Curr Top Med Chem*. 2013;**13(3)**:335-43.

68. Leslie TA, Greaves MW, Yosipovitch G. Current topical and systemic therapies for itch. *Handb Exp Pharmacol*. 2015;**226**:337-56.

69. Weisshaar E, Szepietowski JC, Darsow U, Misery L, Wallengren J, Mettang T, *et al*. European guideline on chronic pruritus. *Acta Derm Venereol*. 2012;**92(5)**:563-81.

70. Papoiu AD, Valdes-Rodriguez R, Nattkemper LA, Chan YH, Hahn GS, Yosipovitch G. A novel topical formulation containing strontium chloride significantly reduces the intensity and duration of cowhage-induced itch. *Acta Derm Venereol*. 2013;**93(5)**:520-6.

71. Papoiu AD, Chaudhry H, Hayes EC, Chan YH, Herbst KD. TriCalm(®) hydrogel is significantly superior to 2% diphenhydramine and 1% hydrocortisone in reducing the peak intensity, duration, and overall magnitude of cowhage-induced itch. *Clin Cosmet Investig Dermatol*. 2015;**8**:223-9.

72. Anacor Pharmaceuticals announces positive results from phase 2 dose-ranging study of AN2728 in adolescents with atopic dermatitis. Palo Alto, California: Anacor Pharmaceuticals; 2013. Available online from: http://investor.anacor.com/releasedetail.cfm?releaseid=750026. Last accessed July 2016.

73. Davis MP, Frandsen JL, Walsh D, Andresen S, Taylor S. Mirtazapine for pruritus. *J Pain Symptom Manage*. 2003;**25(3)**:288-91.

74. Lee JJ, Girouard SD, Carlberg VM, Mostaghimi A. Effective use of mirtazapine for refractory pruritus associated with carcinoma en cuirasse. *BMJ Support Palliat Care*. 2016;**6(1)**:119-121.

75. Hundley JL, Yosipovitch G. Mirtazapine for reducing nocturnal itch in patients with chronic pruritus: a pilot study. *J Am Acad Dermatol*. 2004;50(6):889-91.

76. Mansour-Ghanaei F, Taheri A, Froutan H, Ghofrani H, Nasiri-Toosi M, Bagherzadeh AH, *et al*. Effect of oral naltrexone on pruritus in cholestatic patients. *World J Gastroenterol*. 2006;**12(7)**:1125-8.

77. Jung SI, Seo CH, Jang K, Ham BJ, Choi IG, Kim JH, *et al*. Efficacy of naltrexone in the treatment of chronic refractory itching in burn patients: preliminary report of an open trial. *J Burn Care Res*. 2009;**30(2)**:257-60; discussion 261.

78. Peer G, Kivity S, Agami O, Fireman E, Silverberg D, Blum M, *et al*. Randomised crossover trial of naltrexone in uraemic pruritus. Lancet 1996;**348(9041)**:1552-4.

79. Pauli-Magnus C, Mikus G, Alscher DM, Kirschner T, Nagel W, Gugeler N, *et al*. Naltrexone does not relieve uremic pruritus: results of a randomized, double-blind, placebo-controlled crossover study. *J Am Soc Nephrol*. 2000;**11(3)**:514-9.

80. Dawn AG, Yosipovitch G. Butorphanol for treatment of intractable pruritus. *J Am Acad Dermatol*. 2006;**54(3)**:527-31.

81. Papoiu AD, Kraft RA, Coghill RC, Yosipovitch G. Butorphanol suppression of histamine itch is mediated by nucleus accumbens and septal nuclei: a pharmacological fMRI study. *J Invest Dermatol*. 2015;**135(2)**:560-8.

82. Maley A, Swerlick RA. Azathioprine treatment of intractable pruritus: a retrospective review. *J Am Acad Dermatol*. 2015;**73(3)**:439-43.

83. Ko KC, Tominaga M, Kamata Y, Umehara Y, Matsuda H, Takahashi N, *et al*. Possible antipruritic mechanism of cyclosporine a in atopic dermatitis. *Acta Derm Venereol*. 2016; **96(5)**;624-9.

84. Simon D. Systemic therapy of atopic dermatitis in children and adults. *Curr Probl Dermatol*. 2011;**41**:156-64.

85. Beck LA, Thaci D, Hamilton JD, Graham NM, Bieber T, Rocklin R, *et al*. Dupilumab treatment in adults with moderate-to-severe atopic dermatitis. *N Engl J Med*. 2014;**371(2)**:130-9.

86. U.S. National Institutes of Health. Clinicaltrials.gov. A study of Ustekinumab (STELARA®) in adult Japanese participants with severe atopic dermatitis.. Bethesda: National Institutes of Health; 2016. Available at: https://clinicaltrials.gov/ct2/show/study/NCT01945086?term=ustekinumab+atopic+dermatitis&rank= Last accessed July 2016.

87. Thaci D, Blauvelt A, Reich K, Tsai TF, Vanaclocha F, Kingo K, *et al*. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis: CLEAR, a randomized controlled trial. *J Am Acad Dermatol*. 2015;**73(3)**:400-9.

88. Griffiths CE, Reich K, Lebwohl M, van de Kerkhof P, Paul C, Menter A, *et al*. Comparison of Ixekizumab with Etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. *Lancet*. 2015;**386(9993)**:541-51.

89. Sobell JM, Foley P, Toth D, Mrowietz U, Girolomoni G, Goncalves J, *et al*. Effects of Apremilast on pruritus and skin discomfort/pain correlate with improvements in quality of life in patients with moderate to severe plaque psoriasis. *Acta Derm Venereol*. 2016;**96(4)**:514-20.

90. Schut C, Mollanazar NK, Kupfer J, Gieler U, Yosipovitch G. Psychological interventions in the treatment of chronic itch. Acta Derm Venereol 2016;**96(2)**:157-61.

91. Sidbury R, Tom WL, Bergman JN, Cooper KD, Silverman RA, Berger TG, *et al*. Guidelines of care for the management of atopic dermatitis: Section 4. Prevention of disease flares and use of adjunctive therapies and approaches. *J Am Acad Dermatol*. 2014;**71(6)**:1218-33.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Ulster Med J 2016;**85(3):**174-177

Clinical Paper

Uterotonics for Non-emergent Caesarean Section: Protocol Change During UK-Licensed Drug Shortage

C Malone[1], JR Acheson[2], JD Hinds[3], MH McComiskey[1]

Accepted: 3rd March 2016
Provenance: externally peer-reviewed

Abstract

The aim was to assess the efficacy of Syntometrine ® (500 micrograms ergometrine with 5 units oxytocin) as an appropriate alternative first-line uterotonic for use in elective caesarean section (CS) during a national shortage of UK-licensed IV oxytocin from April-June 2014. An observational study was performed involving 2 groups of 22 women undergoing elective CS in a UK DGH during this period. Primary endpoints included mean estimated blood loss (EBL), haemoglobin drop post-operatively and transfusion requirement. Secondary endpoints were use of antiemetics and mean post-operative nausea and vomiting (PONV) score.

Results for Syntometrine ® groups and syntocinon groups respectively: mean EBL (ml) 527.3 vs. 550.0 (p=0.5820), mean haemoglobin drop (g/dL) 0.977 vs. 0.982 (p=0.98), blood transfusion 1/22 vs. 0/22 (p=1). Intra-operative antiemetics 20/22 vs. 6/22 (p=<0.001), post-operative antiemetics 2/22 vs. 2/22 (p=1), mean PONV score 11.5 vs. 3.5 (p=0.099).

As no significant difference in primary endpoints or PONV scores was observed between regimes, we conclude Syntometrine ® was a safe first-line haemostatic agent for elective CS during oxytocin shortage.

Key words: Drug shortages, patient safety, uterotonic, postpartum haemorrhage, post-operative nausea and vomiting

INTRODUCTION

The nonapeptide oxytocin acts on the uterine myocyte by causing release of prostaglandins leading to contraction of the uterus. It also has a role in cardiovascular regulation, as well as maternal and sexual behaviours. Major maternal adverse effects include hypotension, myocardial ischaemia, arrhythmias, nausea, vomiting, headache and flushing. Heart rate and blood pressure changes are less problematic after administration of a reduced dose of oxytocin (2 IU rather than 5IU) with no reported difference in requests for additional uterotonic agents.[1]

Ergometrine is a naturally occurring alkaloid, first isolated in 1932 and remains the second line intervention for atonic PPH persisting after administration of oxytocin at CS. Ergometrine causes a rapid and sustained contraction of both the pregnant and non-pregnant uterus. Its mode of action is thought to be via calcium channels or an a-receptor in the inner myometrium.[2] Ergometrine causes an increase in mean arterial pressure and there are reported cases of renal and coronary artery spasm as well as myocardial infarction associated with its use. The high incidence of nausea and vomiting after the recommended 0.5 mg dose has discouraged its use as a first-line agent at CS.[3]

Active management of the third stage of caesarean delivery is relatively under-researched and it has been assumed that proven benefits in vaginal delivery are applicable to CS.[4,5,6] The Royal College of Obstetricians and Gynaecologists (RCOG) recommend that oxytocin (5 IU by slow intravenous injection) should be used for women delivering by CS to reduce the frequency of post-partum haemorrhage (PPH).[7] The recommendation goes on to state that Syntometrine ® (Alliance) may be used in the absence of contraindications as it reduces the risk of minor PPH but it does lead to increased reported nausea, vomiting and elevation in blood pressure.

Licensed medicine shortages are becoming a more frequent occurrence due to manufacturing and supply issues.[8,9,10] This leads to consideration of unlicensed preparations or enforced change of perceived optimal patient management as dictated by the availability of safe alternatives. In April and May 2014 there was a UK-wide shortage of IV oxytocin (Syntocinon ®) licensed for UK use. This affected maternity departments where IV oxytocin is routinely used first-line for prevention of postpartum haemorrhage (PPH) during CS, as recommended

[1]Department of Obstetrics and Gynaecology, Craigavon Area Hospital, Southern Health and Social Care Trust, Northern Ireland. [2]Department of Obstetrics and Gynaecology, Daisy Hill Hospital, Southern Health and Social Care Trust, Northern Ireland. [3]Department of Anaesthetics, Craigavon Area Hospital, Southern Health and Social Care Trust, Northern Ireland

cmalone02@qub.ac.uk

Correspondence to Dr C Malone

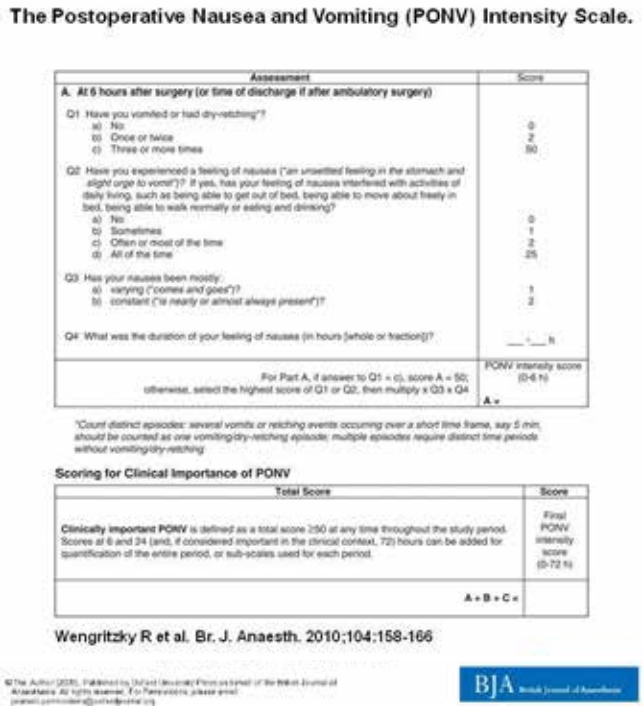
UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

by NICE.[11] Having considered the options presented by the Department of Health,[9] in our unit the protocol was changed from IV oxytocin to IM ergometrine and oxytocin (Syntometrine ® 500 micrograms ergometrine with 5 units oxytocin) as the first-line uterotonic agent in CS.

In order to assess the effect on patients of this enforced change in practice, we aimed to determine the suitability of Syntometrine ® as a first-line uterotonic agent for elective CS in terms of patient safety and outcomes. The primary endpoints of observed (operator estimated) bleeding; and secondary endpoints of post-operative nausea and vomiting and use of antiemetics were employed. These parameters were then compared to women receiving oxytocin when stocks were replenished.

METHODS

This was a prospective observational study, spanning a period of national shortage of Syntocinon ®. During the shortage period between April and May 2014, 22 women in a district general hospital underwent elective CS, facilitated by spinal anaesthesia. First-line PPH prophylaxis protocols were changed from 5 units IV oxytocin after delivery of the baby to 1ml of IM Syntometrine ® (500 micrograms ergometrine with 5 units oxytocin). Blood loss was recorded by surgeon estimated blood loss (EBL). Pre-operative and second day post-operative haemoglobin levels (g/dL) were checked, as well as any requirement for blood transfusion. Antiemetic use was recorded intra- and post-operatively. The incidence of post-operative nausea and vomiting (PONV) was recorded using a validated, standardised face-to-face questionnaire at 24 hours (Figure 1).[12] Wengritzky et al. developed a validated PONV intensity scale to formally assess clinically important PONV, as defined by a score of ≥50 using this tool, as this score is associated with a poorer quality of recovery and more antiemetic use, as well as increased complications. [12] The same data was then collected for the subsequent 22 elective CSs when stocks of UK-licensed oxytocin were replenished in May and June 2014, reverting to the previous protocol for prevention of PPH as above.


The Postoperative Nausea and Vomiting (PONV) Intensity Scale.

Assessment	Score
A. At 6 hours after surgery (or time of discharge if after ambulatory surgery)	
Q1. Have you vomited or had dry-retching*? a) No b) Once or twice c) Three or more times	 0 2 50
Q2. Have you experienced a feeling of nausea ("an unsettled feeling in the stomach and slight urge to vomit")? If yes, has your feeling of nausea interfered with activities of daily living, such as being able to get out of bed, being able to move about freely in bed, being able to walk normally or eating and drinking? a) No b) Sometimes c) Often or most of the time d) All of the time	 0 1 2 25
Q3. Has your nausea been mostly: a) varying ("comes and goes")? b) constant ("is nearly or almost always present")?	 1 2
Q4. What was the duration of your feeling of nausea (in hours [whole or fraction])?	___ . ___ h
For Part A, if answer to Q1 = c), score A = 50; otherwise, select the highest score of Q1 or Q2, then multiply x Q3 x Q4	PONV intensity score (0-6 h) A =

*Count distinct episodes: several vomits or retching events occurring over a short time frame, say 5 min, should be counted as one vomiting/dry-retching episode; multiple episodes require distinct time periods without vomiting/dry-retching

Scoring for Clinical Importance of PONV

Total Score	Score
Clinically important PONV is defined as a total score ≥50 at any time throughout the study period. Scores at 6 and 24 (and, if considered important in the clinical context, 72) hours can be added for quantification of the entire period, or sub-scales used for each period.	Final PONV intensity score (0-72 h)
A + B + C =	

Wengritzky R et al. Br. J. Anaesth. 2010;104:158-166

© The Author [2010]. Published by Oxford University Press on behalf of the British Journal of Anaesthesia. All rights reserved. For Permissions, please email: journals.permissions@oxfordjournals.org

BJA British Journal of Anaesthesia

Fig 1. PONV score[12] reproduced with permission from author P. Myles

Patient demographics in terms of age, BMI, parity, mode of previous deliveries, indication for CS and presence of risk factors for PPH such as placenta praevia were comparable for both groups.

Results were analysed using statistical methods to determine significance. The differences in mean estimated blood loss,

TABLE 1

Observed Peri-Operative Outcomes

Parameter	Syntometrine ® Group	Oxytocin Group	P value
Mean EBL (ml)	527.3	550.0	0.582
Mean haemoglobin drop post-operatively (g/dL)	0.977	0.982	0.98
Blood transfusion	1/22	0/22	1
Intra-operative antiemetics given	20/22	6/22	<0.001
Post-operative antiemetics given	2/22 *	2/22 *	1
Mean 24 hour PONV score	11.5 †	3.5 †	0.099

* In the Syntometrine ® group one woman had clinically important PONV score ≥50; in the oxytocin group no women had clinically important PONV score ≥50

† In the Syntometrine ® group four women had clinically important PONV score ≥50; in the oxytocin group one woman had clinically important PONV score ≥50

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Table 2

Cost Analysis of Syntometrine ® vs Oxytocin

	Syntometrine ® Group	Oxytocin Group	P value
Cost of uterotonic per patient	£ 1.31	£ 0.89	<0.0001
No of patients receiving antiemetic during study	20/22	8/22	0.0006
Cost of antiemetics (total)	£249.38	£76.20	<0.0001
Overall mean cost per patient (uterotonic+ antiemetics)	£12.65	£4.35	<0.0001

post-operative haemoglobin drop and PONV scores between the Syntometrine ® and oxytocin groups were compared using t-test analysis. It was assumed that the two populations had the same variance, were normally distributed and that each value was sampled independently. Chi squared analysis was performed using a 2x2 contingency table for administration of intra-operative antiemetics.

An ethics waiver was issued by Southern Health and Social Care Trust Research and Development Committee as the work was considered as service evaluation.

RESULTS

The results in Table 1 show no significant difference in mean EBL between the Syntometrine ® and oxytocin groups, which is also reflected in a non-significant post-operative drop in haemoglobin between both groups. One woman in the Syntometrine ® group required blood transfusion during the study.

In terms of antiemetic use, significantly more women administered Syntometrine ® received intra-operative antiemetics. There was no statistically significant difference in PONV scoring between groups, or clinically important PONV as defined by a score ≥50 using the validated tool.

In order to ascertain the financial implications of changing CS protocols in favour of Syntometrine ® during the oxytocin shortage, the costs of the standard doses of oxytocin and Syntometrine ® as well as the type, route and number of doses of each antiemetic received by women in both groups during the study period were analysed.[13] The total costs were then used to work out a mean cost per patient of uterotonic plus antiemetics for each group, as summarised in Table 2. This demonstrates a statistically significantly increased cost associated with changing protocols, due to the combined increased antiemetic use and the increased cost of Syntometrine ®.

DISCUSSION

Patient safety had been a legitimate concern when news of the oxytocin shortage came to light. There was little notice of the supply issue and a change of practice had to be implemented with almost immediate effect.

Our data show that Syntometrine ® is a suitable alternative to oxytocin as a uterotonic for use in elective CS in terms of blood loss, haemoglobin drop and transfusion requirement. Available study (syntocinon) patients during this time were limited due to the opportunistic nature of the project and the fact that the control (syntometrine) group was matched 1:1. This left little scope to alter the sample sizes analysed. Although post-hoc power calculation has received criticism as a method for interpreting negative study results[14], our study had 75% power to detect a statistically significant difference in mean estimated blood loss. Further reassurance regarding statistical validity of the project rests in the narrow 95% confidence limits reported (527ml +/- 24ml for the syntometrine group and 550ml +/- 33ml for the syntocinon group).

Intra-operative antiemetic was given more frequently to women who received Syntometrine ® compared to oxytocin, though there was no difference in clinically significant PONV scores.

The studies from which the Royal College of Obstetricians and Gynaecologists (RCOG) and NICE have based their guidelines on management of PPH and CS have consistently established that Syntometrine ® is as effective as IV oxytocin (5IU or 10IU) in preventing PPH >1000ml.[7,11] In fact, the Cochrane review referenced by the RCOG guideline states that there is a greater risk reduction of PPH for the definition of blood loss > 500ml, with Syntometrine ® versus IV oxytocin.[15] The widely reported increase in unpleasant side-effects of nausea and vomiting with Syntometrine ® compared with oxytocin alone are derived from the same studies, but exhibit considerable heterogeneity in reporting of these symptoms.[15] When examined in greater detail, the methods of reporting such symptoms are sub-optimal, with no validated tools used to score PONV.[16] While our study involved a small number of patients, it does use a validated tool for assessing PONV, lending weight to the results. The Syntometrine ® group received significantly more intra-operative antiemetics. It is impossible to say if this was in response to reported symptoms, or merely reflective of an attempt by the anaesthetist to mitigate against predicted problems. It is noteworthy that the Oxford Handbook of Anaesthesia recommends prophylactic antiemetic when giving Syntometrine ®. [17]

The practice of giving antiemetic along with ergometrine is also re-enforced in training manuals / protocols in UK

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

obstetric departments. [18] The 2004 Cochrane review[15] concluded that there was an increased rate of nausea and vomiting with Syntometrine ® – although the PONV scores were generally not using validated tools. The increased use of antiemetics therefore seems engrained in practice and needs to be factored into any economic cost calculation for syntometrine vs. syntocinon. As a result, it is impossible to accurately compare PONV rates between the two drugs due to the presence of bias. This is a clinical bias however, and it now would be unethical (based on well-established data that there is a 4 to 7 fold increase in nausea / vomiting) to withhold antiemetics in the syntometrine group of patients for research or cost reasons.

In the setting of increasingly frequent international drug shortages it is important to have contingency protocols in place. Supply chain issues can be unpredictable and there may be no reliable estimates of the duration of the shortage. In this particular case, there were additional concerns - existing stocks of oxytocin were reserved for circumstances where no alternative exists, e.g., augmentation of labour and for emergencies such as massive PPH.

The effectiveness of Syntometrine ® at preventing PPH at CS - without significantly increased side-effects - raises the possibility of using Syntometrine ® for elective cases where increased blood loss would be expected; for example placenta praevia. The cost issues would make it prohibitive for regular use however, due to the increased use of antiemetics.

We conclude that in the setting of a UK-wide shortage of IV oxytocin, Syntometrine ® is an appropriate safe alternative for first-line prevention of PPH at elective CS. It provides equal haemostasis. There was no significant increase in patient reported post-operative nausea and vomiting. Significantly more intra-operative antiemetic use was observed, though it is unclear if this was due to actual intra-operative nausea and vomiting, or merely reflective of a more aggressive prophylactic approach to antiemesis.

It can also be concluded that patient safety did not appear to be compromised when a shortage of oxytocin mandated the use of Syntometrine ® as an alternative for elective CS. However, the higher cost of Syntometrine ®, combined with the increased use of intra-operative antiemetics, suggests that this particular drug shortage may have had a significant financial consequence for the NHS.

REFERENCES

1. Sartain JB, Barry JJ, Howat PW, McCormack DI, Bryant M. Intravenous oxytocin bolus of 2 units is superior to 5 units during elective CS. *Br J Anaest*. 2008; 101(6):822–6.
2. Dyer RA, van Dyk D, Dresner A. The use of uterotonic drugs during CS. *Int J Obstet Anesth*. 2010; 19(3): 313–9.
3. Balki M, Carvalho JC. Intraoperative nausea and vomiting during cesarean section under regional anesthesia. *Int J Obstet Anesth*. 2005; 14(3):230–41.
4. Murphy J, Carey M, Montgomery AA, Sheehan S, ECSSIT Study Group. Study Protocol. ECSSIT – Elective CS Syntocinon® Infusion Trial. A multi-centre randomised controlled trial of oxytocin (Syntocinon®) 5 IU bolus and placebo infusion versus oxytocin 5 IU bolus and 40 IU infusion for the control of blood loss at elective CS. *BMC Pregnancy Childbirth*. 2009; 9:36.
5. Lokugamage AU, Paine M, Bassaw-Balroop K, Sullivan KR, Rafaey HE, Rodeck CH: Active management of the third stage at CS: a randomised controlled trial of misoprostol versus syntocinon. *Aus NZ J Obstet Gynaecol*. 2001; 41(4):411-4.
6. Munn MB, Owen J, Vincent R, Wakefield M, Cheshunt DH, Hauth JC. Comparison of two oxytocin regimens to prevent uterine atony at caesarean delivery: a randomized controlled trial. *Obstet Gynecol*. 2001; 98(3):386-90.
7. Royal College of Obstetricians and Gynaecologists. *Postpartum Haemorrhage, Prevention and management. (Green-top Guideline No. 52)*. London: Royal College of Obstetricians and Gynaecologists; 2009.
8. European Association of Hospital Pharmacists. *Medicines shortages in European hospitals: the evidence and case for action*. London: EAHP; 2014.
9. NHS. East & South East England Specialist Pharmacy Services. Medicines Information Division. Drug Discontinuation. Shortage of Supply Memos. *Shortage of oxytocin (Syntocinon) injection.* London: Department of Health; 2014.
10. American Society of Health System Pharmacists. Drug Shortages. Current shortages. *Bulletin 876. Oxytocin injection [24 May 2016].* Bethesda, Maryland: ASHP; 2016.
11. NICE Clinical Guideline; 132. *CS.* London: National Institute for Health and Care Excellence; 2011.
12. Wengritzky R, Mettho T, Myles PS, Burke J, Kakos A. Development and validation of a postoperative nausea and vomiting intensity scale. *British Journal of Anaesthesia*. 2010 Feb; 104(2):158-166.
13. British Medical Association, Royal Pharmaceutical Society of Great Britain. *British National Formulary No. 62*: *Oxytocin*. London: BMJ Group and RPS Publishing; 2011.
14. Levine M, Ensom MH. Post-hoc power analysis; an idea whose time has passed? *Pharmacotherapy*. 2001; 21(4): 405-9.
15. McDonald SJ, Abbott JM, Higgins SP. Prophylactic ergometrine oxytocin versus oxytocin for the third stage of labour. *Cochrane Database Systematic Reviews* . 2004. Issue 1. Art No. CD000201.
16. Choy CM, Lau WC, Tam WH, Yuen PM. A randomised controlled trial of intramuscular syntometrine and intravenous oxytocin in the management of the third stage of labour. *BJOG*. 2002; 109(2):173-7.
17. Allman K, Wilson I. Oxford Handbook of Anaesthesia. 4th ed. Oxford: Oxford University Press; 2016.
18. NHS Networks (UK). Postpartum haemorrhage, PPH 2013–15. NHS Networks [internet]. 2015. Available online from: https://www.networks.nhs.uk/nhs-networks/staffordshire-shropshire-and-black-country/documents/Postpartum%20Haemorrhage%202013.pdf. Last accessed July 2016.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Ulster Med J 2016;**85(3):**178-181

Clinical Paper

Re-Staging Following Long-Course Chemoradiotherapy For Rectal Cancer: Does It Influence Management?

McBrearty A, McCallion K, Moorehead RJ, McAllister I, Mulholland K, Gilliland R, Campbell WJ

Accepted: 9th February 2016
Provenance: externally peer-reviewed.

ABSTRACT

Background: In patients with locally advanced or low rectal cancers, long-course chemoradiotherapy (LCCRT) is recommended prior to surgical management.[1] The need for restaging afterwards has been questioned as it may be difficult to interpret imaging due to local tissue effects of chemoradiotherapy. The purpose of this study was to determine if restaging affected the management of patients receiving long-course chemoradiotherapy for rectal cancer.

Methods: A retrospective review of patients with rectal cancer discussed at the South Eastern Health and Social Care Trust Lower Gastrointestinal Multi-Disciplinary Team Meeting (LGIMDT) in 2013 who had received long-course chemoradiotherapy was performed. Patients were identified from the Trust Audit Department, LGIMDT notes and patient records. Imaging results and outcomes from meetings were obtained through the Northern Ireland Picture Archiving and Communications System® (NIPACS) and Electronic Care Record® (ECR). Data including patient demographics, initial radiological staging and LGIMDT discussion, restaging modality and result, outcome from post-treatment LGIMDT discussion and recorded changes in management plans were documented using a proforma.

Results: Seventy-one patients with rectal cancer were identified as having LCCRT in 2013 (M:F 36:35; age range 31 - 85 years). Fifty-nine patients were restaged following long-course treatment with computed tomography (CT) and magnetic resonance imaging (MRI). Twelve patients did not undergo restaging. Data was not available for 6 patients, one patient underwent emergency surgery, two patients were not fit for treatment, one failed to attend for restaging and two patients died prior to completion of treatment. Of the 59 patients restaged, 19 patients (32%) had their management plan altered from that which had been proposed at the initial LGIMDT discussion. The most common change in plan was not to operate. Ten patients had a complete clinical and radiological response to treatment and have undergone intensive follow-up. Nine patients had disease progression, with 3 requiring palliative surgery and 6 referred for palliative care.

Conclusion: Of those patients who were restaged, 32% had their management plan altered from that recorded at the initial LGIMDT discussion. Seventeen per cent of patients in this group had a complete clinical and radiological response to treatment. Fifteen percent demonstrated disease progression. We recommend, therefore, that patients with rectal cancer be restaged with CT and MRI following long-course chemoradiotherapy as surgery may be avoided in up to 27% of cases.

INTRODUCTION

Rectal cancer is a tumour with its lower edge within 15cm of the anal verge. It remains the second most common cause of cancer death in the United Kingdom. 70-80% of patients will present with T3 or node positive disease.[2] Treatment has been modified in recent years with improved imaging techniques, neoadjuvant treatment strategies and the dawn of total mesorectal excision (TME). More recently, chemoradiotherapy has become a standard practice pre-operatively to downstage tumours to achieve sphincter preservation and reduce local recurrence rates.[3] When a tumour fails to respond, aggressive surgery or palliation may be indicated. Imaging is central to such decisions in a multidisciplinary setting. Recent literature has debated the role of re-staging following pre-operative long-course chemoradiotherapy (LCCRT), in particular, the ability to discriminate malignant from non-malignant tissue.[3-8] We performed a retrospective review of patients presented at the LGIMDT to determine the role of re-staging in patients who have received LCCRT for rectal cancer and its impact on their management.

METHODS

A retrospective review of patients discussed at the LGIMDT in 2013 was performed. All patients diagnosed with rectal cancer that received LCCRT and were re-staged prior to re-

Department of General Surgery, Ulster Hospital, Dundonald, Belfast, BT16 1RH

anthonymcbrearty@doctors.org.uk

Correspondence to Mr Anthony McBrearty

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

discussion at the LGIMDT were included. Local research ethic committee approval was obtained. Data were collected using a proforma which included patient demographics, primary radiological staging and initial LGIMDT plan, mode of neoadjuvant treatment, restaging modality and result, outcome of re-discussion at the LGIMDT and changes in the initial treatment plan. Imaging results were obtained through the Northern Ireland Picture Archiving and Communications System® (NIPACS). In accordance with Northern Ireland Cancer Network (NICaN) guidelines, the clinical, histological and radiological findings for each patient were discussed at the LGIMDT.[9] The treatment plan was recorded. For each patient who was deemed to have a potentially threatened or involved margin, pre-operative neoadjuvant therapy was commenced. Treatment options included long-course chemoradiotherapy, short-course radiotherapy, long-course radiotherapy or extensive radical surgery. Only patients receiving LCCRT were included in this study. Following re-staging, patients were again discussed at the LGIMDT and a treatment plan agreed. Options recommended included surgery, regular follow-up or palliative care referral.

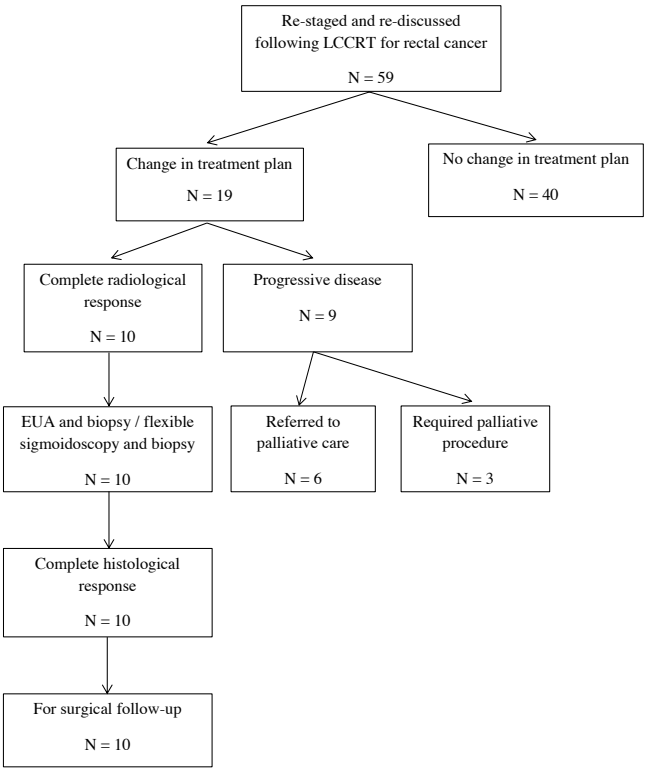


Fig 1.

RESULTS

We identified 71 patients with rectal cancer discussed in 2013 at the LGIMDT who had received LCCRT and were re-staged prior to re-discussion. Thirty-six males, 35 females with age range 31 to 85 years were included. Of these, 6 patients had incomplete data available, 2 patients had died, 1 patient declined further management, 2 patients were deemed not fit for further treatment due to multiple medical co-morbidities and 1 patient had an emergency resection. All of the 59 remaining patients had re-staging magnetic resonance imaging (MRI) of pelvis-rectum and computed tomography (CT) of the chest, abdomen and pelvis (Figure 1). Of the 59 patients re-staged, a change in the original treatment plan occurred in 19 patients (32%). Ten patients (17%) were found to have a complete radiological response to LCCRT. Of these 10 patients, all have remained under regular surveillance with three monthly examination under anaesthetic/flexible sigmoidoscopy and biopsy and 6 monthly MRI pelvis-rectum. One of the 10 patients had died at the time of writing with a synchronous primary lung tumour. The remaining patients were alive at an average of 3.5 years of follow-up. Nine patients were found to have disease progression (15%). Of these, 3 patients required a palliative procedure. The remaining 6 patients were considered for palliative chemotherapy and, where appropriate, referred for palliative care. In total, of the 59 patients included in the study, 16 patients (27%) avoided surgery following re-staging.

DISCUSSION

Chemotherapy and/or radiotherapy followed by total mesorectal excision (TME) is the gold standard treatment for locally advanced rectal cancer increasing the likelihood of sphincter preservation and reducing local recurrence rate. Tumour within 1mm of the circumferential resection margin (CRM) strongly predicts local recurrence and poor survival. Patients with CRM involvement have been reported to have at least 3 times the risk of local recurrence and twice the risk of death.[10] In these patients, pre-operative long course chemoradiotherapy (LCCRT) may facilitate successful TME with a reduction in tumour volume and greater likelihood of a sphincter-saving procedure.[10,11] It is thought that pre-operative treatment of well-oxygenated tissue increases sensitivity to radiotherapy as well as reducing the risk of small bowel radiation injury.[11]

Many authors advocate MRI to determine CRM status before and after LCCRT.[12-16] By contrast, clinical examination understages in approximately 47% of patients and is highly dependent on the examiner's appreciation of tumour mobility and fixation.[17] Endoanal ultrasound (EAUS) tends to overestimate tumour depth and is associated with difficulty in determining tumour from fibrosis/inflammation. There has been a growing interest in positron emission tomography (PET-CT), however, there is a need for standardisation of criteria used to measure response with this modality.[2] In addition, sensitivity and specificity of PET in predicting response to treatment varies from 45 – 100% and 59 – 96% respectively.[2] The MERCURY trial demonstrated that MRI assessment of the CRM is feasible and reproducible.[10] It has also been shown that multidisciplinary discussion of MRI results and implementation of a pre-operative treatment plan leads to significantly reduced positive CRM.[16]

If a complete clinical response occurs, a policy of careful observation may be adopted after discussion with the patient.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Complete response of the primary rectal tumour has been observed in up to 30% of patients after restaging.[18] After neoadjuvant treatment, accurate assessment of the tumour has proved difficult due to local response to LCCRT resulting in fibrosis.[3] Prediction of CRM involvement is reported to be 66-85% while determination of rectal wall invasion and nodal disease after LCCRT have been quoted to be as low as 50% (specificity 35%; sensitivity 100%) and 65% respectively.[7,8,19] The MERCURY group showed an overall accuracy of 91% for predicting CRM in patients going straight to surgery versus 77% in patients undergoing pre-operative LCCRT.[10] Fibrosis of the bowel wall from radiation can easily be misinterpreted as tumour. Furthermore, peri-tumour inflammation and infiltration and vascular proliferation can correlate with peri-lesional enhancement leading to overstaging.[11]

TABLE 1.

Complete responders: initial radiological staging and position of tumour within the rectum.

Initial Radiological Staging	Position of tumour
T3 N0	Lower
T4 N2	Upper
T2 N0	Middle
T3 N1	Upper
T3 N0	Middle
T4 N0	Lower
T2 N0	Lower
T3 N2	Middle
T4 N0	Upper
T2 N0	Middle

Understaging is usually explained by an inability to locate residual tumour encased in fibrotic tissue.[3] This has led to recent literature questioning the role of restaging patients who have had LCCRT and raising doubt as to its clinical and cost-effectiveness.[3,4,20,21] Some studies have concluded that none of the available imaging modalities can accurately determine whether or not there has been a complete pathological response.[5,22,23] We set out to challenge these hypotheses and determine whether there was a role for restaging in patients with rectal cancer treated with LCCRT.

All of our patients were re-discussed following restaging at the LGIMDT. This typically has consultant radiologists, oncologists, the colorectal surgical body and other healthcare professionals present. A colorectal surgeon leads the LGIMDT discussion. Outcomes from the meeting are based on group consensus amongst the specialists present and documented in an accessible online care pathway. Imaging, in particular, is actively discussed and independent second opinions sought where interpretation is difficult. In such cases, comparison of pre- and post-treatment images has proven useful. Re-imaging results are based on the agreement between two independent consultant radiologists who both attend the LGIMDT. Where a complete response was agreed, patients proceeded to timely clinical assessment.

The 10 patients in our group found to have a complete radiological response underwent examination under anaesthetic/flexible sigmoidoscopy and biopsy. None of these patients were found to have residual tumour present following histological analysis. Of these ten patients, 7 were found to have stage II or III disease on initial imaging (Table 1). No direct assessment of response rates between low and locally advanced disease was performed. Follow-up, under direction of the LGIMDT, encompassed re-assessment every 3 months with MRI pelvis-rectum every 6 months. If clinical concerns arose, patients were reviewed earlier and re-discussed. After approximately three and a half years of follow-up 1 patient had succumbed to a synchronous lung tumour and the remaining patients continue on regular surgical follow-up. 16 patients were able to avoid an unnecessary operation as a direct result of restaging. This included patients with disease progression who were able to avoid a major resection and whose care was directed towards symptom control and palliation.

There is recognition that improved imaging techniques will enable better interpretation and more accurate assessment of response. Comparison of pre- and post- treatment images, use of MR volumetry and perfusion MRI are just some approaches suggested.[8] Functional MRI techniques will enable greater understanding of tumour biology, microcirculation, vascular permeability, and tissue cellularity leading to more accurate interpretation and prognostication.[24] Such techniques may enable accurate noninvasive surveillance in a greater number of selected patients.[24]

This study demonstrates that restaging continues to play an important role in the management of patients with rectal cancer. Limitations include a small sample size, retrospective review, limited follow-up and reliance on electronic data. Although all patients were discussed at our local LGIMDT, time from end-of-treatment to re-staging was not standardised. In addition, there was no intention to assess the accuracy of imaging against resected histological specimens as this was not likely to add any further information to current knowledge. Our study does, however, emphasise the essential role of re-imaging in making treatment decisions for patients with rectal cancer.

CONCLUSION

While we acknowledge that restaging techniques require further improvement in order to accurately assess treatment response and assist in surgical planning, we have shown that restaging alters management and avoids surgery in a significant number of patients. Therefore, despite the

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

controversy, we recommend that all patients who receive pre-operative LCCRT for rectal cancer undergo restaging in a multidisciplinary setting.

REFERENCES

1. NICE Clinical Guideline: 131. Colorectal cancer: diagnosis and management. *National Institute for Health and Care Excellence;* 2011.
2. Vignali A, De Nardi, P. Multidisciplinary treatment of rectal cancer in 2014: where are we going? *World J Gastroenterol*. 2014;**20(32)**:11249-61.
3. De Nardi P, Carvello M. How reliable is current imaging in restaging rectal cancer after neoadjuvant therapy? *World J Gastroenterol*. 2013;**19(36)**:5964-72.
4. Lee JH, Jang HS, Kim JG, Lee MA, Kim DY, Kim TH, *et al*. Prediction of pathologic staging with magnetic resonance imaging after preoperative chemoradiotherapy in rectal cancer: pooled analysis of KROG 10-01 and 10-02. *Radiother Oncol*. 2014;**113(1)**:18-23.
5. Hanly AM, Ryan EM, Rogers AC, McNamara DA, Madoff RD, Winter DC, MERRION Study Group. Multicenter evaluation of rectal cancer reimaging post-neoadjuvant (MERRION) therapy. *Ann Surg*. 2014;**259(4)**:723–7.
6. Zhao RS, Wang H, Zhou ZY, Zhou Q, Mulholland MW. Restaging of locally advanced rectal cancer with magnetic resonance imaging and endoluminal ultrasound after preoperative chemoradiotherapy: a systematic review and meta-analysis. *Dis Colon Rectum*. 2014;**57(3)**:388-95.
7. Pomerri F, Pucciarelli S, Maretto I, Zandonà M, Del Bianco P, Amadio L, *et al*. Prospective assessment of imaging after preoperative chemoradiotherapy for rectal cancer. *Surgery*. 2011;**149(1)**:56-64.
8. Kim DJ, Kim JH, Lim JS, Yu JS, Chung JJ, Kim MJ, *et al*. Restaging of rectal cancer with MR imaging after concurrent chemotherapy and radiation therapy. *Radiographics*. 2010;**30(2)**:503-16.
9. NICaN. Regional colorectal cancer network guidelines for the management of colorectal cancer. Belfast: *Northern Ireland Cancer Network;* 2013.
10. MERCURY Study Group. Diagnostic accuracy of preoperative magnetic resonance imaging in predicting curative resection of rectal cancer: prospective observational study. *BMJ*. 2006;**333(7572)**:e779-85.
11. Kye BH, Cho HM. Overview of radiation therapy for treating rectal cancer. *Ann Coloproctol*. 2014;**30(4)**:165-74.
12. Battersby NJ, How P, Moran B, Stelzner S, West NP, Branagan G, *et al*. Prospective validation of a low rectal cancer magnetic resonance imaging staging system and development of a local recurrence risk stratification model: the Mercury II study. *Ann Surg*. 2016;**263(3)**:751-60.
13. Moreno CC, Sullivan PS, Kalb BT, Tipton RG, Hanley KZ, Kitajima HD, *et al*. Magnetic resonance imaging of rectal cancer: staging and restaging evaluation. *Abdom Imaging*. 2015;**40(7)**:2613-29.
14. Kluza E, Rozeboom ED, Maas M, Martens M, Lambregts DMJ, Slenter J, *et al*. T2 weighted signal intensity evolution may predict pathological complete response after treatment for rectal cancer. *Eur Radiol*. 2013;**23(1)**:253-61.
15. Birlik B, Obuz F, Elibol FD, Celik AO, Sokmen S, Terzi C, et al. Diffusion-weighted MRI and MR-volumetry in the evaluation of tumour response after preoperative chemoradiotherapy in patients with locally advanced rectal cancer. *Magn Reson Imaging*. 2015;**33(2)**:201-12.
16. Burton S, Brown G, Daniels IR, Norman AR, Mason B, Cunningham D. MRI directed multidisciplinary team preoperative treatment strategy: the way to eliminate positive circumferential margins? *Br J Cancer*. 2006;**94(3)**:351-7.
17. Brown G, Davies S, Williams GT, Bourne MW, Newcombe RG, Radcliffe AG, *et al*. Effectiveness of preoperative staging in rectal cancer: digital rectal examination, endoluminal ultrasound or magnetic resonance imaging? *Br J Cancer*. 2004;**91(1)**:23-9.
18. Koh DM, Chau I, Tait D, Wotherspoon A, Cunningham D, Brown G. Evaluating mesorectal lymph nodes in rectal cancer before and after neoadjuvant chemoradiation using thin-section T2-weighted magnetic resonance imaging. *Int J Radiat Oncol Biol Phys*. 2008;**71(2)**:456-61.
19. Vliegen RF, Beets GL, Lammering G, Dresen RC, Rutten HJ, Kessels AG, *et al*. Mesorectal fascia invasion after neoadjuvant chemotherapy and radiation therapy for locally advanced rectal cancer: accuracy of MR imaging for prediction. *Radiology*. 2008;**246(2)**:454-62.
20. Bipat S, Glas AS, Slors FJ, Zwinderman AH, Bossuyt PM, Stoker J. Rectal cancer: local staging and assessment of lymph node involvement with endoluminal US, CT and MR imaging – a meta-analysis. *Radiology*. 2004:**232(3)**;773-83.
21. Dickman R, Kundel Y, Levy-Drummer R, Purim O, Wasserberg N, Fenig E, *et al* Restaging locally advanced rectal cancer by different imaging modalities after preoperative chemoradiation: a comparative study. *Radiat Oncol*. 2013;**8**:e278-85.
22. Guillem JG, Ruby JA, Leibold T, Akhurst TJ, Yeung HW, Gollub MJ, *et al*. Neither FDG-PET or CT can distinguish between a pathological complete response and an incomplete response after neoadjuvant chemoradiation in locally advanced rectal cancer: a prospective study. *Ann Surg*. 2013;**258(2)**:289–95.
23. Kuo LJ, Chiou JF, Tai CJ, Chang CC, Kung CH, Lin SE, *et al*. Can we predict pathologic complete response before surgery for locally advanced rectal cancer treated with preoperative chemoradiation therapy? *Int J Colorectal Dis*. 2012;**27(5)**: 613–21.
24. Hötker AM, Garcia-Aguilar J, Gollub MJ. Multiparametric MRI of rectal cancer in the assessment of response to therapy: a systematic review. *Dis Colon Rectum*. 2014;**57(6)**:790-9.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Ulster Med J 2016;**85(3):**182-186

Clinical Paper

Electroconvulsive Therapy - What Do Patients Think Of Their Treatment?

Maguire S, Rea S M, Convery P.

Accepted: 10th February 2016
Provenance: externally peer-reviewed.

ABSTRACT

Background The Regulation and Quality Improvement Authority (RQIA) monitors the administration of electroconvulsive therapy (ECT) in Northern Ireland (NI). As part of their inspection methodology RQIA wished to include feedback from ECT patients. The aim of this report is to summarise the opinions of ECT patients over a 1-year period and to compare their feedback about treatment with the standards of best practice, as defined by the Electroconvulsive Therapy Accreditation Service (ECTAS).

Method RQIA was granted permission to use the ECTAS patient questionnaire. The questionnaire was distributed to all the ECT clinics in NI and staff were requested to give them to patients who had received a course of ECT.

Results A total of 42 individuals returned questionnaires, 24 females (57.1%) and 18 (42.9%) males. The response rate was 26%. Almost half of respondents were detained under the Mental Health (Northern Ireland) Order 1986 (n=19, 45.2%), with one third receiving ECT as a day patient (n=14, 33.3%). Respondents reported having detailed information about ECT, with ECTAS standards 4.2 and 4.3 being affirmed in over 80% of cases. Eighty percent of respondents (n=34) believed they benefited from ECT.

Conclusion The results are mainly favourable towards ECT. The majority felt they benefited from treatment.

Key Words: Electroconvulsive Therapy, User Experience/User Satisfaction, Semi-Structured Interview, Qualitative, Regulation and Quality Improvement Authority, Northern Ireland.

INTRODUCTION

In 2012, the Regulation and Quality Improvement Authority[1] (RQIA), Northern Ireland's (NI) independent health and social care regulator, undertook a review of the practice of Electroconvulsive Therapy (ECT). RQIA used information from the Electroconvulsive Therapy Accreditation Service[2] (ECTAS) to formulate their methodology. ECTAS was set up in England in 2003 by the Royal College of Psychiatrists with the aim of improving the quality of the administration of ECT within the United Kingdom (UK) through a process of assessment and accreditation with an established set of standards.

Despite 70 years of existence and substantial proof of efficacy, ECT still continues to be one of the most controversial and misunderstood treatments in medicine[3]. Convulsive therapy was first introduced in 1934 by Meduna, who believed schizophrenia and epilepsy were antagonistic disorders. He treated patients with chemically-induced seizures. In 1938 Cerletti, an Italian neurologist, successfully treated a patient with electrically-induced seizures and this form of treatment soon replaced chemically-induced seizures.

ECT was originally given "unmodified", i.e., without anaesthesia or muscle relaxants. By the end of the 1950s most hospitals in the UK used "modified" ECT to avoid the serious complications of bone fracture or dislocation. The use of ECT spread throughout the world and was common in UK psychiatric practice during the 1960s and early1970s. At that time, there began some professional and public disquiet over some aspects of its use.

The use of ECT in the UK has been steadily declining since 1985[4] due to the increasing use of effective pharmacotherapy for severe mental disorders. Over the years, many sets of guidelines have been produced by the National Health Service (NHS), the Royal College of Psychiatrists and the National Institute for Care and Excellence to improve standards of administration of ECT. In parallel, the main indication for ECT transformed from first-line to last-resort treatment for medication-resistant and very severe life-threatening conditions. Despite the improvement in all aspects of the delivery of ECT, considerable stigma still surrounds it which undermines public acceptance.

The Regulation and Quality Improvement Authority, 9th Floor, Riverside Tower, 5 Lanyon Place, Belfast, BT1 3BT

team.mentalhealth@rqia.org.uk

Correspondence to Dr Shelagh-Mary Rea,

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

ECT is a safe and effective short-term treatment of depression[5] and other severe psychiatric conditions. In NI it is currently administered to approximately 6 per 100,000 of the general population per year[6]. Recently, a number of reviews have summarised the available literature on patients' experience of ECT[3,7]; however there have been no published studies of local experience.

METHOD

RQIA obtained approval from ECTAS to adapt its patient questionnaire[2] for the purposes of this study. The 32 questions contained in the questionnaire assess demographic details, information given about ECT, consent process, quality of care, side-effects and effectiveness. Questionnaires were distributed by the 7 clinical teams providing ECT within the 5 trusts in NI to patients who had received ECT. These were completed anonymously and returned directly to the RQIA office in Belfast. RQIA provided a stamped addressed envelope to make it easier for respondents.

The data was analysed quantitatively and responses were compared with ECTAS standards for the administration of ECT. The qualitative data was analysed thematically.

An analysis was also carried out, using Fisher's Exact Test, to determine if there were any statistically significant differences between the voluntary group and the detained group of respondents.

RESULTS

A total of 163 patients received ECT in NI between 1 July 2013 and 30 June 2014 and 42 questionnaires were returned giving a response rate of 26%. The ages of the respondents ranged from 37 to 76 years, with a mean of 57 years. More females (n=24, 57.1%) than males (n=18, 42.9%) responded. Almost half of respondents (n=19, 45.2%) were detained under the Mental Health (Northern Ireland) Order 1986 (the Order), with one third (n=14, 33.3%) receiving ECT as a day patient. The majority (n=32, 76.2%) responded to the questionnaire within 6 months of receiving ECT.

Information offered prior to ECT

Almost all respondents indicated that they recall speaking to their doctor before having ECT (n=38, 90.4%); 80.9% (n=34) reported that they were given information about what would happen during ECT; 83.3% (n=35) reported receiving information about why they were having ECT and 83.3% (n=35) reported receiving information about what ECT was likely to do for them. Approximately two thirds of respondents (n=27, 64.3%) received information on side-effects and problems with ECT. Half of the respondents reported receiving information on alternative treatments (n=21, 50%) and information on what would happen if they did not have ECT (n=24, 57.1%). Two thirds of respondents (n=28, 66.7%) recall receiving written information on ECT.

Patient satisfaction with the information they received

The questionnaire invited open comments about how information about ECT could be improved. Of the 26 respondents who provided comment over half (n=16, 61.5%) were satisfied with the information that was given to them. Two respondents (n=2, 7.7%) requested further information on side-effects, while other individuals requested information about appropriate attire for the procedure and an opportunity to speak with those who had had successful treatment with ECT.

Quality of the therapeutic relationship with staff

This study reports that a majority of respondents had a positive relationship with the staff involved in their care. They recalled being accompanied by a staff member to the ECT clinic (n=39, 92.9%); knowing this member of staff (n=35, 83.3%); being introduced to all those present in the theatre (n=28, 66.6%); and the same member of staff being present when they awoke (n=33, 78.6%). Almost all respondents agreed staff were friendly and reassuring and were satisfied the ECT clinic was clean and comfortable (n= 41, 97.6%) and recall being cared for immediately after having ECT (n=41, 97.6%).

Quality of care

Respondents were given the opportunity to provide open comments about the quality of care they felt they received. Twenty-one respondents commented. Almost three-quarters (n=15, 71.4%) stated the care was of the highest quality or could not be better; three (14.3%) found the care satisfactory; and two (9.5%) commented on the professional and competent nature of the staff. No negative comments about the quality of care were received.

The Consent Process

A majority of respondents (n=32, 76.2%) stated they had enough time to discuss their decision to have ECT with a doctor independently. Two-thirds (n=27, 64.3%) agreed to have ECT and recalled signing the consent form; twelve (28.6%) either did not know or did not state whether they signed a consent form and three (7.1%) did not recall signing a consent form. There were nineteen respondents (45.2%) who recalled having ECT as a detained patient, 15 of whom reported that they said to their doctor that they agreed to have the treatment. Whilst the majority recalled their consent for ECT being confirmed immediately prior to ECT, 12 (28.6%) either did not know or did not state whether they provided consent to treatment and 4 (9.5%) recalled that their consent was not checked.

In response to the question "Did you feel pressurised or forced to have ECT" 4 respondents (9.5%) affirmed that they did feel pressurised, 2 from the voluntary group and 2 from the detained group.

Of the respondents who provided open comments on the consent process, 14 (77.8%) were satisfied with the consent process; 2 respondents (11.1%) commented about feeling coerced and one (5.5%) stated it was a family decision.

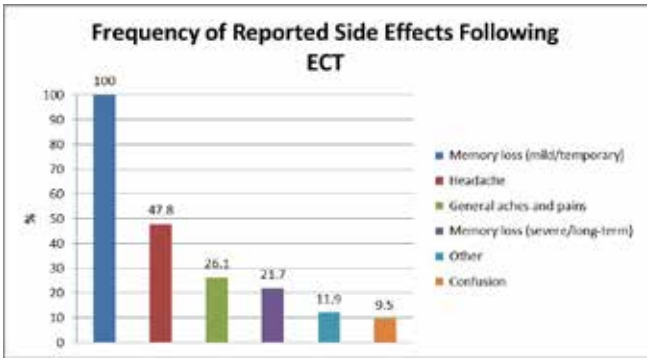
UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Side-effects

Approximately half of the respondents (n=23, 54.8%) reported side-effects with around one quarter (n=11, 26.2%) reporting no side-effects and fewer respondents (n=8, 19%) either not knowing or not stating. Of the 23 respondents reporting side-effects, all reported mild or temporary memory loss and 5 (21.7%) reported severe or long term memory loss. Memory loss was also the most frequent side-effect commented upon in the open question relating to side-effects (n=14, 63.3%). Graph 1 tabulates the frequency of reported side-effects.

Graph 1

Frequency of Reported Side effects Following ECT



Patient Attitudes

Over four-fifths of respondents (n=34, 80.9%) said ECT was beneficial to them, 3 respondents (7.1%) stated it was not beneficial and 5 respondents (11.9%) either did not know or did not state. The qualitative results from the study reflects a highly confident view of ECT with 17 of the 18 comments portraying a positive view of the personal efficacy of ECT and 15 out of 21 commenting on the high quality of care.

Respondents were asked to comment on how their experience of ECT could be improved. The majority of respondents (n=29, 69%) did not provide any specific comment in this section, a small number (n=8, 19%) stated that their care was excellent and could not be improved, 4 respondents (9.5%) suggested "not having to travel" would be an improvement and one respondent (2.4%) commented that there were too many "consultations".

Comparison of voluntary and detained groups of respondents

When the group of 16 voluntary respondents were compared with the group of 19 detained respondents (7 respondents did not give their status) it was found that the voluntary group were statistically significantly younger (p=0.002). There was no significant difference with regard to gender (p=0.841). The voluntary group were statistically significantly more able to recall the information given about problems and side-effects associated with ECT (p=0.010). Four respondents (11%), 2 from the voluntary group and 2 from the detained group admitted feeling pressurised to have ECT. Statistically, there no differences between the groups with regard to feeling pressurised to have the treatment (p=0.859). Almost all respondents in both groups felt that ECT helped them.

ECTAS standards

In relation to the information offered to patients about ECT (Table 1) when the responses obtained from the questionnaire were compared with key ECTAS standards over 80% of respondents affirmed 2 out of 6 standards as having been met. All 6 standards were met by 50% of respondents.

Table 1

Questions asked, ECTAS standards and quantitative results for information offered to patients prior to ECT

Questions	ECTAS standards	Yes	No	Don't know Can't remember	Not stated
Were you given information about what would happen during the treatment?	4.2	34 (81)	1 (2.4)	4 (9.5)	3 (7.1)
Were you given information about why you were having ECT?	4.3	35 (83.3)	1 (2.4)	2 (4.8)	4 (9.5)
Were you given information about what ECT was likely to do for you?	4.3	35 (83.3)	1 (2.4)	3 (7.1)	3 (7.1)
Were you given information about problems and side effects?	4.4	27 (64.3)	10 (23.8)	3 (7.1)	2 (4.8)
Were you given information about other treatments you could have instead?	4.6	21 (50)	12 (28.6)	7 (16.)7	2 (4.8)
Were you given information about what would happen if you didn't have ECT?	4.5	24 (57.1)	7 (16.7)	8 (19.1)	3 (7.1)
Did you receive any written information on ECT	4.11	29 (69)	6 14.3	5 11.9	2 4.8

In relation to the quality of care (Table 2) over 80% of respondents affirmed 4 out of 6 standards. All 6 standards were affirmed by over 60% of respondents.

Table 2

Questions asked, ECTAS standards and quantitative results for quality of care.

Questions	ECTAS Standard	Yes (%)	No (%)	Don't know can't remember (%)	Not stated (%)
Did a member of staff accompany you to the ECT clinic?	3.28	39 (92.8)	1 (2.4)	0 (0)	2 (4.8)
Did you know the member of staff who accompanied you?	3.29	35 (83.3)	3 (7.1)	1 (2.4)	3 (7.1)
When you arrived at the clinic were you introduced to all those who would be present during your treatment?	3.31	28 (66.6)	6 (14.3)	6 (14.3)	2 (4.8)
Did clinic staff check that you still agreed to have ECT before your treatment?	4.41	26 (61.9)	4 (9.5)	10 (23.8)	2 (4.8)
Were clinic staff friendly and reassuring and was the clinic clean and comfortable?	1.2	41 (97.6)	0 (0)	0 (0)	1 (2.4)
Do you feel you properly cared for immediately after the treatment?	7.5	41 (97.6)	0 (0)	1 (2.4)	0 (0)

DISCUSSION

Strengths and weaknesses

The main strength of this study was its use of a national questionnaire developed by ECTAS to examine patient experience when assessing ECT centres in England and Wales for accreditation. The clinical teams administering ECT in NI were asked to invite all patients who had received a course of ECT to complete the questionnaire in order to obtain a representative sample. A further strength was that patients were made aware that their responses were anonymous.

The main limitation of the study is the low response rate of 26%. Although measures were put in place to try to maximise the response rate, RQIA were only indirectly involved in the administration of the questionnaires in order to preserve anonymity and were unable to do a re-mailing of the

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

questionnaire. We cannot therefore be sure that all patients received the questionnaire. More active outreach to the ECT clinics might have increased response rate. The fact that ECT is often used for severely depressed patients who may have a degree of cognitive impairment could also have been a factor.

Main findings

Our response rate of 26% compares with 37% in a large study of patients attending ECTAS accredited clinics and a 57% response rate in an Irish ECT clinic.[8,9] Gathering the views of a representative sample of patients is challenging for organisations not directly providing clinical care. Coulter et al refer to surveys on patient experience by the NHS in England which have response rates similar to ours and found a falling response rate to postal surveys, suggesting an element of "survey fatigue"[10].

Demographic analysis of our sample corresponds with the annual trend[1] in NI for more females (67%) than males to receive ECT. The mean age of our respondents is also similar to the mean age of patients receiving ECT here. While our sample was not representative in terms of location or detained/voluntary/day patient status, it did contain patients who received their ECT under all of these circumstances.

The majority of respondents reported receiving general information about ECT. However, information about alternative treatments, possible outcomes if ECT was not given and side effects received lower ratings and were either less well recalled or were perhaps not always included in the discussions with doctors. Similar percentages recall receiving written information on ECT in our study and the study by Rush et al[9]; 69% and 68% respectively. The importance of detailed discussions with patients and their families, supported by written information in a patient-appropriate form, should be emphasised to clinicians.

Overall, with regard to the consent procedures, the majority of respondents felt they had time to discuss their decision with their doctor and were satisfied with the consent procedures. Again, the majority of respondents reported a good therapeutic relationship with staff (Table 2). The question with the fewest positive responses related to the recall of whether consent to ECT was checked immediately prior to the treatment. Difficulty with recall may be partly due to a degree of retrograde amnesia caused by the procedure.

Myers[11] found refusal of or agreement to ECT on sufferance was linked to an unfavourable view of ECT so it was expected that patients in this study who were treated under the Order would have had a less favourable view. In fact, there were no differences between voluntary and detained groups when considering factors related to quality of care or the beneficial nature of treatment. Neither were there differences between groups with regard to feeling pressurised to have ECT. Of the 4 respondents who felt pressurised to have ECT, 2 were actually from the voluntary group. Therefore, it is likely that influences from sources other than detention under the Order can contribute to patients feeling under pressure to consent. Clinicians may inadvertently put pressure on patients during discussions about treatment or patients may feel under obligation to accept the treatment being offered. One respondent commented that the decision to have treatment was made by the family.

This study revealed a relatively low level of perceived coercion by respondents (one tenth). The Irish study by Rush et al[9] reported an even lower level of perceived coercion in contrast to others who reported coercion rates among respondents of about one fifth to one third. [3,12]

Chakrabarti et al[3] reported that on average 2/3 of their patients reported adverse effects following ECT: roughly 60% in their review reported memory problems and in about 40%, this persisted from several weeks to several years. Philpott et al[13] found that 45% of their patients reported persistent memory loss. In our study, 50% of the respondents reported side-effects and 21.7% reported long term memory loss. Whether ECT results in long-term changes in memory performance is a controversial issue[14] which has not yet been resolved with any certainty. It is, therefore, important that clinicians attend to cognitive factors when recommending ECT and employ strategies within the treatment regime that minimise possible longer term effect on cognitive function.

Although some consider ECT to be effective and potentially life-saving, others regard it as harmful and campaign energetically for it to be banned[15]. An extensive review of the literature on the attitudes of patients to ECT by Chakrabarti et al[3] found evidence that the vast majority of patients perceived ECT to be helpful and had positive views regarding treatment. In our study, 4/5 of respondents felt ECT was beneficial. The majority of open comments referred to the high quality of care received and a small number stated that their experience of ECT could not be improved. Not having to travel long distances for ECT was suggested as an improvement and this should be taken into account by those responsible for planning services.

Kershaw et al[8] reported that the anxiety of patients having ECT may be reduced by personal attention and reassurance from clinical staff known to the patient. The importance of the continuity of staff accompanying the patient on the journey through ECT should be stressed.

Bias

Reliable interpretation of survey data depends on having full information about the survey population, the sample obtained and a high response rate[10]. Our study does not have a detailed profile of responders and non-responders and produced a relatively low response rate which carries a risk of producing bias. A further bias may be due an over representation of day patients amongst respondents who may have had a more positive attitude as they did not have to experience hospitalisation or may have been less ill than in-patients.

Memory loss, which is a frequent side effect of ECT, may have impacted on an individual's ability to accurately recall the information sought by the questionnaire and may have

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

been reflected in the number of "don't know/can't remember" or "not stated" replies. In light of the positive findings of our study, it is possible that patients whose attitude was more favourable towards ECT were more likely to return our questionnaire.

CONCLUSION

Although the majority of respondents were satisfied with the quality of care that they received, not all the selected ECTAS standards were affirmed by the respondents in this study.

REFLECTIONS ON THE PAST

There is no doubt that when senior psychiatrists reflect on the use of ECT, they feel that it was over-used in the 1960s and 1970s but it is important to understand that the range of treatment options was much lower at that time. During a session of ECT, up to 10 in-patients and 30 out- patients may have received ECT whereas now it is unusual to have more than 3 or 4 patients receiving ECT per session. Today, due to the stigma, ECT may in fact be under-used and patients whose depressive conditions could respond to ECT remain unwell despite high doses of medication. Standards of administration of ECT have certainly risen and the technical aspects of treatment have improved to achieve optimal clinical outcomes whilst minimising side-effects. Most psychiatrists would wish to retain the option of giving ECT and would hold the opinion that, in the severely depressed or suicidal patient, it is a life-saving treatment. When applied appropriately, the outcome of its use is very favourable in the short term but measures, including medication, must be put in place for the patient to maintain their recovery.

FUTURE CONSIDERATIONS

Two ECT suites in Northern Ireland have ECTAS accreditation and RQIA will continue to encourage the five other suites to apply for accreditation. RQIA will also seek to improve the patient journey through this treatment by continuing to monitor and inspect ECT services.

LEARNING POINTS

- If appropriate, information about alternative treatments and the consequences of not having ECT should be discussed and recorded
- If appropriate, consent to ECT should be sought prior to each treatment and recorded
- The issue of perceived coercion merits further study.
- Clinicians must take steps to minimise cognitive side-effects and monitor cognition with standardised tests
- Distance to reach the ECT clinic and opportunities to meet those previously treated with ECT should be considered by those planning services
- Continuity of nursing staff accompanying the patient through ECT should be ensured

The authors have no conflct of interest.

ACKNOWLEDGEMENTS

We would like to thank Mike Stevenson, Department of Statistics, Queen's University, Belfast, for the statistical analysis, Professor R Murray and Dr Judy Laing, University of Bristol, Professor R McClelland and Dr C Kelly for their helpful contribution and Claire Henry for her secretarial support.

REFERENCES

1. RQIA Report on the review of electroconvulsive therapy in Bluestone Unit, Craigavon Area Hospital. Belfast: Regulation and Quality Improvement Authority (RQIA); 2013. Available from: http://www.rqia.org.uk/cms_resources/Craigavon%20Area%20Hospital,%20SHSCT%20-%203%20December%202013.pdf. Last accessed May 2016.
2. Buley N, Hailey E, Hodge S. ECT accreditation service (ECTAS): standards for the administration of ECT. 13th ed. London: Royal College of Psychiatrists; 2016. Available from: http://www.rcpsych.ac.uk/workinpsychiatry/qualityimprovement/ccqiprojects/ectclinics/ectas/ectasstandards.aspx. Last accessed May 2016.
3. Chakrabarti S. Grover S, Rajagopal R. Electroconvulsive therapy: a review of knowledge, experience and attitudes of patients concerning the treatment. *World J Biol Psychiatry*. 2010; **11(3)**: 525-37.
4. Eranti SV, McLoughlin DM. Electroconvulsive therapy – state of the art. *Br J Psychiatry*. 2003; **182 (1)**: 8.
5. UK ECT Review Group. Efficacy and safety of electro-convulsive therapy in depressive disorders: a systematic review and meta-analysis. *Lancet*. 2003; **361(9360)**: 799-808.
6. Rea S, Convery P. Report on the administration of electroconvulsive therapy in Northern Ireland. Belfast: Regulation and Quality Improvement Authority (RQIA); 2014. Available from: http://www.rqia.org.uk/cms_resources/ECT%20Report%202013_14.pdf. Last accessed May 2016.
7. Rose D, Fleischmann P, Wykes T, Leese M, Bindman J. Patients' perspectives on electroconvulsive therapy: systematic review. *Brit Med J*. 2003; **326(7403)**: 1363.
8. Kershaw K, Rayner L, Chaplin R. Patients' views on the quality of care when receiving electroconvulsive therapy. *Br J Psych Bull*. 2007; **31(11)**:414-7.
9. Rush G, McCarron S, Lucey J V. Consent to ECT: patients' experiences in an Irish ECT clinic. *Br J Psych Bull*. 2008; **32(1)**:15-7.
10. Coulter A, Locock L, Ziebland S,Calabrese J. Collecting data on patient experience is not enough: they must be used to improve care. *Brit Med J*. 2014; 348; g2225.
11. Myers DH. A questionnaire study of patients' experience of electroconvulsive therapy. *J ECT. 2007*; **23 (3)**:169-74.
12. Rose DS, Wykes TH, Bindman JP, Fleischmann PS. Information, consent and perceived coercion: patients' perspectives on electroconvulsive therapy. *Brit J Psychiatry*. 2005, **186 (1)** 54-9.
13. Philpot M, Collins C, Trivedi P, Treloar A, Gallacher S, Rose D. Eliciting users' views of ECT in two mental health trusts with a user-designed questionnaire. *J Ment Health*. 2004;**13(4)**:403-13.
14. MacQueen G, Parkin C, Marriott M, Begin H, Hasey G. The long-term impact of treatment with electroconvulsive therapy on discrete memory systems in patients with bipolar disorder. *J Psychiatry Neurosci*. 2007; **32(4)**: 241-9.
15. Carney S, Geddes J. Electroconvulsive therapy. *Brit Med J*. 2003; **326(7403)**: 1343-4

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Ulster Med J 2016;**85(3):**187-192

Clinical Paper

Systemic Therapy In Acquired Haemophilia – A Single Institute Experience

Lawless Sarah[1], Das Prantik[2], Benson Gary [1].

Accepted: 7th December 2015
Provenance: externally peer reviewed

ABSTRACT

A cornerstone of the management of Acquired Haemophilia A (AHA) involves inhibitor eradication. First line immunosuppressive agents are usually steroids, either alone or in combination with cyclophosphamide.

We present the use of Rituximab, cyclophosphamide, vincristine and prednisolone (RCVP) combination as immunosuppressant in AHA in a small cohort of patients in order to control their symptoms and eradicate inhibitors.

This was a retrospective analysis of all AHA patients treated at the Northern Ireland Haemophilia centre over a six year period. During this time, a total of six patients were newly diagnosed with AHA. Four of these patients failed to respond conventional therapy of steroids and cyclophosphamide, they were however successfully treated with RCVP/ RCV.

All patients achieved complete remission with this regimen after 1 to 2 cycles of treatment. Remission has been maintained for an extended time period (range 33-69 months).

As AHA is related to immune modulation and, in some cases, underlying malignancy we decided to use this regime as it is effective in either condition.

From our experience, we demonstrate that RCVP combination is a promising treatment in patients with AHA who fail to respond to steroids alone or who have been on pre-existing immunosuppression.

Key words: acquired haemophilia, inhibitor eradication, RCVP

Acquired haemophilia is a rare but serious bleeding disorder which occurs due to the development of autoantibodies (inhibitors) directed against coagulation factors, most commonly factor VIII. The overall incidence of acquired haemophilia is 1.4 per million per year[1]. Given the population of Northern Ireland, we expect 2 new cases per year.

The majority of patients are elderly and in 50% of cases, the aetiology of autoantibodies is idiopathic. In the remainder of patients, autoantibodies may be associated with underlying haematological or solid cancers, pregnancy and autoimmune diseases[2]. Eradicating the autoantibody requires immunosuppression.

Between 2008 and 2012 6 patients were newly diagnosed with Acquired Haemophilia A (AHA) and were referred to the Regional Centre for Thrombosis and Haemostasis in Northern Ireland. Four of these patients received a combination of immunosuppressive agents with RCVP to successfully eradicate their inhibitors. Treatments were administered at 3 weekly intervals (Rituximab 375 mg/m^2, cyclophosphamide 750 mg/m^2, vincristine 1.4mg/m^2 with maximum dose 2mg and prednisolone1mg/kg body weight). A maximum of 2 cycles were administered (median of 1).

To our knowledge there are no published reports of this specific combination to date.

CASE DISCUSSION

Case 1

A 76 year old female presented with a three month history of spontaneous bruising. She had a past medical history of polymyalgia rheumatica, for which she was taking prednisolone 5mg.

She was found to have an isolated prolonged APTT of 68.10. This initially corrected with a 50:50 mix with normal plasma to 35.60. However, after a two hour incubation period the APTT was recorded at 87.90.

Her Factor VIII level was <1% and Factor VIII inhibitor level was 28 Bethseda units (BU) consistent with AHA.

[1]Northern Ireland Regional haemophilia Centre, Belfast City Hospital, Belfast, Northern Ireland. [2]Northern Ireland Cancer Centre, Belfast City Hospital, Belfast, Northern Ireland

sallylawless@hotmail.com

Correspondence to Dr Sarah Lawless

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

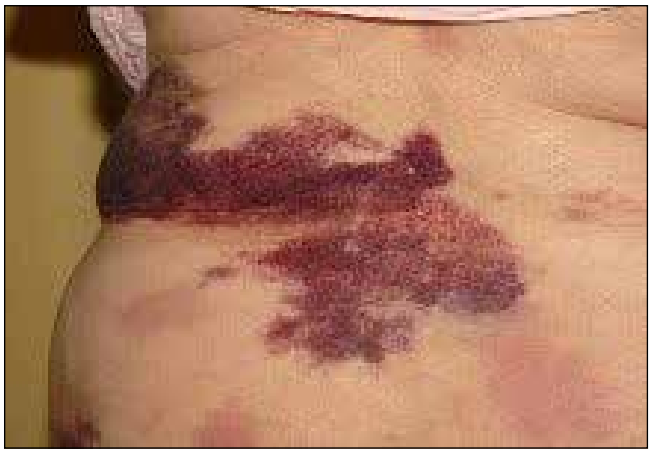


Fig 1. Extensive ecchymosis

Her prednisolone was escalated to 1mg/kg (60mg daily). A CT chest, abdomen and pelvis was performed, there was no evidence of malignancy.

Despite high dose steroids, this patient's treatment course was complicated by severe retroperitoneal bleeding, atrial fibrillation and anginal pain. By day 10 her FVIII level was 5%, but her inhibitor titre had risen to 37 BU.

She required activated recombinant activated factor VII to manage her retroperitoneal bleed.

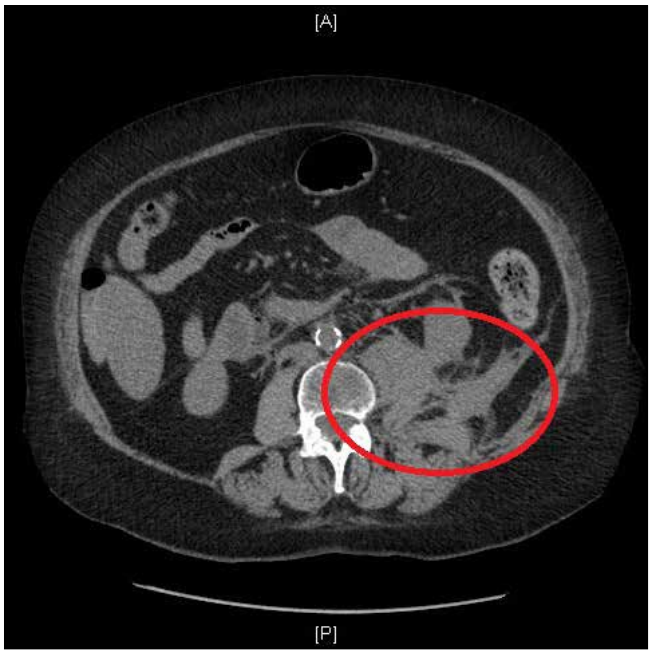


Fig 2. Retroperitoneal haematoma (red circle) on CT scan

A decision was made to commence Rituximab. This was given at a dose of 375mg/m^2 on day 10. The initial plan was to administer this weekly for 4 weeks.

Despite the addition of Rituximab the patient developed a significant right thigh haematoma on day 21. This was associated with a 20g/l drop in her haemoglobin. She required further bypassing agents to achieve haemostasis. Oral cyclophosphamide was commenced at a dose of 100mg daily on day 22 to add additional immunosuppression.

She developed a urinary tract infection, which required antibiotics and had an episode of acute psychosis presumably secondary to high dose steroids. The episode of acute psychosis was extremely distressing to both patient and family. She had ongoing haemorrhagic symptoms. We recognised the need to reduce her steroids back to maintenance dose as soon as possible. Following a multidisciplinary meeting, a decision was made to use a combination of cyclophosphamide, vincristine and prednisolone.

The regimen was the same as the RCVP regimen used in the treatment of Non-Hodgkin Lymphoma (NHL). Vincristine was given at 1.4mg/m^2 and cyclophosphamide 750mg/m^2, both drugs were given intravenously. Prednisolone was given at a dose of 40mg/m^2 orally, which equated to 100mg prednisolone, for 5 days the gradually weaned. This combination was given for the first time on day 48. Rituximab had already been given at 375mg/m^2 weekly and therefore was not given on day 48.

The rationale behind this treatment was that it would provide a boost in immunosuppression and only required 5 days of high dose steroids. It is a commonly used regimen in the treatment of NHL and therefore haematology staff were familiar with its administration and side effect profile.

CVP was well tolerated. By day 66 her FVIII level was 5% and her inhibitor had reduced to 3.83 BU.

CVP was administered again after 21 days, on this occasion Rituximab was also given. She received this second course on day 69.

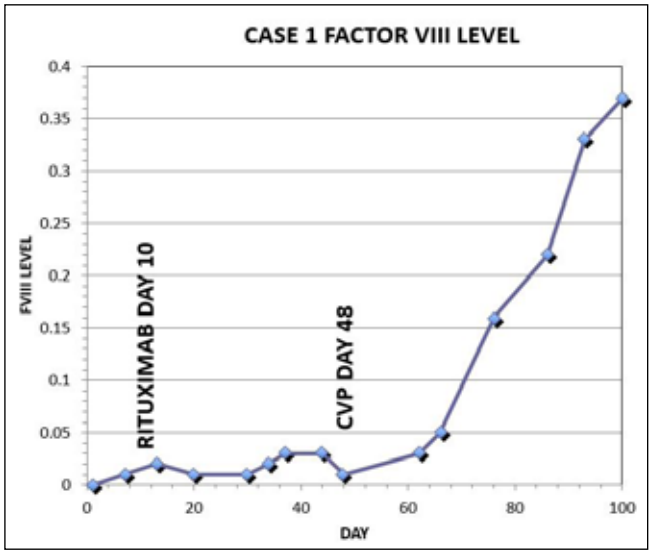


Fig 3. Factor VIII levels with each treatment

By day 76, her FVIII level had risen to 23% and her inhibitor had been suppressed to 0.5 BU. By day 86, her inhibitor had become undetectable, this was 10 days post cycle 2 RCVP. She was on 5mg of prednisolone daily on discharge, which was her maintenance dose for her polymyalgia rheumatica.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

She remains in remission from her acquired haemophilia 69 months after discharge.

It is impossible to determine if this patient experienced a delayed response to Rituximab or benefited from the high dose cyclophosphamide.

Case 2

A 75 year old male presented with haematemesis. A CT scan revealed a dilated oesophagus (filled with fluid and debris) and pancreatitis. On day 4 of his admission, an OGD was unsuccessful due to poor visualisation. On day 11 he had a significant haematemesis therefore OGD was repeated. This revealed a large oesophageal clot measuring 21cm x 34cm. He aspirated during the procedure and was intubated and transferred to intensive care. He was referred to haematology when his coagulation screen revealed an isolated prolonged APTT of 44.30 seconds. This initially corrected to 35.20 seconds with an APTT 50:50 mix. His factor VIII level was found to be 2% and he had a detectable Factor VIII inhibitor at 17.49 BU.

He required a laparotomy to remove the oesophageal haematoma. Given the need for major surgery he underwent plasma exchange with FFP to remove the inhibitor and replace FVIII. He required extensive treatment with factor VIII bypassing agents (FEIBA) and activated recombinant FVII.

On day 8 post laparotomy, wound healing was complete and his pancreatitis had resolved, at this point he was commenced on combination immunosuppression with Rituximab, cyclophosphamide and vincristine. He received 375mg/m^2 of rituximab, 1.4mg/m^2 of vincristine and 750mg/m^2 of cyclophosphamide intravenously. Given his pancreatitis steroid use was avoided.

By day 4 post RCV his FVIII level had risen to 41% and his inhibitor was now 0 BU. His FVIII level continued to make a steady recovery and was 110% on discharge. This patient has had a sustained remission of 52 months to date.

Case 3

A 66 year old female presented with a one week history of widespread bruising. She had a background history of bullous pemphigoid managed with prednisolone 5mg and azathioprine 25mg. She also had a history of laryngeal carcinoma treated with chemotherapy and radiotherapy. She remained on PEG feeding. Other comorbidities included type II diabetes and hypothyroidism.

Her APTT was prolonged at 62.70. She was found to have a Factor VIII level of 2% and AHA was confirmed by the presence of a FVIII inhibitor at 16 BU.

The dose of prednisolone was increased from 5mg to 1mg/kg (70mg) daily. A CT scan was performed and there was no evidence of malignancy

As she was already taking two immunosuppressant medications a decision was made to offer this patient combination Rituximab, cyclophosphamide, vincristine and prednisolone. Given her multiple comorbidities, a 50% dose reduction in cyclophosphamide was made. She received 375mg/m^2 Rituximab, 1.4mg/m^2 vincristine and 325mg/m^2 cyclophosphamide intravenously.

Following the first treatment her factor VIII level was recorded at 10% on day 7 post cycle 1 RCVP. She developed aspiration pneumonia and required intravenous antibiotics. She was not neutropenic. She also required an insulin sliding scale to control her blood glucose while taking steroids. Prior to commencing cycle 2 RCVP her FVIII level was 22%. Following her second cycle her FVIII level continued to rise to 33% on day 7 post cycle 2 RCVP and to 89% by day 23 post cycle 2. No further treatment was required.

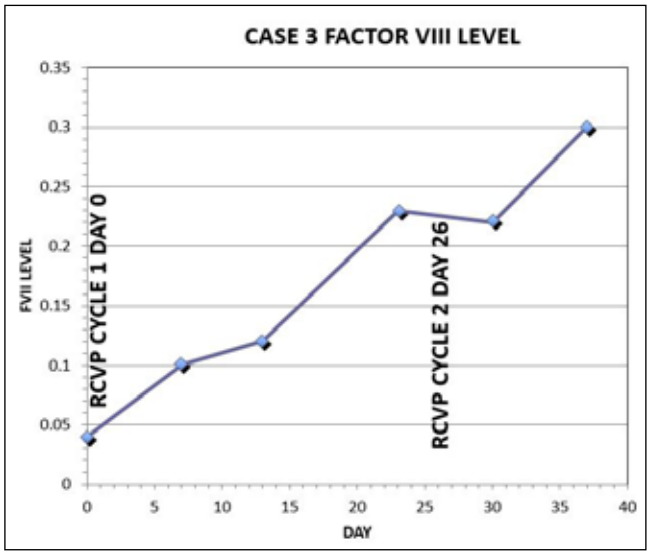


Fig 4. Factor VIII levels in case 3.

Case 4

A 77 year old male presented with continuous bleeding from his tongue after accidently biting it. He had a background of myasthenia gravis treated with 15 mg of prednisolone daily.

His coagulation screen revealed a PT of 14.3 APTT 73.9 and fibrinogen 4.11. His FVIII level was <1% and his inhibitor was recorded at 1200 BU.

His prednisolone dose was increased to 1mg/kg. There was no evidence of malignancy on CT scan.

His FVIII level failed to improve with steroids alone and given the extremely high level of inhibitor, he underwent plasma exchange. Following this, he was commenced on Rituximab 375mg/m^2 intravenously weekly for 4 weeks. This was initially successful in inducing a remission and he was discharged after 2 months with a factor VIII level of 29%. This continued to rise to 120% post 4 cycles of single agent Rituximab. His prednisolone was gradually reduced back to his maintenance dose of 15mg daily.

At routine clinic appointment 5 months later, his FVIII level

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Table 1:

Patients Characteristics:

Age Sex	Presentation	Associated disease	Immuno-suppression prior diagnosis	Factor VIII concent units	Inhibitor Level BU	Haemostatic treatment	Systemic therapy	Complete Remission (CR)duration (months)
76 F	Bruising	Polymyalgia Rheumatica	Prdnisolone 5 mg	<0.01	28	recombinant human coagulation Factor VIIa	RCVPx2	69 months
75 M	Haemoptysis	none	none	0.02	17.49	FEIBA, recombinant human coagulation Factor VIIa	RCVx1	52 months
66 F	Haematoma	Bullous Pemphigoid	Prenisolone 5mg, Azathioprine 25 mg	0.02	16		RCVPx2	33 months
77 M	Bruising	Myasthenia Gravis	Prednisolone15 mg	0.01	1200		RCVP x1	46 months

was found to be 16% with an inhibitor of 1.91 BU. Given our success with other patients, a decision was made to treat this patient with RCVP. He received one course with each drug given at the usual dose. This has been successful in inducing a sustained remission for more than 46 months. The patient is back on maintenance dose steroids.

TOXICITIES

One patient was pyrexic while neutropenic. One patient developed aspiration pneumonia (non neutropenic) and was treated with intravenous antibiotics. No one required GCSF. Transfusion of packed red cells was given in one patient due to bleeding which was not related to a complication of systemic therapy. One patient with a background of type 2 diabetes required an insulin sliding scale due to fluctuating blood sugar related to high dose steroids. No patient developed neuropathy symptoms.

DISCUSSION

All patients with acquired haemophilia should be managed in a comphrensive care haemophilia unit. The principles of treatment consist of;

- arrest bleeding
- protect the patient against trauma and non-essential invasive procedures
- inhibitor eradication
- treatment of precipitating cause if present

Our discussion will focus on inhibitor eradication only.

INHIBITORS ERADICATION:

Inhibitor eradication should be started immediately after confirmation of the diagnosis, as untreated, the mortality of AHA is high. Severe bleeds may be seen in up to 90% of patients with mortality rates ranging between 8-42%[3,4].

A meta-analysis by Delgado *et al* claimed that achieving inhibitor eradication had a significantly better clinical outcome[5].

As AHA is such a rare disorder, randomised trials have not been possible, therefore there is no convincing data that one immunosuppressive regimen is better than another. To date much of the evidence regarding immune suppression comes from case series. The choice of regimen is not determined by the inhibitor titre or FVIII level but should be individualised to the patient.

Prednisolone

First line therapy typically involves steroids, usually prednisolone 1mg/kg daily which can eradicate the inhibitor in approximately 30% of patients[6,7]. Steroids can be used alone or in combination with cyclophosphamide which has been shown to improve response rate significantly[8,9].

Cyclophosphamide

Data from the European Acquired Haemophilia Registry (EACH2) indicated combined therapy of steroids and cyclophosphamide achieved higher stable remission rates. Furthermore a meta-analysis by Delgado *et al* demonstrated higher complete remission rates in those treated with combined steroid and cyclophosphamide therapy rather than steroids alone (89% vs 70%). Higher response rates did not translate into better survival[5]. Another observational study of 172 patients also failed to reveal any significant difference in mortality between patients treated with steroids alone

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

and a combination of steroids and cytotoxic agents mainly cyclophosphamide[1].

Cyclophosphamide is normally used in oral form in most of the published data. EACH2 data included only a very small proportion of patients (9) who had received intravenous cyclophosphamide[10]. We used cyclophosphamide intravenously. We could postulate that an intravenous dose of 750mg/m^2 enhances the effectiveness of the RCVP regimen compared to the standard 2g/kg dose of cyclophosphamide.

As an alkylating agent, cyclophosphamide can result in myelosuppression, infertility, alopecia and increased risk of secondary malignancies. It is therefore not suitable in a pregnant or post-partum patient and should be used with care in the elderly. EACH registry data demonstrated a higher incidence of adverse effects in the group receiving combined treatment (41%) than in those receiving steroids alone (27%)[10]. Meta-analysis by Delgado *et a*l also revealed substantial proportion of patients die as a result of complications associated with this agent, mainly neutropenia-related infections. Indeed, 15% of all deaths in the overall population resulted from infectious complications[5].

Rituximab

Rituximab is a monoclonal antibody directed against the surface molecule CD20 expressed by pre-B cells and memory B lymphocytes. It is administered as an intravenous infusion at a dose of 375mg/m^2 at weekly intervals for four weeks. EACH2 reported 59% of patients had complete remission with a rituximab based regime[10]. A review by Franchini *et al* on 65 patients treated with rituximab and systemic agents showed a CR rate of 90%[11]. However rituximab monotherapy is normally effective in patients with low inhibitor titers[12]. Field *et al* suggested that in patients with high titres, single agent Rituximab alone may be effective but unable to achieve a sustained response and combination with other therapies may provide a better result[13]. The Rituximab-based regimens take longer time to achieve complete inhibitor eradication and normalise FVIII than other agents[10.] The current consensus is that Rituximab should be considered in patients who are resistant to first-line therapy.

Rituximab is not licensed for the treatment of acquired haemophilia, therefore applications for use and funding may delay administration.

Vincristine

Vincristine in combination with cyclophosphamide and prednisolone (CVP) was found to be effective in a small retrospective series of 6 patients[14]. The authors described 5 patients achieving a complete response with no significant adverse effects[15].

Our Experience

We report encouraging results with combination therapy of rituximab, cyclophosphamide, vincristine and prednisolone in patients with AHA. This combination is more commonly used in the treatment of NHL[16]. RCVP has also been used in steroid refractory chronic immune thrombocytopenic purpura[17,18]. As AHA is related to immune modulation and underlying malignancy, we decided to use a regime which is effective in either condition.

Interestingly, 75% of our patients were already taking immunosuppression with either steroids or azathioprine. This leads to the question that if a patient is already on immunosuppressive therapy, is more potent immunosuppression required to induce a remission?

All patients achieved complete remission in this case series. There were no unacceptable toxicities despite patients being in their 6th and 7th decades. Patients in our cohort achieved remission after 1 to 2 cycles (median 1) of treatment. None of the patients relapsed and follow up ranged from 33 -69 months.

This shorter duration of treatment is beneficial to minimise treatment related cumulative toxicities and may prove to be cost effective by reducing hospital visits.

CONCLUSION

While we are unable to conclude that RCVP or RCV is superior to other regimens we suggest that it is a safe alternative treatment option in patients with acquired haemophilia A who are not responding to standard treatment with no additional toxicities observed.

Ideally, this regimen should be investigated further in prospective multicentre trials. However as the disease occurs so infrequently, such studies are very difficult to perform.

ACKNOWLEDGEMENTS

The authors state that they have no conflicts of interest.

REFERENCES:

1. Collins PW, Hirsch S, Baglin TP, Dolan G, Hanley J, Makris M, Keeling DM, *et al*. Acquired hemophilia A in the United Kingdom: a 2-year national surveillance study by the United Kingdom Haemophilia Centre Doctors Organisation. *Blood*. 2007; **109(5)**: 1870–7.
2. Ma AD, Carrizosa D. Acquired factor VIII inhibitors: pathophysiology and treatment. *Hematology Am Soc Hematol Educ Program*. 2006; 432–7.
3. Franchini M, Lippi G. Acquired factor VIII inhibitors. *Blood*. 2008;**112(2)**:250–55.
4. Collins PW, Chalmers E, Hart D, Jennings I, Liesner R, Rangjaragan S, *et al*. Diagnosis and management of acquired coagulation inhibitors: a guideline from UKHCDO. *Br J Haematol*. 2013; **162(6)**:758-73
5. Delgado J, Jimenez-Yuste V, Hernandez-Navarro F, Villar A. Acquired haemophilia: review and meta-analysis focused on therapy and prognostic factors. *Brit J Haematol*. 2003; **121(1)**: 21–35.
6. Green D, Lechner K. A survey of 215 non-hemophilic patients with inhibitors to Factor VIII. *Thromb Haemost*. 1981. **45(3)**, 200–3.
7. Spero JA, Lewis JH, Hasiba U. Corticosteroid therapy for acquired F VIII: C inhibitors. *Brit J Haematol*. 1981; **48(4)**: 635–42.
8. Green D, Rademaker AW, Briet E. A prospective, randomized trial of prednisone and cyclophosphamide in the treatment of patients with factor VIII autoantibodies. *Thromb Haemost*. 1993; **70(5)**: 753–7.
9. Shaffer LG, Phillips M, Successful treatment of acquired hemophilia with

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

oral immunosuppressive therapy. *Ann Intern Med*. 1997; **127(3)**: 206–9.

10. Collins P, Baudo F, Knoebl P, Lévesque H, Nemes L, Pellegrini F, *et al*., EACH2 registry collaborators. Immunosuppression for acquired hemophilia A: results from the European Acquired Haemophilia Registry (EACH2). *Blood*. 2012; **120(1)**:47-55.
11. Franchini M. Rituximab in the treatment of adult acquired hemophilia A: a systemic review. *Crit Rev Oncol Hematol*. 2007; **63(1)**:47–52.
12. Stasi R, Brunetti M, Stipa E, Amadori S. Selective B-cell depletion with rituximab for the treatment of patients with acquired hemophilia. *Blood*. 2004; **103(12)**: 4424–8
13. Field JJ, Fenske TS, Blinder MA. Rituximab for the treatment of patients with very high-titre acquired factor VIII inhibitors refractory to conventional chemotherapy. *Haemophilia*. 2007; **13(1)**: 46–50.
14. Lian EC, Villar MJ, Noy LI, Ruiz-Dayao Z. Acquired factor VIII inhibitor treated with cyclophosphamide, vincristine, and prednisone. *Am J Hematol*. 2002; **69(4)**: 294–5.
15. Lian EC, Larcada AF, Chiu AY. Combination immunosuppressive therapy after factor VIII infusion for acquired factor VIII inhibitor. *Ann Intern Med*. 1989; **110(10)**: 774–8.
16. Marcus R, Imrie K, Belch A, Cunningham D, Flores E, Catalano J, *et al*. **CVP chemotherapy plus rituximab compared with CVP as first-line treatment for advanced follicular lymphoma.** *Blood*. 2005, **105(4):**1417-23.
17. Hasan A, Michel M, Patel V, Stasi R, Cunningham-Rundles S, Leonard JP, *et al*. Repeated courses of rituximab in chronic ITP. *Am J Hematol*. 2009; **84(10)**: 661–5.
18. McMillan R. Long-term outcomes after treatment for refractory immune thrombocytopenic purpura. *New Engl J Med*. 2001;**344(18)**:1402–3.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Ulster Med J 2016;**85(3):**193-195

Case Report

Radial Multi-Site, Longitudinal Multi-Polar Epicardial Left Ventricular Pacing In Tricuspid Valve Disease

Ernest W Lau,[1] Tony McEntee,[2] Kyle B Ashfield, [1] Alastair N Graham [3]

Accepted 21st February 2016
Provenance: externally peer-reviewed

ABSTRACT

Tricuspid valve (TV) disease (which includes surgical repair) can impede transvenous endocardial right ventricular pacing. A lead crossing the TV can damage and be damaged by the valve, especially in the presence of mechanical prostheses (valve, annuoplasty ring, artificial chordae). Surgical epicardial lead placement requires sternotomy or thoracotomy and pericardotomy, with associated morbidity and mortality. Surgical epicardial leads perform less well than endocardial leads over time and may induce pericardial adhesions. With the possibility of radial and longitudinal multi-site pacing and pulse generators with versatile programmability, transvenous epicardial lead placement through the coronary sinus has become robust and reliable, and may provide the best approach for achieving permanent ventricular pacing in patients with TV disease.

CASE HISTORY

A 75 year old male patient underwent tricuspid valve (TV) repair for severe regurgitation due to a flail anterior leaflet caused by chordal rupture after a motor vehicle accident. The anterior leaflet was re-attached to the papillary muscle with 4 artificial chordae made of sutures at the tip, and sutured to the septal and posterior leaflets at the base. The tricuspid annulus was buttressed with an annuloplasty ring with a gap over the septal region for atrio-ventricular node (AVN) and His bundle preservation. With these measures, tricuspid competence was achieved. Coronary artery bypass grafting was performed at the same time. The patient made an uneventful recovery from his cardiac surgery. However, he developed multiple arrhythmias, including sinus rhythm with complete heart block (CHB) and narrow complex escape rhythm (Fig 1a), paroxysmal atrial fibrillation (AF) with left (Fig 1b) and right (Fig 1c) bundle branch block (BBB), and paroxysmal atrial flutter with 2:1 A:V conduction (Fig 1d), over a 3 week period.

The management of the patient's multiple arrhythmias, which included both bradycardia and tachycardia, posed several clinical challenges. The patient displayed evidence of significant AVN and infra-Hisian conduction system disease, and hence required permanent pacing. Transvenous endocardial right ventricular (RV) pacing required crossing the TV with a lead, not ideal given the previous disease and recent surgical repair. Surgical epicardial pacing required repeat sternotomy and pericardotomy, an especially unattractive option soon after cardiac surgery. Transvenous epicardial left ventricular (LV) pacing through the coronary sinus (CS) avoided these concerns and was deemed the best approach.[1-3]

The patient suffered from atrial flutter, but successful cavo-tricuspid isthmus ablation would be difficult and potentially dangerous in the presence of an annuloplasty ring (the ablation catheter needed to get under the ring; risk of ring dehiscence and para-prosthetic leakage). The patient was also likely to develop persistent or permanent AF over time, even with anti-arrhythmic drugs or ablation. Based on these considerations, it was decided the patient's atrial tachyarrhythmias would be best controlled by AVN ablation, especially as he already had a class I indication for permanent pacing. However, AVN ablation with the intentional induction of iatrogenic CHB placed a heavy burden on the reliability of permanent pacing. Transvenous epicardial LV pacing through the CS may fail post-operatively due to lead dislodgement, elevation of pacing threshold and phrenic nerve stimulation.[4, 5] Even though the patient had normal LV function, it was decided the patient should have 2 leads placed in 2 different side branches of the CS if technically feasible in case one of the leads failed post-operatively.[1] Radially separated multi-site LV pacing may also provide an alternative form of cardiac resynchronization therapy (CRT).[6]

During permanent pacemaker implantation, the CS was found to have a large antero-lateral vein (ALV) and a middle cardiac vein (MCV) suitable for lead placement (Fig 2a). A quadripolar Quartet LV lead (St Jude Medical, Sylmar, CA, USA) was first positioned in the ALV with the tip advanced as distally as possible. The distal bipole (D1-M2, marked by § in Fig 2b) produced the best pacing parameters. A bipolar Quickflex µ LV lead (St Jude Medical) was next positioned in the MCV with the tip advanced as distally as possible. However, all the distal lead tip positions near the

[1]Department of Cardiology and [3]Department of Cardiac Surgery, Royal Victoria Hospital, Belfast, Northern Ireland [2]PEI Surgical Limited, Dublin, Republic of Ireland

ernest.lau@btinternet.com

Correspondence to Dr E W Lau

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

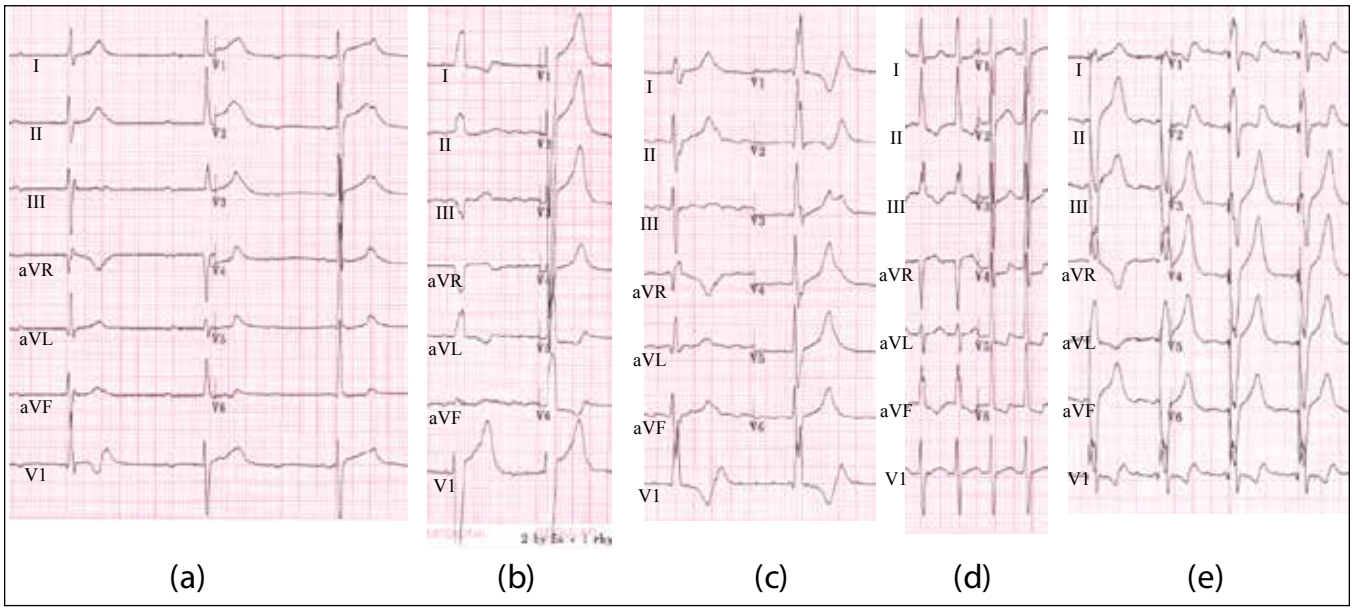


Fig 1. Electrocardiograms of arrhythmias and multi-site epicardial left ventricular pacing

(a) Complete heart block with narrow complex escape rhythm (b) Atrial fibrillation with left bundle branch block (c) Atrial fibrillation with right bundle branch block (d) Atrial flutter with 2:1 A:V conduction (e) Multi-site epicardial left ventricular pacing

apex (including into smaller second order side branches) failed to produce pacing capture of the LV. The only lead tip position that produced acceptable pacing parameters was very proximal (marked by * in Fig 2b) with a high risk of dislodgement. Based on the existent knowledge of the pacing characteristics at different sites, it was decided a better long term outcome for the patient would be achieved by swapping the quadripolar and the bipolar LV leads around (Fig 2c). The most distal bipole (D1-M2) of the quadripolar lead delivered the largest sensed R wave at 9.7mV whereas the most proximal bipole (M3-P4) delivered the best pacing threshold of 1.25V at 0.4ms, with no diaphragmatic stimulation. The bipolar lead delivered a small sensed R wave and the best pacing threshold was 1.75V at 1ms with no phrenic nerve stimulation with the tip-to-can pulse configuration. The lead configuration of the 2 LV leads was accepted. An active fixation pacing lead was positioned in the right atrium. The leads were connected to the Allure Quadra biventricular pacemaker pulse generator (St Jude Medical), programmed to sense the R wave from the LV (the most proximal bipole of the quadripolar lead in the MCV) instead of the RV port. AVN ablation produced CHB with a right BBB pattern escape rhythm at around 45bpm. The patient felt substantially better post procedure with control of both his bradycardia and tachycardia (Fig 1e). The chest X-rays (Fig 3) and pacing check were all satisfactory. He was discharged home the day after his procedures.

DISCUSSION

TV disease (which includes surgical repair) poses special problems for transvenous endocardial RV lead placement. A lead crossing the TV can induce stenosis[7] and regurgitation,[8] either through the physical presence of the lead or other biological processes such as fibrosis, thrombosis or infection.[9] In this case, such a lead might interfere with the artificial chordae and cause recurrent TV regurgitation, defeating the main therapeutic aim of the original cardiac surgery. The TV leaflets might abrade against the lead, causing failure through outside-in abrasion of insulation[10, 11] and even conductor fracture,[12] especially in the presence of an annuloplasty ring.[13] Surgical epicardial lead placement requires sternotomy, thoracotomy and pericardotomy, with associated morbidity and mortality. Epicardial leads do not last as long as endocardial leads in general, and often suffer from a rising pacing threshold as well as insulation breach and conductor fracture over time.[4, 14] Epicardial leads may induce pericardial adhesions, making subsequent replacement difficult. In contrast, transvenous epicardial LV pacing through the CS avoids all these issues and may provide the best approach for patients with TV disease.

However, transvenous epicardial LV pacing through the CS suffers its own inherent limitations, including lack of suitable side branches, lead dislodgement, phrenic nerve stimulation, and less reliable pacing and sensing characteristics.[4, 5] The quadripolar lead was specifically developed to address these issues, and the Quartet was the first such lead commercially available. Similarly, the Allure Quadra is currently the only available biventricular pacemaker capable of accepting a quadripolar LV lead. One functional feature which proved pivotal in this case was the Allure Quadra's versatility in sensing the ventricles from either the RV port or the LV port (with the choice of multiple bipoles, independent of the pacing pulse configuration). Other manufacturers may wish to replicate this versatility in developing their comparable pulse generator models.

Transvenous epicardial LV pacing through the CS produces satisfactory long term performance and pacing outcomes.[15]

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

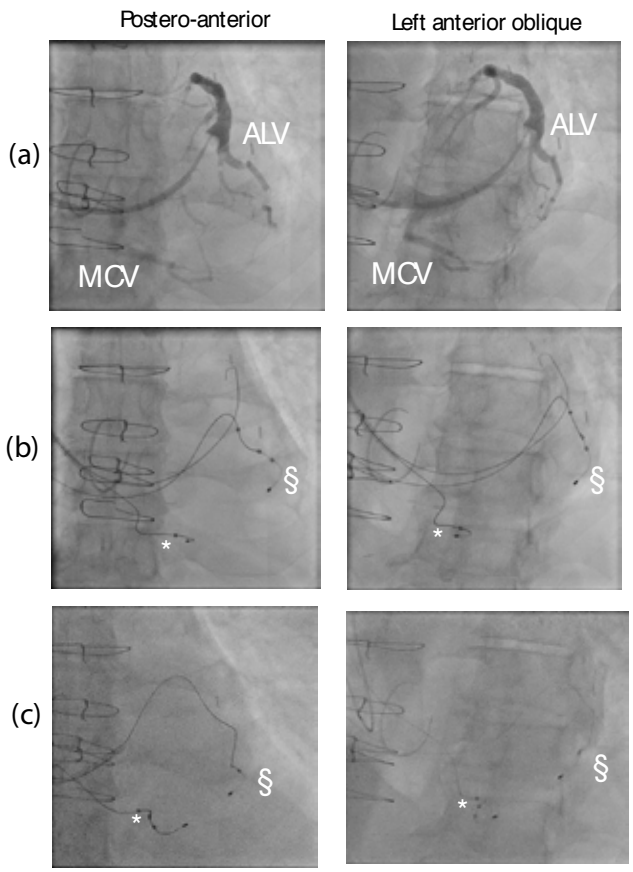


Fig 2. Radial multi-site longitudinal multi-polar epicardial left ventricular pacing

(a) Coronary sinus venogram revealed an antero-lateral vein (ALV) and middle cardiac vein (MCV) suitable for lead placement. (b) A quadripolar lead was placed in the ALV (best pacing site marked by §) and a bipolar lead in the MCV (best pacing site marked by *). There was concern the bipolar lead might dislodge from the MCV given the proximity of the tip position. (c) The quadripolar and bipolar leads were swapped around to achieve the optimal combination of positional stability and pacing parameters for both leads.

With extension of operators' experience in CRT and advances in lead and pulse generator technologies offering ever expanding options, radial multi-site longitudinal multi-polar epicardial LV pacing should be the preferred approach for delivering permanent pacing to patients with TV disease.

Conflicts of interest: EWL consultancy for St Jude Medical

REFERENCES

1 Bos HS, Pop GA, Stel EA, van Gelder BM. Dual site coronary sinus pacing in a patient with an artificial tricuspid valve prosthesis. *Pacing Clin Electrophysiol*. 2004;27(10):1451-52.

2 Nguyen LS, Swaroop S, Prejean CA. Pacing in the middle cardiac vein in a patient with tricuspid prosthesis. *Pacing Clin Electrophysiol*. 2002;**25(2)**:243-4.

3 Herre JM, Bullaboy CA, Derkac WM, Dow MT. Permanent transvenous dual-chamber pacing using the coronary sinus in a patient with a mechanical prosthetic tricuspid valve. *Pediatr Cardiol*. 2004;**25(1)**:65-6.

4 Lau EW. Achieving permanent left ventricular pacing-options and choice. *Pacing Clin Electrophysiol*. 2009;**32(11)**:1466-77.

5 Lau EW. Cardiac resynchronization therapy - the remaining challenges. *J Innovation Card Rhythm Manag*. 2012;**3(Apr)**:747-57.

6 Padeletti L, Colella A, Michelucci A, Pieragnoli P, Ricciardi G, Porciani MC, Tronconi F, et al. Dual-site left ventricular cardiac resynchronization therapy. *Am J Cardiol*. 2008;**102(12)**:1687-92.

7 Cassagneau R, Jacon P, Defaye P. Pacemaker lead-induced severe tricuspid valve stenosis: complete percutaneous extraction under extracorporeal life support. *Europace*. 2013;**15(9)**:1248.

8 Baquero GA, Yadav P, Skibba JB, Banchs JE, Linton-Frazier LN, Lengerich EJ, *et al*. Clinical significance of increased tricuspid valve incompetence following implantation of ventricular leads. *J Interv Card Electrophysiol*. 2013;**38(3)**:197-202.

9 Polewczyk A, Kutarski A, Tomaszewski A, Brzozowski W, Czajkowski M, Polewczyk M, *et al*. Lead dependent tricuspid dysfunction: Analysis of the mechanism and management in patients referred for transvenous lead extraction. *Cardiol J*. 2013;**20(4)**:402-10.

10 Lau EW. External insulation breach near the tip of a single ventricular pacing lead. *J Innovation Card Rhythm Manag*. 2012;**3(Feb)**:668-70.

11 Novak M, Dvorak P, Kamaryt P, Slana B, Lipoldova J. Autopsy and clinical context in deceased patients with implanted pacemakers and defibrillators: intracardiac findings near their leads and electrodes. *Europace*. 2009;**11(11)**:1510-6.

12 Clarke B, Jones S, Gray HH, Rowland E. The tricuspid valve: an unusual site of endocardial pacemaker lead fracture. *Pacing Clin Electrophysiol*. 1989;**12(7 Pt1)**:1077-9.

13 Hauser RG, Abdelhadi RH, McGriff DM, Kallinen Retel L. Failure of a novel silicone-polyurethane copolymer (Optim) to prevent implantable cardioverter-defibrillator lead insulation abrasions. *Europace*. 2013;**15(2)**:278-83.

14 Tomaske M, Gerritse B, Kretzers L, Pretre R, Dodge-Khatami A, Rahn M, *et al*. A 12-year experience of bipolar steroid-eluting epicardial pacing leads in children. *Ann Thorac Surg*. 2008;**85(5)**:1704-11.

15 Grimard C, Clementy N, Fauchier L, Babuty D. Ventricular pacing through coronary sinus in patients with tricuspid prosthesis. *Ann Thorac Surg*. 2010;**89(6)**:e51-2.

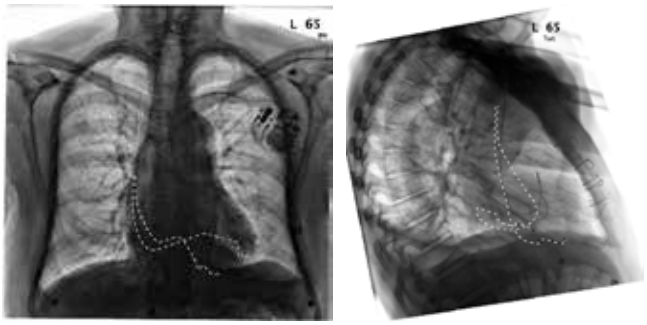


Fig 3. Chest X-rays showing bipolar and quadripolar leads in different side branches of the coronary sinus

The tricuspid annuloplasty ring can be clearly seen in the left anterior oblique projection.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Ulster Med J 2016;**85(3):**196-202

Medical History

Orthopaedic Surgery in World War II: Military and Medical Role of Northern Ireland

John Hedley-Whyte, Debra R. Milamed

Accepted: 12th June 2016
Provenance: externally peer-reviewed

INTRODUCTION

Belfast, Boston Massachusetts, Oswestry Shropshire and Oxford were the sites of publications on the regionalisation of Orthopaedic Surgery centres which have led to our present trauma centres. Professors Andrew Fullerton and Thomas Sinclair of Queen's Belfast were under the Allied Command of Sir Alfred Keough, head of the RAMC who appointed Robert Jones of Oswestry as Commander of Allied Orthopaedics for World War I. Both Jones and Keough established orthopaedic regional centres and orthopaedic hospitals in England, France and Scotland. In total, they comprised 30,000 beds. Jones also treated as patients and trained as surgeons: Harry Platt, Gathorne Robert Girdlestone, Henry Osmond Clark and Reginald Watson-Jones, who were later to become prominent consulting professorial orthopaedic surgeons.

INTERVAL BETWEEN WORLD WAR I AND WORLD WAR II

Realising that 70% of Allied World War I war wounds involved bone injuries[1,2], Professor Lord Moynihan, Leeds and Professor Gerald Gask, Barts, agreed that a committee should be set up to consider all aspects of orthopaedic staffing and equipment[3]. This committee first met at Bath during August 1925 under the auspices of the British Medical Association (BMA). Later, the BMA, the RAMC and the British Orthopaedic Association informed the American Orthopedic Association that the regionalisation of Orthopaedics instituted by Generals Sir Robert Jones and Sir Alfred Keough would be continued as British policy.[1,3,4] The results were superior when regionalisation had been deployed.[3]

Five months before Hitler gained power in Germany, Professor and Mrs. Gathorne Robert Girdlestone were invited to Harvard, New York and Baltimore and to address the American Orthopedic Association[5]. Both spoke. Professor Girdlestone was "the great missionary of regional orthopaedics with its central orthopaedic hospital, satellite clinics and unified staff" and "the hospital was an extension of… home life which was made idyllically happy by his wife Ina."[6] Professor and Mrs. Girdlestone discussed and delineated Orthopaedic regionalisation and planning at Harvard University for a week, and then with Massachusetts General Hospital staff and Harvard students. The Girdlestones continued on to New York and Baltimore, back to Boston, thence to Buffalo, NY and Toronto, where the American Orthopedic Association was meeting.

Fig 1. Gathorne Robert Girdlestone (1881-1950), oil on canvas, 29.5" by 24.5", by Frank S. Eastman (1878-1964), Photography by Lafayette Ltd. Reproduced with permission of Oxford Health NHS Foundation Trust, Oxfordshire Health Archives, Oxfordshire History Centre and Lafayette Ltd. solely for this Medical History.

On July 20, 1932, Girdlestone (Figure 1) wrote to Sir Robert Jones, about the excellent Platt (Fig. 2)[7,8,9] who had trained at the Massachusetts General Hospital.

In November 1937, Lord Nuffield gave £26,000 "to develop orthopaedics in Northern Ireland[5,10]" . In addition, Lord Nuffield promised to "Provide for honoraria to help young surgeons specialise in orthopaedic surgery." (Table 1) This announcement was written at Nuffield's request by Girdlestone, now elected Nuffield Professor of Orthopaedics at Oxford University[5].

The Travelling Surgeons Club (a group of 20 WWI

David S. Sheridan Professorship in Anaesthesia and Respiratory Therapy, Harvard University, 1400 VFW Parkway, Boston, MA 02132-4927 USA

john_hedley-whyte@hms.harvard.edu

Correspondence to Prof. Hedley-Whyte

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Fig 2. Sir Harry Platt, 1886-1986. Oil on canvas by Sir William Oliphant Hutchison PRSA (1889-1970), 37" x 31.5". Reproduction courtesy of the Hunterian Museum at the Royal College of Surgeons of England and reproduced with their permission solely for this Medical History.

surgeons), along with the Surgical Travellers[14], at their spring 1939 meeting in Belfast suggested that a Northern Ireland Orthopaedic Committee be formed under the Chairmanship of David Lindsay Keir, Vice Chancellor of Queen's University[14,15] (Fig 3). He read Philosophy and Modern Languages at Glasgow University from where he volunteered for the Royal Scottish Borderers. Wounded twice at the Somme[16] and Arras he became acquainted with Jones's organisation for Allied wounded triage and treatment. Keir completed his undergraduate study at Oxford and was there elected to a fellowship at University College. Called to Harvard for 1923 and 1924 as tutor, he became cognisant of a very strong Orthopaedic Department described by Platt in a panegyric on his Harvard training at the Massachusetts General Hospital[9]. Keir returned to University College, Oxford University to assume Bursarial duties[17,18,19,20,21,22,23,24]. These responsibilities led to friendship with Sir William Morris, later Lord Nuffield, and Professor Girdlestone, Nuffield Professor of Orthopaedics. Girdlestone, Irish Amateur golf Champion and Oxford golf blue[25], enjoyed golfing with W. Rowley Bristow, a Scratch Player, Nuffield Head of Orthopaedics at St. Thomas's Hospital, London and designate of the RAMC[26].

KEIR COMMITTEE EXECUTIVE AND PLENARY

Vice Chancellor Keir of Queen's chaired the committee beginning with its first meeting on Monday, March 11, 1940, to discuss a "draft scheme drawn up for Northern Ireland by the Central Council for the Care of Cripples[15,27]." The Committee's aims were "A. The recognition of orthopaedics

TABLE 1.

Nuffield Orthopaedic Benefactions, 1935-1942[10,11,12]

DATE	Original Amount	2015 £ equivalent[13]	Recipient
1935	£275,000	£15,867,500	Nuffield Fund for Cripples
1935	£321,800	£18,567,860	Nuffield Fund for Orthopaedic Services in Australia, New Zealand, and the Union of South Africa
1935	£8,000	£461,600	Radcliffe Infirmary, New Wards
1935	£16,000	£923,200	Nuffield Institute of Medical Research
1936	£10,000	£572,000	Albert Dock Hospital (Fracture Clinic)
1936	£2,000,000	£114,400,000	Medical School Trust
1936	£100,000	£5,720,000	Higher Studies Fund
1937	£300,000	£16,620,000	Oxford Hospitals and Nursing Services
1937	£26,000	£1,440,400	Northern Ireland Allocation
1937	£25,000	£1,385,000	Princess Elizabeth Orthopaedic Hospital, Exeter
1938	£31,380	£1,697,658	Wingfield-Morris Orthopaedic Hospital
1940	£250,000	£11,875,000	Royal Air Force Benevolent Fund
1941	£1000 Nuffield Block Grant authorized	£42,900	Northern Ireland Council for Orthopaedic Development (NICOD)
1942	£2000 requested	£79,800	Request by NICOD for funds for medical training and treatment
TOTAL		£189,652,918	

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Fig 3. Sir David Lindsay Keir, LL.D (1895-1973). Oil on canvas, 47" by 33" , by Allan Gwynne-Jones, 1960. Reproduced with permission of the Master and Fellows of Balliol College, solely for this Medical History.

as a specialty in the University and B. A central open-air Orthopaedic Hospital for long-stay cases[27]." The consensus was that both objectives, including the appointment of a full time Orthopaedic Surgeon and Professor of Orthopaedics at Queen's, had to be deferred until defeat of Germany. The creation of regional orthopaedic clinics in Northern Ireland on the Robert Jones model was strongly endorsed and realised with Nuffield money (Table 1). Personnel were sent to Oswestry and Oxford to be trained as Orthopaedic Sisters and technicians. A Northern Irish Orthopaedic instrument and device industry was launched, again[28] with Nuffield support[10,15] (Table 1). Watson-Jones, Civilian Advisor to the Royal Air Force was invited and accepted an invitation to address the Northern Ireland Council for Orthopaedic Development (NICOD) on 11 September 1941[15,29,30]. The regional directors of the North West England Emergency Medical Service Hospitals were engaged in mutual support in patient transfers. The RAF and U.S. Army Air Force provided NICOD with air transport facilities for patients, medical consultants and needed support staff. Planning was undertaken for the desired entry of the United States into the war. The Executive committee decided that public plenary meetings of NICOD should be chaired by the Duchess of Abercorn, DBE. Northern Irishman, Mr. R Jimmy W Withers, a surgeon of proven executive ability, should be co- opted as leader and guarantor of the future of orthopaedics in Northern Ireland. Withers had gained first-class honours from Queens in 1930. He was MD Gold Medalist then M.Ch. highly commended. Sir Ian Fraser, the host of the 1939 Surgical Travellers meeting in Belfast of 15 members had successfully proposed Withers as a member for being "the best of good crack". Withers was a Rugby Blue and an excellent golfer: fluent in French and German. He was popular in the "intellectual rugby team" of the Surgical Travellers founded in 1927.[14,15] Fraser, was thanked for his service on the Executive Committee. Fraser was now surgeon to the Allied Medical Services to the Mediterranean Theatre[14]. As a result of this NICOD meeting, there was publicity on Northern Ireland not having another orthopaedic surgeon. This adverse publicity was at least partially countered by my*father now working at Musgrave Park[31] , who said that since he had worked as surgeon to the UK Coal Trade since 1936, and Fraser had worked as surgeon at St. Helens, both were experienced in orthopaedics and trauma. Withers, together with Thomas B. Quigley[32], and Queen's University were funded by Nuffield to send three potential assistant surgeons for further training at Oxford, Oswestry and Exeter. The RAF (and from June 1942, the U.S. Army Air Force) agreed to fly essentially all patients with combined orthopaedic and neurological injuries to Oxford; Neurosurgery at Saint Hilda's College under Cairns and Calvert. The treatment of Orthopaedic lesions was under the purview of Girdlestone and Joseph Trueta of Spanish Civil War Fame[5].

Major Quigley, former intern of Harvey Cushing and head of Orthopaedics at Musgrave Park from May to December 1942[32], was de facto senior orthopaedic consultant for Northern Ireland. Later, when I worked with him at Harvard, he stated that Belfast was as hard as interning for Harvey Cushing. Quigley pointed out that without more trained and devoted physiotherapists, nurses, occupational therapists and plasterers, return to health and duty was delayed or thwarted[33]. Platt (Fig. 2) and Watson-Jones promised better and faster training as an Allied priority[30,33,34]. Watson-Jones, Civilian Consultant to the RAF and constant visitor to Air Stations, with Sir Archibald Sinclair, Minister of Air in the British Cabinet agreed. With increased training, Air Crew Hospitals, limitation of mandatory tours of duty, results and times of return to flying improved. Osmond-Clarke, also Harvard trained[1,2] (Fig. 4), on the recommendation of Platt became Air Commodore and Head of Orthopaedics for the RAF.

US DEPLOYMENTS

In January and February 1943, Bristow, as Head of Orthopaedics, RAMC, was sent to the US by Churchill's War Cabinet to advise that U.S. Army deployments of orthopaedic surgeons were not realistic for the invasion of France[26]. In the Mediterranean, with an Allied Command structure, therapy and evacuation were reasonably satisfactory. Since in France, Medical Services were to be divided, where were

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

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

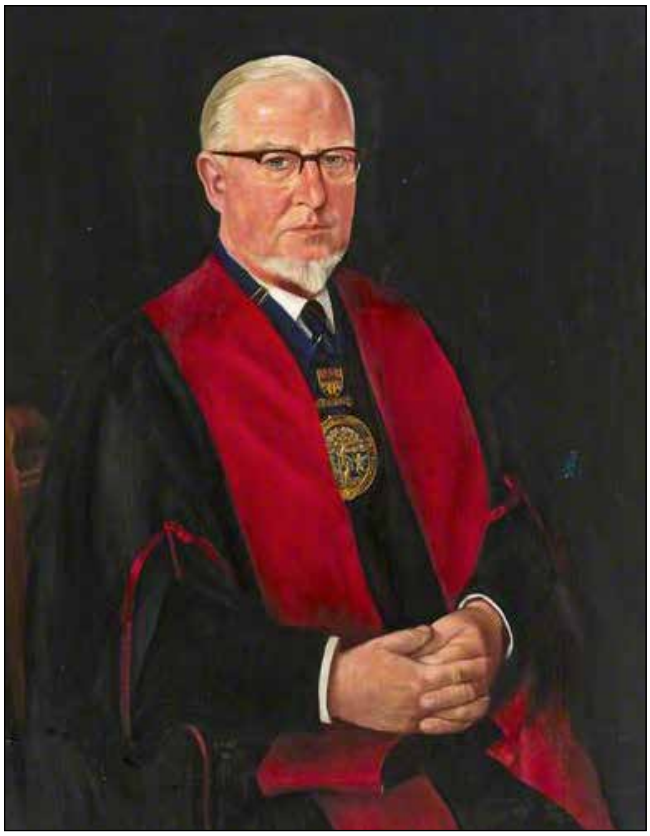


Fig 4. Sir Henry Osmond-Clarke, KCVO, CBE, Portrait, Oil on Canvas, Artist Unknown.

the U.S. orthopaedic plans? Robert Jones who died in 1933, had divulged them to the U.S. before his death, but they were still classified 'Secret'. With 70% of wounds of the Allies having an orthopaedic component[1,2,35], this lack of preparation was another reason for no trans-Channel invasion in 1943. Eventually after D-Day, the U.S. orthopaedic surgeons were more rationally deployed[36]. The American Medical Association achieved their object on June 1, 1943 of getting Kirk, an orthopaedic surgeon who had studied briefly at Johns Hopkins University Hospital, Baltimore and the Massachusetts General Hospital, appointed U.S. Army Surgeon General, after the firing of his Donegal-born predecessor Magee[36,37].

U.S. NAVY ORTHOPAEDICS

The U.S. Navy Surgeon General Ross McIntire, had been since 1935, President Franklin D. Roosevelt's personal physician, accompanying him almost everywhere. On the Presidential train his accommodation was in the Communications Car. He flew with FDR and heard from him how "My Navy must have the best"[38]. Admirals King and Leahy concurred. Joseph Barr, Head of Orthopaedics Designate at the Massachusetts General Hospital was appointed Head of the U.S. Naval Hospital, Bethesda, Maryland, FDR's Hospital (Fig. 5)[39]. Joe Barr met his friend McIntire frequently and was put in charge of U.S. Navy Medical Deployment. Barr, having pioneered and developed successful disc surgery[40,41] was famous from 1935. He knew the best orthopaedic and general surgeons. Excellent orthopaedic surgeons were deployed under Nimitz to the Carrier Battles, Leyte, Iwo Jima, Okinawa and the Kamikaze attacks. These medics helped design and operate the pipeline nitrogen purging systems to quench fires and prevent explosions.

As a consultant (1964-74) to the U.S. Naval Hospital, Boston, I read and taught on the oxygen monitoring devices and their care of the ship-borne wounded and near-drowned. Barr was also appointed head of instruction visuals under FDR as C in C[41]. In the 1960s I worked with Barr in the operating rooms of the Massachusetts General Hospital; as Buckminster Brown Professor, he was an excellent and enlightened head of Harvard Orthopaedics.

Fig 5. Joseph S. Barr, oil on canvas, 44" by 33" (framed 50" by 40"), by Pietro Pezzati (1902-1993), 1964[39], from the Massachusetts General Hospital, Archives and Special Collections,reproduced with permission of the Paul S. Russell Museum of Medical History.

EVACUATION TO REGIONAL ORTHOPAEDIC CENTRES IN THE UK

While splints, even those improvised on site from sticks, boards and even a soldier's rifle, could be applied in a Battalion Aid Station or in the field, these were temporary measures. It was generally accepted that plaster casts should not be applied until after surgical cleansing of the affected limbs. The inherent difficulties of its use in the field resulted in plaster not being applied until patients had reached the clearing stations and field hospitals[16,42]. Innovations including the plaster traction splint for compound fractures , improved traction cradles and revolving traction frames resulted from

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Table 2.

Cross-channel aeromedical evacuation, D-Day through May 1945[14,45] (70% Of evacuees had orthopaedic injuries)

MONTH	NO. EVACUATED
June 1944	7,947
July 1944	19,490
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	361,056

*From 16 August 1944, evacuated represents Allied control under SHAEF[45].

the combined efforts of U.S. Orthopaedic Surgeons now Lt. Col. Quigley[32,34], Maj. Marshall R. Urist and Capt. Lincoln Ries at the 22nd General Hospital in the 802nd Hospital Centre in Blandford, England[34].

Ultimate responsibility for the regionalised orthopaedic centres in the UK in the aftermath of D-Day, June 6, 1944, was divided de facto between Air Commodore Osmond-Clarke for the RAF, Colonel Grow for the U.S. Army Air Force, Bristow for the RAMC with Girdlestone responsible for Southern England and Bristow and my father responsible for the North of the UK. Responsibility was aided by Sir Alexander Hood's firm role as Director General, RAMC, and General Paul Howley's much-praised role as Chief U.S. Surgeon for the European Theater of Operations. Watson-Jones held a position similar to that held by Jones in World War I. Ten RAF orthopaedic units of up to 150 beds were created, backed by residential rehabilitation centres: 77 % of these patients were returned to full active RAF duty, while 18

% were retrained or returned to modified duty: only one in twenty needed invalid discharge[30,43]. By October of 1943, the

U.S. Army had implemented training programs for physical therapists. While occupational therapists were not accorded military status, 96-hour army orientation programs for these professionals were also established at three U.S. locations[33].

These great patient results were due to superb air evacuation and nursing[44,45] (Table 2). U.S. Army engineers put into operation sixty new airfields and by 15 September 1944 the RAF had built a total of seventy-six airfields[46]. Bristow used to say that steel air strips were among the greatest advances in World War II orthopaedics.

NIGHTINGALES

This appellation is generally applied to nurses who have graduated and stayed to work at St. Thomas's Hospital, London. During World War II "Nightingale" was also applied to U.S. Army Air Force qualified air evacuation nurses and to Princess Mary's Royal Air Force nurses. Groups of Nightingale nurses were collectively superb—the Allied air evacuation in-flight mortality for the European Theatre was almost zero. Princess Mary, also known as the Princess Royal (Fig 6), based her selected World War II 'Mary Nightingales' in Necerne Castle on Lough Erne and in Castle Archdale, Northern Ireland. The Princess Royal also had jurisdiction over 30,000 UK EMS beds—just sufficient for the casualties from Normandy, St Lô, Arnheim, V1 and V2 bombs and the Battle of the Bulge[48]. Close cooperation of British and U.S. Orthopaedic leadership led to excellent results in World War II. Early skilled triage and evacuation are keys to success in warfare[49,50]. Viscount Nuffield's generosity aided Allied victory in World War II.

ACKNOWLEDGEMENTS

The authors thank Mr. Liam O'Reilly and Ms. Alyson Stanford of the Public Records Office of Northern Ireland (PRONI) for expert assistance with the Archives of the Northern Ireland Council for Orthopaedic Development

Fig 6. Her Royal Highness, Princess Mary, the Princess Royal CI, GCVO, CBE, RRC (1897-1965), by Sir James Jebusa Shannon (1862-1923), 1914[44,47]. Princess Mary, The Princess Royal, trained at Great Ormond Street. During World War I she founded the Princess Mary RAF Nurses[44]. During World War II she oversaw expansions of UK Emergency Hospitals[46]; Commandant of the ATS with the rank of General in the British Army.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

(NICOD). The authors thank Ms. Martha Stone, M.S., AHIP, Coordinator for Reference Services, Treadwell Library and Mr. Jeff Mifflin, Archivist, Massachusetts General Hospital, for assistance with Massachusetts General Hospital Archives. The authors thank Mr. Jeffrey Wright, Archives Assistant, Oxford Health NHS Foundation Trust, Oxfordshire Health Archives, Oxfordshire History Centre, and Mr. Warwick Baggaley, BA (Hons) BSc, Head of Photography, John Radcliffe Hospital, Headington, Oxford, and Lafayette Ltd. for arranging permission to reproduce the portrait of G.R. Girdlestone. The authors thank Ms. Sarah Pearson, Curator, Hunterian Museum and Mr. Bruce Simpson of the Royal College of Surgeons of England for arranging permission to reproduce the portrait of Sir Harry Platt. The authors thank Ms. Anna Sander, Archivist and Curator of Manuscripts, Balliol College, Oxford for arranging permission to reproduce the portrait of Sir David Lindsay Keir. The authors thank Ms. Michelle Marcella, Office of Public Affairs, Paul S. Russell Museum of Medical History and Innovation, Massachusetts General Hospital History Program at the Massachusetts General Hospital, for arranging permission to reproduce the portrait of Professor Joseph Seaton Barr.

REFERENCES

1. Osmond-Clarke H. Half a century of orthopaedic progress in Great Britain. *J Bone Joint Surg* 1950;**32B(4):**620-75.
2. Osmond-Clarke H, Crawford Adams J. General review of orthopaedic surgery. Chapter 6., Orthopaedic surgery. In: Cope Z ed. *Surgery*. London: HM Stationery Office, 1953, p.234-70.
3. Cooter R. The meaning of fractures: Orthopaedics and the reform of British hospitals in the inter-war period. *Med Hist* 1987;**31**:306-32.
4. Thompson SV. Sir Alfred Keogh—the years of reform 1899-1910. *JR Army Med Corps* 2008;**154(4):**269-72.
5. Trueta J. *Gathorne Robert Girdlestone*. Oxford: Oxford University Press, 1971.
6. Seddon HJ. In memoriam. Gathorne Robert Girdlestone, 1881-1950. *J Bone Joint Surg* 1951;**33B(1):**130-3.
7. Platt, Sir Harry (1886-1986). Biographical Entry. Plarr's Lives of the Fellows Online, Royal College of Surgeons of England. http://livesonline.rcseng.ac.uk/biogs/E000232b.htm (last accessed 16 June 2016)
8. Smith R. Sir Harry Platt: 100 not out. *Brit Med J* (Clin Res Ed)1986 Oct 4; **293(6551)**: 864-66.
9. Platt H. Orthopaedic surgery in Boston. *Medical Chronicle* 1914;**58**:473-4.
10. Andrews PWS, Brunner E. *The Life of Lord Nuffield: A study in enterprise and benevolence*. Oxford: Basil Blackwell, 1955.
11. Northern Ireland Council for Orthopaedic Development (NICOD). Minute Book. 1941 Annual Report; Minutes of the Meeting of 31st July and 11th September 1941. Belfast: Public Records Office of Northern Ireland (PRONI), www.proni.gov.uk.
12. Northern Ireland Council for Orthopaedic Development (NICOD). Minute Book. Minutes of the Meeting of 10th February 1942. Belfast: Public Records Office of Northern Ireland (PRONI), www.proni.gov.uk.
13. Measuring Worth Website. http://www.measuringworth.com/ppoweruk/ (last accessed 16 June 2016).
14. Hedley-Whyte J, Milamed DR. Surgical Travellers: Tapestry to Bayeux. *Ulster Med J* 2014;**83(3)**:171-7.
15. James WV. Orthopaedics and the Northern Ireland Council for Orthopaedic Development (NICOD). *Ulster Med J* 1984; **53(2):**111-6.
16. Purvis J. Editorial. Following a physician's footsteps in Flanders: The Centenary of the Somme. *Ulster Med J* 2016;85(2):69-70.
17. Keir DL. Papers of Sir David Keir. Administrative/Biographical History. Bodleian Library. University of Oxford. Special Collections Ref. No. GB 0162 MSS.Brit.Emp.s393. http://www.bodley.ox.ac.uk/dept/ scwmss/wmss/online/blcas/keir-david.html (last accessed 16 June 2016).
18. Lieutenant David Lindsay Keir. Biography of Lieutenant David Lindsay Keir. University of Glasgow. http://www.universitystory.gla.ac.uk/ww1-biography/?id=1299 (Last accessed 16 June 2016).
19. Obituary. Sir David Lindsay Keir. Former Master of Balliol. *Times* [London, England]. 4 Oct. 1973 p.25. The Times Digital Archive Web, 18 Sept. 2015.
20. Keen MH. Keir, Sir David Lindsay (1895-1973), historian and university administrator. *Oxford Dictionary of National Biography*. Downloaded through the Harvard University Libraries at http://www. oxforddnb.com/ezp-prod1.hul.harvard.edu/view/article/31300 (Last accessed 16 June 2016).
21. Keir DL. *The Constitutional History of Modern Britain*, 1485-1937. London: A. and C. Black, 1938.
22. Keir DL, Lawson FH. *Cases in Constitutional Law*. Oxford: The Clarendon Press; 1928.
23. Keir DL. Western medicine in the modern world. *Lancet* 1954 Oct 23;267(6843):823-5.
24. Ollerenshaw P. *Northern Ireland in the Second World War. Politics, economic mobilization and society, 1939-45*. Manchester, UK: University of Manchester Press; 2013. p.211.
25. Oxford University Golf Club, http://www.ougc.co.uk; Gillum J., *The Oxford and Cambridge Golfing Society: 100 Years of Serious Fun*, Grant Books, 1997.
26. Bristow WR. Orthopaedic lessons of the war. *JR Army Med Corps* 1945;Dec. **85**:271-5.
27. Northern Ireland Council for Orthopaedic Development (NICOD). Minute Book. Minutes of the Meeting of Monday, 11th March 1940. Belfast: Public Records Office of Northern Ireland (PRONI), www.proni.gov.uk.
28. Northern Ireland Council for Orthopaedic Development (NICOD). Minute Book. Minutes of the Meeting of April 14, 1941. Belfast: Public Records Office of Northern Ireland (PRONI), www.proni.gov.uk.
29. Northern Ireland Council for Orthopaedic Development (NICOD). Minute Book. Minutes of the Meeting of Thursday, September 4, 1941. Belfast: Public Records Office of Northern Ireland (PRONI), www.proni.gov.uk.
30. Watson-Jones R. Rehabilitation in the Royal Air Force. *Brit Med J*. 28 March 1942; **4238**:403-7.
31. Hedley-Whyte J. Epidemic jaundice: Harvard's 5th General Hospital at Musgrave Park in World War II. *Ulster Med J*. 2005;**74(2):**122-5.
32. Hedley-Whyte J., Milamed DR. American surgeons at Musgrave Park Hospital in World War II: Surgical giants. *Ulster Med J* 2016;**85(2):**107-12.
33. Mullins WS, Parks RJ, eds. *Medical Training in World War II*. Washington, DC: Office of the Surgeon General, Department of the Army; 1974. p.152-3, 235.
34. Medical Department United States Army. *Surgery in World War II. Orthopedic Surgery in the European Theater of Operations*. Cleveland M., ed. Washington DC: Office of the Surgeon General, Department of the Army; 1956.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

35. Welch SCR. The Royal Air Force Medical Services. Medical Statistics. In: Mellor WF, ed. *Casualties and Medical Statistics*. London: HM Stationery Office; 1972. Table 3(b), p.498-9.

36. Hedley-Whyte J, Milamed DR. Our blood your money. *Ulster MedJ* 2013;**82(2)**:114-20.

37. U.S. Army Medical Department. Office of Medical History. Surgeons General. Norman Thomas Kirk. http://history.amedd.army.mil/surgeongenerals/N-Kirk2.html (last accessed 16 June 2016).

38. McIntire RT. *White House Physician*. New York: G.P. Putnam's Sons, 1946.

39. Massachusetts General Hospital, Boston, MA. Museum at Massachusetts General, Catalog. http://history.massgeneral.org/catalog/Detail.aspx?itemId=42&searchFor=Pictures,%20Portraits%20and%20Plaques (Last accessed 16 June 2016).

40. Mixter WJ, Barr JS. Rupture of the intervertebral disc with involvement of the spinal canal. *New Engl J Med* 1934; **211:**210-4.

41. Joseph Seaton Barr (1901-1964) Obituary. *J Bone Joint Surg* 1965;**47-A:**1446-8.

42. Bosworth BM. Splints and casts in the treatment of war injuries. *Am J Surg*. 1946;**72(3)**:385-92.

43. In Memoriam: Sir Reginald Watson-Jones 1902-1972. *J Bone Joint Surg Br* 1972;**54B(4)**:569-75. Osmond-Clarke H. Comments, p.572-3.

44. Mackie M. *Wards in the Sky: The RAF's Remarkable Nursing Service*. Stroud, Gloucestershire: The History Press; 2014.

45. Futrell RF. *Development of Aeromedical Evacuation in the USAF, 1909-1960*. USAF Historical Studies No. 23. (Draft) IV. Aeromedical evacuation comes of age in Europe 1943-1945; air evacuation in the United Kingdom and Normandy. Washington, DC: USAF Historical Division Research Studies Institute; 1960. p.202,211,213,225,228,233, 239,240,242,245,248,251,252. Available online from: http://www.afhra.af.mil/shared/media/document/AFD-090602-048.pdf (Last accessed 16 June 2016).

46. Hedley-Whyte J, Milamed DR. Battle of the Atlantic: Military and medical role of Northern Ireland (After Pearl Harbor). *Ulster Med J*. 2015;**84(3):**182-7.

47. *Princess Mary's Gift Book*. London: Hodder & Stoughton, 1914. https://archive.org/details/princessmarysgif00mary (Last accessed 16 June 2016).

48. Craven WF, Cate JL. *The Army Air Forces in World War II. Vol 3. Europe: Argument to V-E Day. January 1944 to May 1945*. Chicago, IL: University of Chicago Press; 1951. p.568-9.

49. Watson-Jones R. Chapter IX. Reduction and immobilization of fractures. In: *Fractures and Other Bone and Joint Injuries*. Baltimore, MD: Williams and Wilkins Co., 1940; p. 118-42.

50. Spence R, Spence R. Surgery of the troubles: Lessons for the future. IS Ravdin Lecture in the Basic and Surgical Sciences. *J Am Coll Surg* 2014; **219(2):**171-80.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Letters

ABUSE OF FENTANYL ANALGESIC PATCHES

Editor,

A 34-year-old male with a background history of drug abuse, alcohol dependence and depression was recently admitted to our ICU. The patient had acquired a Fentanyl patch, of unknown brand name. He removed the gel matrix containing the active drug, ignited it and inhaled the fumes generated through a rolled-up tin foil.

He immediately lost consciousness and was found by a friend who called the Ambulance Service, who in turn found him comatose with vomitus visible in the mouth. He was given Naloxone and regained consciousness and was brought into hospital, complaining of dyspnoea. He was admitted under the respiratory team with suspected aspiration pneumonia. A chest x-ray on admission showed mild bibasal infiltrates (Figure 1). Over the next 12 hours he deteriorated, developing diffuse bilateral infiltrates and hypoxic respiratory failure in keeping with Acute Respiratory Distress Syndrome (ARDS) requiring tracheal intubation and mechanical ventilation. He spent 1 month in our ICU, undergoing tracheostomy on day 15. His respiratory function remained poor for around 21 days before slowly improving and weaning from ventilation. His overall diagnosis was chemical pneumonitis due to both aspiration and the direct toxic effects of the inhaled fumes.

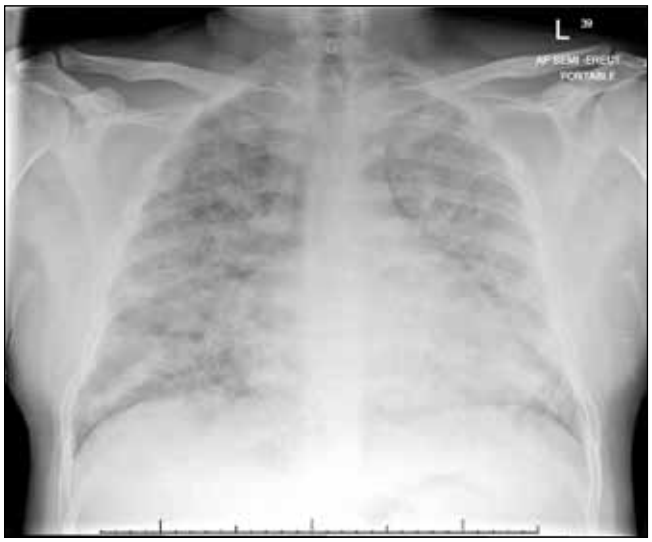


Fig 1. Chest X-Ray showing diffuse widespread air space opacification bilaterally. Appearances would be compatible with the clinical suspicion of widespread aspiration / pneumonitis.

This case highlights the dangers of smoking opioid based patches, both in terms of the potential for rapidly absorbing an extremely high dose of the drug systemically and inhaling the fumes of the ignited matrix. We have not identified another case report of chemical pneumonitis resulting from smoking a Fentanyl patch, but there is at least one report of a patient developing alveolar proteinosis after smoking [1]. Indeed, there are several media reports of deaths from smoking Fentanyl patches recently. [2-3]

It is worrying that a simple internet search engine query for smoking "Fentanyl Patch" reveals a large number of websites of forums devoted to the subject, with many references to the fact that opioid based patches are often worn by the elderly with chronic pain conditions, making them an easy target for theft.

Diarmaid Dillon and Finbarr O'Neill

Regional Intensive Care Unit, Royal Victoria Hospital , 274 Grosvenor Road, Belfast BT12 6BA Northern Ireland UK

Correspondence to: diarmaiddillon@gmail.com

REFERENCES:

1. Chapman E, Leipsic J, Satkunam N, *Churg A. Chest.* 2012;**141(5)**:1321-3.
2. Martin R. Addicts die after smoking pain-relief patches. The Local SE, Sweden's news in English. 2012 Jan 18. Available from: http://www.thelocal.se/20120118/38570. Last accessed May 2016.
3. Ghebreslassie M, Layson G, Doucette T. Fentanyl kills 'perfect wife' and other addicts in Ontario City. CBS News. 2012 Jul 20. Available from: http://www.cbc.ca/news/canada/windsor/fentanyl-kills-perfect-wife-and-other-addicts-in-ontario-city-1.1155726. Last accessed May 2016.

HYPERTROPHIC OSTEOARTHOPATHY ASSOCIATED WITH NON-METASTATIC RENAL CELL CARCINOMA; REPORT OF AN UNUSUAL CASE.

Editor,

Hypertrophic Osteoarthropathy (HOA) is an uncommon syndrome comprising periostitis of long bones, digital clubbing and synovial effusions. HOA is divided into primary and secondary forms[1]. Secondary HOA is associated with a variety of medical conditions, including malignancy. The vast majority of malignancy-associated HOA is in the setting of

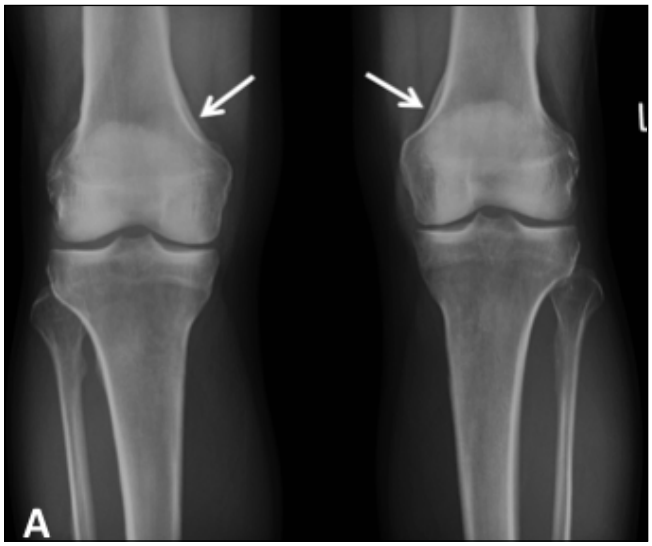


Fig 1A: Weightbearing anteroposterior radiograph of boths knees demonstates a periosteal reaction along the distal femoral metaphyses, best appreciated on the medial aspects (arrows). The appearances are classical for hypertrophic osteoarthropathy.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

thoracic malignancy. Association with extrathoracic, non-metastatic malignancy is very rare. We report a case of hypertrophic osteoarthopathy associated with non-metastatic renal cell carcinoma (RCC).

A 60-year old gentleman was referred by his General Practitioner to our department for radiographs of both knees, having reported a short history of right-sided knee pain, with mild tenderness on examination. He was a non-smoker and had no significant medical history. Radiographs of both knees demonstrated periosteal reaction at the medial and lateral aspects of both distal femora (Figure 1A), in keeping with HOA. Radiographs of both ankles demonstrated a similar periosteal reaction in both distal tibiae. The patient did not have any clinical features of pacchydermoperiostosis (primary HOA) or a known underlying condition to account for the development of secondary HOA. A chest radiograph was normal. Given that no cause for the patient's HOA was apparent, a decision was made to perform a Computed Tomography (CT) scan of the thorax, abdomen and pelvis to evaluate for an underlying malignancy. This demonstrated a 3.5 cm right renal mass, suspicious for a renal cell carcinoma (Figure 1B). There were no metastases or other abnormality identified. The patient was referred to the local Urology Service and underwent an open partial nephrectomy. Histological analysis confirmed a grade II renal cell carcinoma. The patient recovered well and remains disease free at six months following surgery.

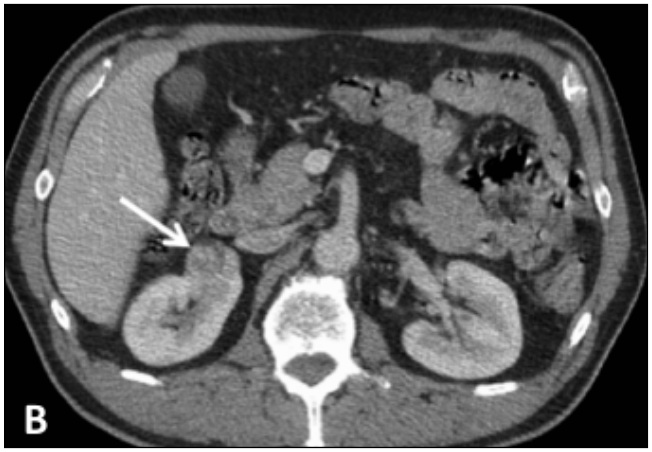


*Fig 1B: Axial CT image demonstrates a 3.*5 cm right renal mass suspicious for a renal cell carcinoma (arrow).

It was Virchow in 1895 who first described HOA in the setting of malignancy[2], in a patient with pulmonary metastases. A strong association of HOA with malignancy has since been established. Given the preponderant association of HOA with thoracic malignancy, it has been commonly referred to as "hypertrophic pulmonary osteoarthropathy". The small number of reported cases associated with an extra-thoracic malignancy have predominantly been in the young adult and paediatric populations.

On review of the English medical literature we identified seven other cases of HOA associated with renal cell carcinoma[3,4]. In five of the reported cases, the development of HOA was seen in patients with pulmonary metastases. The other two cases reported HOA in patients with renal cell carcinoma without pulmonary metastases. Recent evidence has implicated vascular endothelial growth factor (VEGF) as a key factor in the pathogenesis of HOA[5]. Over expression of VEGF has been well documented in renal cell carcinoma and we hypothesize that this had a role in the development of HOA in this case.

In conclusion, this is the third case in the English medical literature of HOA associated with renal cell carcinoma without pulmonary metastases. It emphasises the importance of further investigation when a patient presents with HOA without an apparent cause. In rare cases an extra-thoracic malignancy may be present.

The authors have no conflict of interest.

Redmond CE, Healy GM, Redmond PL.

Department of Radiology, Midland Regional Hospital Tullamore, Co. Offaly.

REFERENCES:

1. Pineda C, Martinez-Lavin M. Hypertrophic osteoarthropathy: what a rheumatologist should know about this uncommon condition. *Rheum Dis Clin North Am*. 2013;**39(2):**383–400.
2. Virchow R. (1895) Veränderungen des Skelets durch Akromegalie. *Berliner Klinische Wochenschrift*, 1895;**32:** 1102.
3. Chen YC, Tiu CM, Bai LY, Liu JH. Hypertrophic pulmonary osteoarthropathy associated with disease progression in renal cell carcinoma. *J Chin Med Assoc*. 2003;**66(1):**63-6.
4. Pandita KK, Afaq S, Singh D, Mushtaq D, Masood I. Finger clubbing in a patient of myelofibrosis with renal cell carcinoma. *J Assoc Physicians India*. 2012;**60:**124–6.
5. Silveira LH, Martinez-Lavin M, Pineda C, Fonseca MC, Navarro C, Nava A. Vascular endothelial growth factor and hypertrophic osteoarthropathy. *Clin Exp Rheumatol*. 2000;**18(1):**57–62.

HEPATOCELLULAR CARCINOMA EXTENDING INTO THE RIGHT ATRIUM.

Editor,

Cardiac tumours are rare and often secondary, rather than primary in origin. The commonest malignant primary tumours are sarcomas (95% of malignant primary cardiac tumours) and the commonest benign primary tumours are myxomas (mostly left sided in origin).[1] Tumours which locally invade the heart are frequently lung and breast cancers, although hepatocellular carcinoma (HCC) can extend via the inferior vena cava into the right atrium and this is seen in approximately 1-4% of HCC.[2] This phenomenon of extension is more commonly seen with renal cell carcinomas.

A 62-year-old man presented to Antrim Area Hospital with a short history of rapidly progressive dyspnoea. Four weeks previously, he had been able to walk 2 miles with no difficulty but this had reduced to 10-20 metres by the time of presentation. He had noticed increasing abdominal girth and ankle swelling. Of note, in his social history, was heavy

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

alcohol intake over many years, although not in the last 10 years. D-Dimer was elevated at 573ng/ml so he proceeded to CT pulmonary angiogram to rule out a pulmonary embolus (PE). This demonstrated a small sub-segmental PE, but more significantly, a right atrial mass. This was further investigated with an echocardiogram which showed the mass extending through the tricuspid valve into the right ventricle. A large liver mass in segments IVa and VIII and extending into the middle hepatic vein, IVC and right atrium was then found on subsequent CT scanning. The atrial mass was felt to be an extension of an HCC (Figure 1).

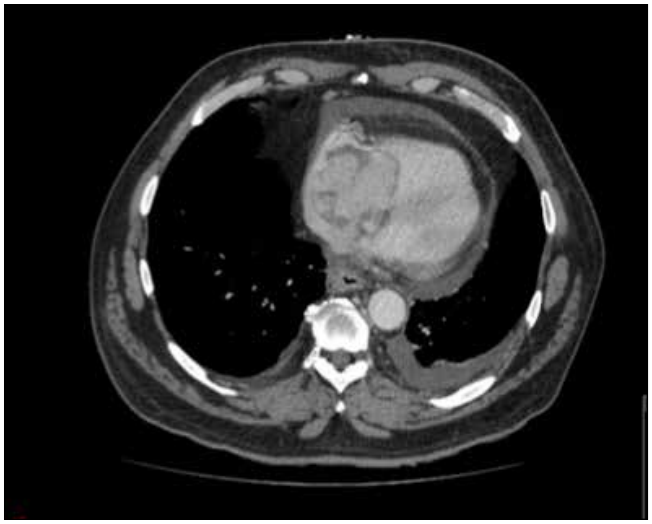


Figure 1: CT scan with white arrow pointing at tumour tissue in right atrium

The patient became increasingly dyspnoeic at rest and was transferred to the Royal Victoria Hospital, Belfast, where he underwent surgery to remove the atrial component of the tumour (Figure 2). Histology confirmed HCC. Following liaison with the hepatobiliary team, trans-catheter arterial chemoembolization (TACE) was felt to be the best treatment option. The patient was greatly improved following the surgery with symptoms of dyspnoea completely resolved and he was restored to normal mobility at the time of discharge (10 days post-surgery).

Fig 2: Excised atrial component of the HCC

TACE involves delivery of chemotherapeutic agents and concurrent embolization which intends to deliver a highly concentrated dose of chemotherapy to tumour cells, prolong the contact time between the two and minimise systemic toxic effects. The concentration of chemotherapy achieved at the site of the tumour is thought to be around 100 times higher than systemic chemotherapy.[3] The process is based upon the observation that agents delivered by the hepatic artery are preferentially taken up by hepatic tumours in comparison to normal liver parenchyma which is preferentially supplied from the portal venous system. Due to the dual blood supply of the liver, the treatment does not compromise healthy liver tissue. Survival rates vary after TACE but two randomised control trials showed 1 year survival between 57%-82%, and 2 year survival rates between 31%-63%, in patients with unresectable HCC undergoing TACE.[4]

McNeice A[1], Graham ANJ[2], Trouton TG[1]

[1] Department of Cardiology, Antrim Area Hospital

[2] Department of Cardiothoracic Surgery, Royal Victoria Hospital, Belfast

REFERENCES

1. Shapiro LM. Cardiac tumours: diagnosis and management. *Heart*. 2001;**85(2)**:218-22.
2. Vallakati A, Chandra PA, Frankel R, Shani J. Intra-atrial tumor thrombi secondary to hepatocellular carcinoma responding to chemotherapy. *N Am J Med Sci*. 2011;**3(9)**:435-7.
3. Konno T. Targeting cancer chemotherapeutic agents by use of lipiodol contrast medium. *Cancer*. 1990;**66(9)**:1897-903.
4. Ramsey DE, Geschwind JFH. Chemoembolization of unresectable hepatocellular carcinoma: a review. *Appl Radiol*. [Internet]. 2004;**33**(3). Available from: http://appliedradiology.com/articles/chemoembolization-of-unresectable-hepatocellular-carcinoma-a-review. Last accessed May 2016.

GENERAL SURGICAL TRAINING AND SURGICAL TRAINEE WORKING PATTERNS.

Editor,

Surgery, as a craft-based speciality, relies on hours of practical apprenticeship to acquire technical skills.[1] To ensure these skills are developed, the Joint Committee on Surgical Training (JCST) has provided guidelines of indicative numbers for procedures required for Certificate of Completion of Training (CCT).

The New Deal and European Working Time Directive (EWTD) have reduced the amount of time doctors spend in work, increased staffing requirements for service provision and thereby diluted training[2]. A new junior doctor contract to replace the New Deal has recently been the subject of much controversy across the United Kingdom. Additional emphasis has been placed on service provision and limited attention paid to the need for effective training. It has been suggested that to ensure optimal training with adequate time for exposure and to provide high quality patient care with increased continuity, it is necessary to return to a working

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

week of approximately 65 hours [3].

The aim of this study was to examine the impact of changes in rota pattern and working hours on operative experience for specialty registrars in General Surgery.

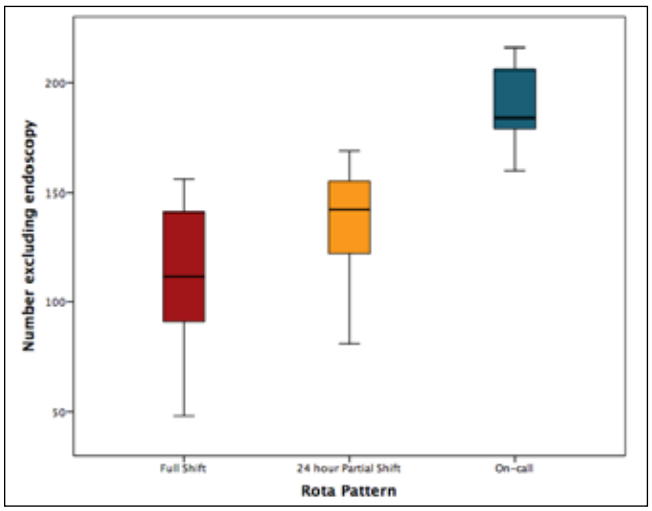


Fig 1. Boxplot of total number of surgical cases to exclude endoscopy for each rota pattern (Kruskal-Wallis p=0.005)

Methods

Surgical registrar working patterns and operative experience were assessed in a district general hospital providing elective and emergency General Surgical services to a population of approximately 400,000. Over a period of 18 months, the working pattern changed progressively each six months, from a full shift rota (48 hours per week) to a 24-hour partial shift rota (56 hours per week), and ultimately to an on-call rota (65 hours per week). Trainee operative experience was compared for each rota pattern.

TABLE 1.

Operative experience in our unit extrapolated over a six-year higher surgical training rotation

	Full shift	24 hour partial shift	On-call	Indicative numbers for CCT
Inguinal Hernia	72	108	120	60
Cholecystectomy	102	156	252	50
Emergency Laparotomy	168	150	228	100
Appendicectomy	192	234	300	80
Total Number of cases excluding endoscopy	1338	1704	2208	1600

Results

When working on a 48 hour per week full shift rota, the Specialty Registrars in our unit had a reduced operative experience. Operative experience did not increase significantly when working a partial shift pattern, but was significantly increased by working a 65 hour per week on-call rota (Figure 1). Operative experience did not vary with grade of registrar.

Differing operative experience was evident for the total number of operations excluding endoscopy (p=0.005) and for individual procedures with regards to the number of cholecystectomies (p=0.020). There was no significant difference in the number of emergency cases (p=0.262), endoscopy (p=0.958), inguinal hernia repair (p=0.058), emergency laparotomy (p=0.266) or appendicectomy (p=0.055) between rota patterns although the number of doctors involved were small.

Results for each six-month period were extrapolated over a six-year period to allow for assessment of the training delivered by each rota pattern in the context of the JCST indicative numbers for CCT (Table 1). On a full shift rota, the total operative numbers required for CCT would not be achieved.

Conclusions

Concerns raised by the Royal Colleges of Surgeons and the Association of Surgeons in Training with regards to the impact of the EWTD on surgical training appear to have been well founded[3,4]. Unless a national or specialty specific opt-out is made available, surgical trainees are likely to be disadvantaged by the EWTD when attempting to gain the experience necessary to achieve excellence. Contract negotiations should prioritise training within this context. We would encourage all possible attempts to allow doctors within craft specialties such as surgery to work outside the constraints of the EWTD in order to produce highly qualified consultants with the requisite experience to deliver high quality patient care.

Ethical approval for this study was not required.

R. Scott McCain[1,3], R. Stephen McCain[1], David A Mark [1], Kevin McCallion[2], Eamon J Mackle[1].

[1] Department of Surgery, Craigavon Area Hospital, 64 Lurgan Road, Portadown

[2] Department of Surgery, The Ulster Hospital, Upper Newtownards Road, Belfast, BT16 1RH.

[3] Centre for Public Health, Queen's University Belfast.

Corresponding author.

R. Scott McCain

e-mail: smccain01@qub.ac.uk

REFERENCES

1. Purcell Jackson G, Tarpley J. How long does it take to train a surgeon? *BMJ*. 2009; **339** (b4260).

2. Maxwell AJ, Crocker M, Jones TL, Bhagawati B; Papadopoulos MC, Bell BA. Implementation of the European Working Time Directive in neurosurgery reduces continuity of care and training opportunities. *Acta Neurochir (Wien)*. 2010; **152**(7): . 1207-10.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

3. Creswell B, Marron C, Hawkins W, Harrison E, Fitzgerald E, von Roon A. Optimising working hours to provide quality in training and patient safety: a position statement. London: *The Association of Surgeons in Training*; 2009.

4. Royal College of Surgeons of England. Surgeons and trainees. Surgical standards. Working practices. Workforce. Working Time Directive. Summary of personal responses to the European Working Time Regulations (EWTR) taskforce consultation. London: *Royal College of Surgeons of England*; 2010.

DUAL POSTERIOR LIP AUGMENTATION DEVICES FOR RECURRENT INSTABILITY OF A CHARNLEY TOTAL HIP REPLACEMENT

Editor,

An 85-year-old female presented with a posterior dislocation of a right Charnley total hip replacement (THR) despite previous posterior lip augmentation. Past medical history included myocardial infarction, left ventricular dysfunction, dual antiplatelet therapy, atrial fibrillation and Alzheimer's disease.

Her original arthroplasty was performed in 1983 via a posterior approach. The acetabular component was revised in 1998 due to dislocations associated with acetabular loosening, but the femoral component remained well fixed. Due to continuing instability, a posterior lip augmentation device (PLAD) was inserted in 2004 following a third dislocation. The hip remained stable until 2011 when a further dislocation occurred. Radiographs revealed a fracture of the PLAD through the middle screw hole. This was revised with a new 22mm PLAD to the postero-superior rim of the acetabular component, which was noted to have significant wear.

The patient had a further posterior dislocation following a fall in March 2015 (Figure 1).

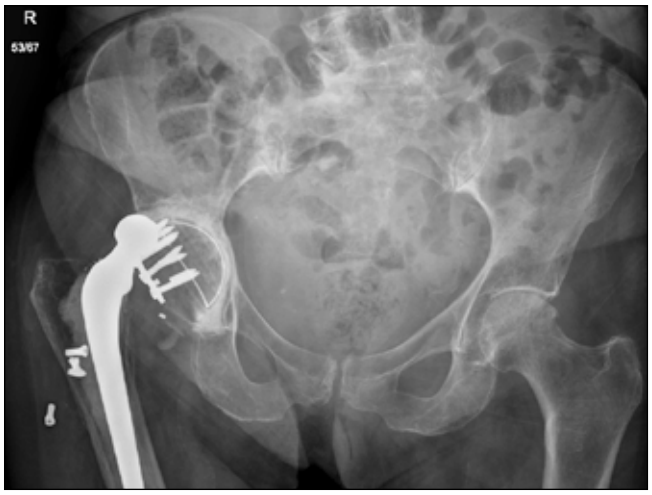


Fig 1. Antero-posterior radiograph showing posterior dislocation of the Charnley total hip replacement previously augmented with a PLAD. Note remnants of the previously fractured PLAD in the soft tissue and acetabular liner.

An open reduction revealed significant wear of the acetabular component and inferior aspect of the PLAD with inferior instability on flexion and internal rotation. The femoral head had multiple abrasions from rubbing on the exposed metal of the PLAD, with significant metal debris in the surrounding soft tissues. The femoral and acetabular components were well fixed. Due to the significant co-morbidities, revision arthroplasty was not felt to be appropriate by the multidisciplinary team. A second 22mm PLAD was placed on the postero-inferior aspect of the acetabular component, overlapping the two inferior holes of the existing PLAD. This appeared to address the issue of inferior instability (Figure 2).

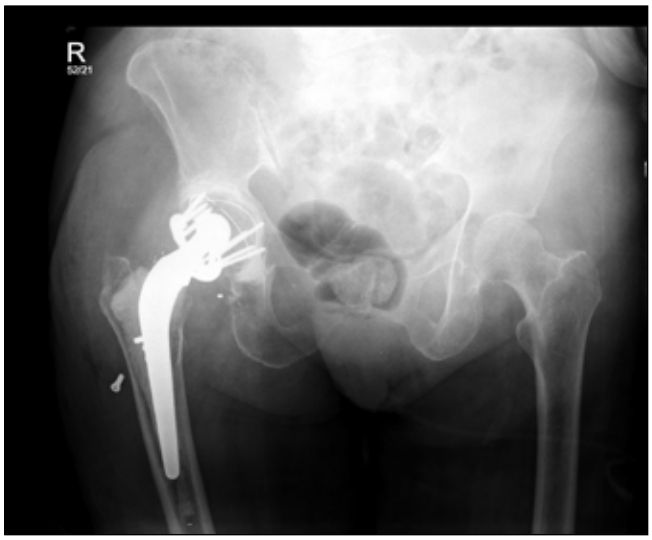


Fig 2. Post-operative antero-posterior radiograph showing the dual PLAD configuration

The approach was by partial re-incision of the previous scar with an operative time of 49 minutes. There were no peri-operative complications.

The PLAD was developed as an alternative to revision surgery for the management of recurrent posterior instability following Charnley THRs in the setting of well fixed, correctly positioned components[1]. It consists of a contoured ultra-high molecular weight polyethylene bearing and stainless steel backing. This is attached to the posterior aspect of the existing acetabular component via five 4.5mm cortical screws. Previous studies have reported dislocation rates following PLAD insertion ranging from 0-10% and revision rates of between 1.3-3.7%[1-5]. Charlwood et al[2] reported that operative time, blood loss, and hospital stay were all significantly reduced in patients treated with PLAD when compared to revision surgery with no significant difference in Oxford Hip Scores in short and long term follow-up. Campbell et al[3] reported two cases or recurrent dislocations past a PLAD which were subsequently treated with excision arthroplasty. Yeung et al[5] have advocated the use of a postero-lateral and antero-medial augmentation to manage recurrent dislocations instead of a constrained liner. Interestingly, the first PLAD in this case had fractured through a screw hole which has only been documented once before[5].

We propose that in the setting of recurrent dislocation

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

past a PLAD the use of a second PLAD to supplement the augmentation over a wider circumference can be successful in patients who are of low functional demand.

Mr Kevin J Donnelly, Mr Graham Finlayson, Mr Chris Andrews

Department of Trauma and Orthopaedic Surgery, Royal Victoria Hospital, 274 Grosvenor Road, Belfast, Northern Ireland BT12 6BA

Correspondence addressed to:

Mr Kevin Donnelly

Email: kevdonnelly@hotmail.com

REFERENCES

1. Charlwood AP, Thompson NW, Thompson NS, Beverland DE, Nixon JR. Recurrent hip arthroplasty dislocation: good outcome after cup augmentation in 20 patients followed for 2 years. *Acta Orthop Scand.* 2002 Oct;**73(5)**:502-5

2. Charlwood AP, Thompson NW, Brown JG, Nixon JR. The Belfast Posterior Lip Augmentation Device (PLAD) in the management of recurrent posterior dislocation following primary total hip arthroplasty. *J Bone Joint Surg [Br] Orthop Proc*. [Online]. 2002; 84-B(Suppl II):154. Available from: http://www.bjjprocs.boneandjoint.org.uk/content/84-B/SUPP_II/154.2. Last accessed May 2016.

3. Campbell D, Muthusamy K, Sturdee S, Finlayson D, Stone M. The Posterior Lip Augmentation Device for Recurrent Dislocation. *J Bone Joint Surg [Br] Orthop Proc*. [Online]. 2001;84(Suppl II):154. Available from: http://www.bjjprocs.boneandjoint.org.uk/content/84-B/SUPP_II/154.3

4. McConway J, O'Brien S, Doran E, Archbold P, Beverland D. The use of a posterior lip augmentation device for a revision of recurrent dislocation after primary cemented Charnley/Charnley Elite total hip replacement: results at a mean follow-up of six years and nine months. *J Bone Joint Surg Br.* 2007;**89(12)**:1581-5.

5. Yeung D, Rourke K, Pradhan N. Use of two posterior lip augmentation devices for recurrent total hip arthroplasty dislocation in select patients. *Ann R Coll Surg Engl.* 2013 Mar; **95(2)**: 156

MUTYH ASSOCIATED POLYPOSIS [MAP] - A 'LESSER KNOWN' POLYPOSIS SYNDROME!

Editor,

Familial Adenomatous Polyposis (FAP) and Hereditary Non-Polyposis Colorectal Cancer (HNPCC) are well recognised syndromes that increase the risk of colorectal carcinoma (CRC). First described in 2002, MUTYH associated polyposis (MAP) results in colorectal polyposis and increased risk of malignancy, with a lifetime risk of CRC of >90%[1,2]. Like FAP and HNPCC, extracolonic manifestations can occur in MAP including duodenal and gastric polyps. Similarity to other polyposis syndromes may lead to diagnostic confusion and underrecognition of MAP in clinical practice.

To illustrate this we report the case of a 67 year old female, who was first diagnosed with colorectal cancer and synchronous tubulovillous adenomata aged 40. Consequently she underwent a subtotal colectomy with ileorectal anastomosis and lifelong rectal surveillance in 1988. Following this, she was ascribed the diagnosis of HNPCC leading to annual surveillance colonoscopy and identification of further rectal polyps. In 2008, an oesophagogastroduodenoscopy (OGD) for dyspepsia identified extensive periampullary polyposis, since managed by endoscopic excision and annual surveillance OGDs. In October 2014, following investigations by the clinical geneticists, a diagnosis of MAP was made. Despite the impressive periampullary carpeting (Figure 1) surveillance biopsies have shown stable low grade dysplasia. Endoscopic ultrasonic surveillance has been enlisted to ensure confinement of disease to the mucosa.

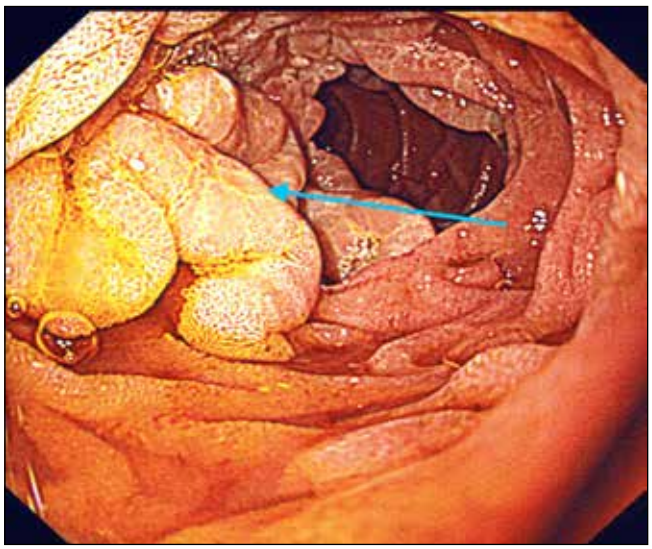


Fig 1. Extensive Periampullary Polyposis in a patient with MUTYH associated polyposis (Blue arrow indicates location of polyposis, around the ampulla of Vater. Image taken in second part of the patient's duodenum)

MAP is an autosomal recessive disorder characterised by biallelic germline mutations in the *MUTYH* gene (chromosome 1p34.1). It has been estimated that 2% of the British population are heterozygous for a *MUTYH* mutation; however no accurate figures exist for the prevalence of MAP. MAP is usually diagnosed at an older age than classical FAP (mean 45 to 56 years), similar to attenuated FAP[3].

Concomitant neoplasms are common in colonic polyposis syndromes and like FAP, duodenal polyposis is a feature of MAP. The prevalence of duodenal polyposis in MAP is 17-25%, as compared to 90% in FAP, with a lifetime risk of duodenal cancer of 4%. Gastric adenomas and fundic gland polyps are also described in MAP. Like HNPCC, cutaneous sebaceous tumours can also occur[4].

The propensity for polyposis of the periampullary region in FAP and MAP is noteworthy. Bile acids can induce production of DNA-damaging reactive oxygen species. This is of particular relevance to MAP as the *MUYTH* gene is responsible for repair of oxidative DNA damage[5]. Furthermore, bile removed from FAP patients has enhanced mutagenic capacity as compared to bile from non-FAP patients. This has not yet been demonstrated in patients with MAP[6].

This case highlights the need for awareness of this rarer polyposis disorder that increases the risk of gastro-intestinal

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

and non-gastrointestinal tumours. The phenotypic spectrum of MAP may lead to diagnostic confusion with other syndromes such as FAP, HNPCC and serrated polyposis syndrome or failure to recognise this as an inheritable condition.

A diagnosis of MAP should be considered when: there is a family history of CRC suggestive of a condition inherited in an autosomal recessive manner; CRC with a c.34G>T mutation in codon 12 of the *KRAS* gene; multiple synchronous colorectal polyps, including hyperplastic/serrated polyps, (typically >10, or 1-10 prior to age 40) in the absence of a mutation in the *APC* gene. For those diagnosed with MAP, the British Society of Gastroenterology recommend biannual surveillance colonoscopy from the age of 25, and 3-5 yearly OGDs[2].

Cathal Hannan[1], Paul Kelly[2], Barry Clements[1]

[1] Upper GI Surgery Unit, BCH

[2] Department of Pathology, RVH.

Contact email – cathalhannan@icloud.com

REFERENCES

1. Al-Tassan, Chmiel, Maynard, Fleming, Livingston,Williams et al.Inherited variants of MYH associated with somatic G:C to T:A mutations in colorectal tumors. *Nat Genet*. 2002; **30**:227 – 232.
2. Cairns SR, Scholefield JH, Steele RJ, Dunlop MG, Thomas HJ, Evans GD et al; British Society of Gastroenterology; Association of Coloproctology for Great Britain and Ireland. Guidelines for colorectal cancer screening and surveillance in moderate and high risk groups (update from 2002). *Gut*. 2010; **59(5):**666-89.
3. Lindor NM. Hereditary colorectal cancer: MYH-associated polyposis and other newly identified disorders. *Best Pract Res Clin Gastroenterology*. 2009; **23(1)**:75-87.
4. Vogt S, Jones N, Christian D, Engel C, Nielsen M, Kaufmann A et al. Expanded extracolonic tumor spectrum in MUTYH-associated polyposis. *Gastroenterology*. 2009; **137(6)**: 1976-85.
5. Slupska MM, Baikalov C, Luther WM, Chiang JH, Wei YF, Miller JH. Cloning and sequencing a human homolog (hMYH) of the Escherichia coli mutY gene whose function is required for the repair of oxidative DNA damage. *J Bacteriol*. 1996;**178(13)**:3885-92.
6. Scates DK, Spigelman AD, Nugent KP, Phillips RK, Venitt S. DNA adducts, detected by 32P-postlabelling, in DNA treated *in vitro* with bile from patients with familial adenomatous polyposis and from unaffected controls. *Carcinogenesis*. 1993;**14**:1107–1110

THE COST OF HISTORY REPEATING ITSELF: A REVIEW OF LABORATORY INVESTIGATIONS ON THE MANAGEMENT OF TONSILLITIS AND QUINSY IN THE SECONDARY CARE SETTING.

Editor,

Tonsillitis and Quinsy are common acute admissions into hospitals throughout Northern Ireland. Patients are frequently referred from the community due to worsening symptoms or failure to respond to initial treatments. While there are guidelines[1-3] for management in the community, there are no specific guidelines for those admitted into secondary care facilities and as such, management and investigations are often guided by anecdotal and historical practice rather than being evidence based. To explore this, we assessed the current investigative practice for patients admitted to Antrim Hospital with tonsillitis and quinsy during 2014.

Data was collected for patients admitted during 2014 with a diagnosis of sore throat, Tonsillitis, Glandular Fever, Infectious Mononucleosis, Quinsy or peri-tonsillar abscess including the length of stay, diagnosis, type of investigations performed, and the type of treatment received by the patients.

Sixty-nine patients accounting for 72 admission episodes in 2014 were assessed. The average length of stay of patients was 1.34 days. Fifty-seven percent of admissions had investigations such as throat culture or monospot testing with 8% having both. A total of 18 throat cultures were performed, but only 83.3% came back with a positive results requiring an average of 3.61 days for colonisation. Thirty-five monospot tests were performed with only 8.8% being positive. Antibiotics were prescribed in 68 of the cases admitted to hospital, with 10.8% receiving corticosteroids, and all patients presenting with a quinsy undergoing surgical drainage.

Our data suggests that additional laboratory investigations have a limited impact on the acute management of patients presenting with tonsillitis or quinsy given the short period of time that the patients spend in hospital (p: 0.597). Our figures estimate that it would cost £911.76 to detect a positive monospot test and £450 to grow a positive culture for every 100 patients admitted with these ailments.

The potential of complications and subsequent litigation has driven clinicians to perform multiple investigations without considering the effect on overall patient management and the cost to the healthcare system. Throat culture has a wide sensitivity range between 40% - 95%[4, 5] and is restricted by the temporal factor of time, and as such will have limited effect on immediate management. While monospot testing can help guide patient management (such as antibiotic avoidance and restrictions on subsequent contact sports), a blanket policy for its routine use is ill advised as only 8.8% showed a positive result in this series. Often, routine laboratory findings and clinical factors will point to a diagnosis of Infectious Mononucleosis and we would suggest the monospot test be used to confirm this suspicion rather than to make a diagnosis.

The authors suggest that tonsillitis and quinsy are primarily clinical diagnoses and that additional laboratory testing is of limited use. Given that the vast majority of these patients are successfully treated with a 24-hour course of intravenous antibiotics, allocation of funding to short stay facilities may be a better use of resources than the excessive investigation that we currently carry out.

The authors have no conflict of interest.

Mr Mohd Afiq Mohd Slim, Mr Philip Robert Bell, Mr Marcel Valko

Department of Otorhinolaryngology, Antrim Area Hospital, 45, Bush Road, Antrim, BT41 2RL, Northern Ireland.

Correspondence to: bellpr@hotmail.co.uk

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

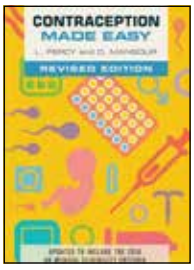
REFERENCES:

1. SIGN National Clinical Guideline; 117. *Management of sore throat and indications for tonsillectomy*. Edinburgh: Scottish Intercollegiate Guidelines Network; 2010. Available from: http://www.sign.ac.uk/pdf/sign117.pdf.
2. ESCMID Sore Throat Guideline Group, Pelucchi C, Grigoryan L, Galeone C, Esposito S, Huovinen P, Little P, *et al*. Guideline for the management of acute sore throat. *Clin Microbiol Infect*. 2012;**18 (Suppl 1)**:1-28.
3. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, *et al*. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2012;**55(10)**:1279-82.
4. Wakode PT, Gawarle SH, Joshi SV, Bajoriya R. Throat swab culture & sensitivity reports - an overview. *Indian J Otolaryngol Head Neck Surg*. 2003;**55(2)**:76-80.
5. Choby BA. Diagnosis and treatment of streptococcal pharyngitis. *Am Fam Physician*. 2009;**79(5)**:383-90.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Book Reviews

CONTRACEPTION MADE EASY.



L.Percy, D. Mansour, 170 pages. ISBN-13: 978-1907904929. Scion Publishing Limited 2015. RRP: £18.99

The books title 'Contraception made easy' delivers on its promise.

In order to do so undoubtedly the best feature is the user-friendly and consistent nature of the format. Each method of contraception has a dedicated chapter with an identical outline showcasing factual and practical content using bulleted text, tables and pictograms.

This consistency allows the reader to quickly become familiar with the contraceptive being discussed but also how it compares and contrasts to the other types of contraceptives.

At the end of each chapter a clinical scenario is provided which acts as a useful adjunct to bring in 'real-life' situations but also provides solutions to problems that may be encountered in every day clinical practice.

The book itself is patient centered from the outset. The 'Contraceptive Consultation' chapter should empower the reader with the tools to elicit a thorough history paying particular attention to the patients own knowledge, experience and expectations in order to individualise the information and treatment options relevant to the patient.

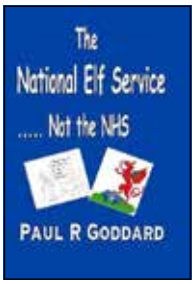
A valuable approach given that so many contraceptive options exist!

The wider issues surrounding contraception are also explored including unplanned pregnancy, abortion, sexually transmitted diseases and sterilization giving the reader a more rounded approach when thinking about the topic of contraception.

This book would be useful for medical students that are 'new' to the subject as previously mentioned the outline of the chapters lends itself to seamless grasping of new information. However the practical application of the factual information is ideal for both gynaecological and family planning trainees, nurses that work within the field and general practitioners.

Dr Suzanne Price. ST7 Obstetrics and Gynaecology.

THE NATIONAL ELF SERVICE …… NOT THE NHS. Author: Paul R Goddard. Publisher: Clinical Press, 2016. ISBN: 9781854570895. Cost: £6.99



This little book of satire is composed of cartoons, written and drawn by Paul Goddard. The author is a retired Radiologist. This is a book for a read on a train or short plane journey and is inexpensive (less than 2 gallons of petrol!). While the book will be of interest to 'mature' consultants, especially those approaching retirement (or even retired) as a reminder of "times gone by" – it should be read by others – including younger consultants and trainees.

In an easy to read and well-illustrated little book Professor Goddard touches with gentle satire – such topics as – super-specialisation, over investigation, rising malpractice, clinical freedom, mentorship, rising political and societal expectations, drug interactions, complexity of medicine, the loss of Matron, working time directives and much more. Throughout there are satirical comments on modern NHS management.

At first sight it is a book of satire, it is readable and would be valuable for senior and junior doctors and their managers to browse through – not all in the past was good but not all was bad either – we can learn from the past as the NHS of the future unfolds – this little book is a useful, painless way of so doing.

Professor Roy Spence, OBE, MA, MD, LLD (Hon), FRCS, Consultant Surgeon

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Ulster Med J 2016;**85(3):**212-218

Abstracts

Annual Trainee Doctors' Prize Evening, Thursday 20th November 2014.

North Lecture Theatre, Medical Biology Centre, Queens University Belfast.

ORAL PRESENTATIONS

In the Name of God

Rona Anderson, Bill McCallion

Introduction: Circumcision is an operation performed worldwide. Indications are either therapeutic such as phimosis or non-therapeutic, that is; in the name of culture or in the name of God. The BMA has recommended that circumcision only be performed were therapeutic indications are present and as such Primary Care Trusts in both England and Wales make independent decisions about whether to provide a circumcision service when it is requested on cultural grounds. Here in Northern Ireland these continue to be conducted in the NHS. The aims of this study were two-fold. Firstly: to determine the indication with which circumcision was performed on boys in Northern Ireland in a 16 month period. Secondly: to estimate the cost of cultural circumcision to the NHS.

Method: Data was collected for a 16 month period (03/01/12-24/05/13) from the Ulster hospital and the Royal Belfast Hospital for Sick Children (RBHSC) theatre lists. A retrospective analysis was conducted regarding the indication for circumcision-therapeutic or non-therapeutic.

Results: In a16 month period (03/01/12-24/05/13) within the Ulster hospital and the RBHSC 134 circumcisions were performed; 47% (63) were performed for cultural or religious reasons. A further 12 were sent to private hospitals as NHS cases. The cost of cultural circumcisions to the NHS in this period: £100,000.

Conclusions: Performing circumcision for non-therapeutic reasons is an issue consistently raised within HSCB. Suggestion to remove it from the NHS using the EUR policy as it was classified as a low value procedure (Plastic surgery and cosmetic non-therapeutic procedures) has aided its removal in England and Whales however is more complicated for us in Northern Ireland due to Section 75 of the Northern Ireland Act 1998 which places more restraints on us with issues such as these due to our strict laws regarding discrimination. Within the current economic climate can the NHS really the NHS really afford this elective procedure in its budget?

Monitoring Patients at High Risk of Developing Type 2 Diabetes

Virginia Christodoulou

Introduction: HbA1c is now the recommended test for diagnosing diabetes in the UK. The cut off level for diagnosis of type 2 diabetes is 48 mmol/mol. Patients with a level between 42-47 are categorised as high risk of developing Type 2 diabetes. WHO guidelines recommend that these patients have an annual HbA1c to monitor for progression to diabetes.

Aims: To identify all patients within 2 GP practices over 1 year who had a HbA1c level between 42-47 and to ensure they were coded as high risk, informed of this, advice given and annual HbA1c performed.

Methods: We identified these patients using Population Manager Audit tool and found 61 patients who had a HbA1c within this range.

Results: Of these, 32 were not coded and 31 were due repeat HbA1c in 2014. These patients were contacted via telephone to arrange review and coded. Of the 31 who needed a repeat in 2014, 100% were contacted and reviews made resulting in 68% having their HbA1c repeated within 1 month.

Discussion: This project highlights the importance of coding patients at high risk of developing diabetes to ensure they are adequately followed up.

Clinical Ethics Reasoning Through Simulation (CERTS): Exploring the Authenticity of Undergraduate Experience

Gareth Lewis, Peter Maxwell, Margaret Sterling, Melissa McCullough, Gerry Gormley

Introduction: Students transitioning into professional practice feel underprepared to deal with the emotional complexities of real-life ethical situations. The few published attempts at authentic ethics simulation have not generated sufficiently deep accounts of student experience to inform pedagogy.

Aims: To study the lived experiences of medical undergraduates as they engage with a complex ward-based simulated ethics scenario and to explore how students handle stress, complexity, uncertainty and negotiate professional hierarchies.

Methods: Eight 4th year medical students at Queen's University Belfast participated in the realistic CERTS environment. They wore headcams that recorded footage during the simulation. Whilst performing a clinical task a series of ethically challenging encounters with multiple parties unfolded. Students were interviewed immediately after the scenario and headcam footage played back to them. An interpretative phenomenological analysis was conducted on verbatim interview transcripts.

Results: Six main themes emerged: i) Simulation, ii) Emotions, iii) Ethical Boundaries, iv) Role and Identity, v) Prior Experiences, vi) Balancing. Students described a wide range of emotion, they felt

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

CERTS was true to life and beneficial in developing ethics reasoning and navigating interprofessional hierarchies.

Discussion: CERTS provides an authentic environment, acceptable to students, that has potential to assist undergraduates in exploring the impact of emotion and stress on ethical decision making.

A pilot study to determine the feasibility of using a three-dimensional scaffold to deliver endothelial progenitor cells (EPCs) to a wound

Sandra McAllister, James Bojdo, Christina O'Neill, Emma Reid, Jasenka Guduric-Fuchs, Reinhold Medina, Alan W Stitt

Introduction: Chronic wounds, such as decubitus and diabetic ulcers, affect some 200,000 people in the UK, at an estimated annual cost of over £3 billion. Although the aetiology is multifactorial, ischaemia of the wound microenvironment is a central factor.

Aim: To determine the feasibility of using dermal scaffolds to deliver pro-angiogenic stem cells to wounds.

Methods: Two fully characterised endothelial progenitor cell subpopulations were isolated from human adult peripheral blood and umbilical cord blood. Outgrowth endothelial cells (OECs) and myeloid angiogenic cells (MACs) were seeded alone or in combination onto a commercially-available dermal substitute (Glyaderm® or Matriderm®), or a collagen control scaffold (Optimaix). Scaffolds were implanted subcutaneously into an immunocompromised murine model.

Results: OECs formed three-dimensional microtubular structures in scaffolds; formation was potentiated by co-culture with MACs, but MACs did not incorporate into tubules. Cells persisted in vivo and formed functional vessels.

Discussion: Personalised pro-angiogenic cells could provide cell-based therapies for wounds, but using the optimum method to deliver cells to the wound is central to the potential efficacy of treatment. Dermal scaffold-cell constructs demonstrate great promise.

Biodegradable oesophageal stents for benign and malignant oesophageal strictures.

Stephen McCain, Scott McCain, Barry Quinn, Ronan Gray, Paul Rice

Introduction: Oesophageal strictures have a benign or malignant aetiology. Benign oesophageal strictures refractory to pneumatic dilatation may benefit from biodegradable stent insertion. Biodegradable stents may also have a role in management of malignant strictures to facilitate enteral nutrition while staging or neo-adjuvant treatment is completed.

Aims: To review the safety and efficacy of biodegradable stents in the management of benign or malignant oesophageal strictures.

Methods: All patients who had biodegradable stent insertion atttempted were included for analysis. Data gathered included patient demographics, indication, pathology, pre and post-stent dysphagia scores and 30-day morbidity and mortality.

Results: Stents were deployed in 28 patients (17 benign, 11 malignant). There was one failure of deployment. There were no serious complications or 30-day mortality. Mean dysphagia scores improved signifcantly (benign- 2.65 to 1.00, $p<0.001$, malignant 3.27 to 1.36, $p<0.001$. Surgical resection was not compromised following stent insertion in the malignant group.

Conclusions: Biodegradable stent insertion is a safe and efficacious adjunct in the treatment of both benign and malignant oesophageal strictures. In malignant disease, biodegradable stent insertion can maintain enteral nutrition while staging or neo-adjuvant therapy is completed without adversely impacting on surgical resection.

POSTER PRESENTATIONS

Clinical Research

What Happens to Patients with Colorectal Cancer who do not undergo Resectional Surgery?

Stephen McCain

Introduction: Management of colorectal cancer depends on the stage of disease at presentation, fitness for surgery and personal choice.

Aim: The aim of this study was to follow a cohort of patients in the colorectal multi-disciplinary team recommended non-resectional management of the primary tumour.

Methods: Between January 2006 and January 2014, 975 patients were discussed at the colorectal multi-disciplinary meeting in the Belfast Trust. Data was collected prospectively by a research nurse but reviewed retrospectively and patients were followed until the 01/08/2014. Data collected included the reason for non-resection and other treatment received. The cause of death was categorised.

Results: 136 patients were included. The median age was 84 (range 69-94). Reasons for non-resection included; 94 patients had advanced disease, 31 were deemed unfit for surgery, 10 refused surgery and 1 had a synchronous ENT malignancy. Of the 94 patients with advanced incurable disease 28 patients required a surgical procedure and 14 had colonic stenting. 58 patients received palliative radiotherapy, chemotherapy or a combination. Of the 31 patients that were unfit for surgery, 1 required a palliative procedure. 9 died due to their colorectal cancer and 22 died secondary to medical conditions. None of these patients developed obstruction.

Conclusion: This study demonstrates the importance of careful MDT assessment of patients with a new diagnosis of colorectal cancer. Non-resectional management is acceptable in patients with advanced incurable disease and severe co-morbidities. Palliative surgical procedures were required in 1 in 5 cases.

Colonoscopy Associated Morbidity: A One Year Retrospective Study

Aaron McCloskey

Introduction: Colonoscopy in considered to be a reliable way of diagnosing a range of bowel conditions. Recognised complications include perforation (0.04%) and significant bleeding (0.25%). Around 0.25% require surgical intervention following colonoscopy.

Aims: To perform a retrospective study of colonoscopy associated morbidity in Belfast City Hospital (BCH) over a 1-year period.

Methods: The trust's Surgical Command software was used to obtain a list of patients who had undergone colonoscopy in the Endoscopy Suite from 01/08/2013 to 31/07/2014. Patients' unique identifying numbers were entered into the Electronic Care Record, emergency admissions within 2 weeks of the procedure were recorded.

Results: Data on 1,678 colonoscopies was collected. 3 patients were admitted with significant bleeding (0.18%). 3 patients were admitted with abdominal pain with no significant pathology found (0.18%).

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

2 patients were admitted with medication omission associated morbidity (0.12%). 1 patient was admitted with a reaction to the sedative midazolam (0.06%). 1 patient was admitted following a vasovagal episode (0.06%). There were no perforations. No patients required surgical intervention.

Discussion: Colonoscopy is a safe procedure. Complication rates in BCH are in line with national figures.

Review of Mortality and Long-term Effects on Renal Function in Patients that Received Continuous Renal Replacement Therapy in the Intensive Care Unit at Antrim Area Hospital

Ryan Murray

Introduction and Aims: Acute Kidney Injury long-term effects are understudied. We reviewed the outcomes of patients with AKI admitted to an ICU to assess their overall mortality and effects this had on their subsequent kidney function.

Methods: All patients requiring Renal Replacement Therapy (RRT) In Antrim Area Hospital ICU over 1-year were obtained via the Intensive Care National Audit and Research Centre system (64 patients). eGFR and creatinine measurements were obtained before their ICU admission and again at 30-days, 90-days and 1-year post-RRT commencement. Primary reason for ICU admission, mortality rates and requirement for ongoing RRT were also analysed after 1-year.

Results: The average age for patients receiving RRT in ICU was 63.8 years (66 % male, 34% female). Their baseline eGFR was 51.6mls/min. The most common cause for admission to ICU was septic shock (22%). The average eGFR at time of RRT commencement was 23.8mls/min. At 30-days, 90-days and 1-year post-RRT their average eGFR was 40.5mls/min, 42.0mls/min, and 42.6mls/min respectively. At 1-year post RRT 36% patients who had received RRT in ICU had died and 1 patient had established renal failure requiring maintenance dialysis therapy.

Discussion: Our review strongly emphasizes the poor outcomes associated with this condition, particularly high mortality rates and overall reduction in renal function.

Quality improvement / Patient safety

Screening for Alcohol Misuse Disorders in our Emergency Departments

Richard Cherry

Introduction: Screening for alcohol misuse disorders with the delivery of brief interventions in the emergency department (ED) has been shown to reduce rates of alcohol consumption, re-attendance rates, hospitalisation and overall alcohol-related morbidity and mortality. This is currently not standard practice in Northern Ireland.

Aims: To establish the point prevalence of alcohol misuse disorders amongst individuals attending Belfast's two EDs, over a one-week period, in order to drive service development with respect to the introduction of routine alcohol screening with brief interventions.

Method: As far as possible, all individuals over 18 years, attending the EDs were screened using the Audit-C at the time of triage. Patients who were medically unfit, intoxicated or refused were counted but not screened.

Results: 1114 (77.2%) of attendees completed the Audit- C. 49% (547) of those met the criteria for an alcohol misuse disorder. 28% (312) met the criteria for harmful drinking while 235 (21%) were drinking at potentially dependent levels.

Discussion: All individuals attending the ED should be routinely screened for an alcohol misuse disorder at the time of triage. For those screening positive appropriate interventions should be offered.

Fluid Balance Chart Record Keeping and Prescribing'

Laura Davis

Aim: Examine whether record keeping is adequate and prescribing appropriate.

Methods: 34 charts were assessed against the hospital policy. We noted whether the correct chart was used, identification, ward, weight, date, previous days total I/O/B, cumulative totals on previous days charts, prescription indication, date, time, prescriber's signature and checks were recorded . Date last U&E taken was noted and whether an appropriate fluid +/ electrolyte prescribed.

Results: Wrong charts were used in 2 cases. 1 chart had no patient identification. Ward, weight and date weren't recorded on 23, 34 and 8 charts respectively. Previous days I/O/B weren't documented in 21, 20 and 27 charts respectively. 3 previous days charts had no cumulative I/O recorded. The previous days total I/O/B weren't calculated correctly in 8,4 and 2 charts respectively. No indication, date, time and prescribers signature in 24, 31, 10 and 32 charts respectively. 25 charts had a U&E taken the same day. A total of 4 prescriptions were not appropriate.

Conclusion: Fluid balance record keeping is not being completed adequately or accurately. In terms of patient safety and accuracy of prescribing can we be sure standards are being met? The results of this audit have highlighted that more training of staff is needed.

The A-Z Guide to Being a FY1 – A Peer-delivered Handbook and Complementing Workshop

Matthew Macartney

Introduction: Transitioning from medical student to FY1 is challenging and covering all the nuances of the FY1 role is beyond the scope of assistantship and induction. This intellectual shortfall has consequences ranging from efficiency of practice to resource utilisation.

Aims: Utilise experiential knowledge from outgoing FY1s to prepare new FY1s for practice.

Objectives: 1. Systematically compile a list of key learning points gleaned during FY1 (presumed intellectual shortfall) to a user friendly guide. 2. Optimise educational impact with FY1-led workshop concurrent to induction.

Methods: 1. Emailed FY1 staff asking for key tips gleaned during FY1. 2. Developed A-Z guide, distributed to new FY1 staff pre-induction. 3. FY1-led workshop systematically covered the guide, reinforcing key information. 4. Compiled feedback on the program to assess relevance, effectiveness and impact on self-reported confidence.

Results: 1. 100% FY1s returned 5/5 rating for every aspect of the workshop and guide. 2. Free text comments included - "practical, helpful, should be trust wide, interactive, feel at ease, relevant, most useful aspect of induction."

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Conclusions: Providing practical experiential knowledge alongside a peer-led workshop supports the transition to FY1.

Recommendations: 1. Program should be adopted trust-wide. 2. Core components are regionally applicable, wider role should be explored. 3. Engage outgoing FY1s in annual cyclical program development to embed practice and sustain a vibrant contemporaneous resource.

The Use of Aspirin for Prevention of Pre-Eclampsia in High-Risk Pregnancies

Catherine Malone

Aims: Assess compliance with NICE clinical guidelines (all women with one high/ two moderate risk factors for developing pre-eclampsia should be prescribed aspirin 75 mg once/day from 12 weeks).

Methods: Retrospective chart review of 100 postnatal patients to determine the proportion of patients who fit the criteria above and who received aspirin.

Results: 12% of patients were moderate or high risk for hypertensive disease in pregnancy at booking (33.3% of whom developed hypertension). None were commenced on aspirin. Guidelines were highlighted during multidisciplinary meetings and wall charts of the NICE guidance provided in each consulting room. After re-audit of 100 patients one year later;

10% of patients were moderate or high risk for hypertensive disease in pregnancy at booking (30% of whom developed hypertension), 10% were commenced on aspirin

Discussion: This audit highlights the lack of awareness among health professionals regarding high-risk patients requiring aspirin therapy.

Recommendations: Wall charts of NICE guidance in each consulting room, Further education of staff regarding risk factors for pre-eclampsia requiring aspirin, Incorporation of risk factor assessment into maternity notes as per existing gestational diabetes guidelines.

The Importance of Early AKI Risk Assessment

Serena Martin

Introduction:AKI complicated up to 18% of admission with costs >£15 million a year in Northern Ireland. NCEPOD 2009 highlighted up to 20% of AKI cases are predictable and potentially avoidable. Trust wide audits revealed less than 50% are adequately risk assessed. We felt the design of the AKI tool was contributing to this.

Aims: Stage 1: Initial audit of AKI risk assessment compliance, Stage 2: Peer education and new design of AKI assessment tool, Stage 3: Re-audit AKI compliance

Methods: Initial audit of 50 acute medical patients admitted to DHH. Audit of risk assessment compliance and validation of the risk score attributed to see if we were correctly risk assessing admissions and identifying those at risk.

Results: 42% of assessments were completed and 29% of these were completed incorrectly. Only 30% of patients were adequately risk assessed on admission.

Discussion: After initial poor results we re-designed the assessment tool and educated peers on the importance of AKI risk assessment. We introduced this to the admission pro-forma then re-audited a further 50 patients. Our revised pro-forma has resulted in a 98% adherence to AKI risk assessment. The new regional eAlert for AKI will allow for accurate AKI incidence rates which will help evaluate the impact of our pro-forma on AKI rates, severity, length of stay and costs.

Nutritional Screening and Management in Acute Stroke

John McGoran

Introduction: NICE guidelines on stroke advocate prompt nutritional screening and management, with appropriate swallow assessment, for acute admissions. Patients with acute stroke stand to benefit greatly from a concerted approach to ensuring adequate feeding.

Aims: The primary aim was to assess nutritional screening and management in a cohort of patients diagnosed with acute stroke. Furthermore, swallow screening measures were identified.

Methods: Stroke admissions from May-July 2013 (n=42) were assessed for adherence to guidelines on nutritional screening. The results were published and quality improvement measures were commenced. Admissions from March-May 2014 (n=31) were compared with those previous.

Results: 30/31 patients were admitted to the stroke ward compared with 29/42 previously. Pre-MUST screening improved from 69.0% to 87.1% with over a third qualifying for MUST however only 5/11 patients had this. Admission weighing improved from 57.1% to 74.2%. Despite educational efforts swallow assessment failed to improve.

Discussion: Improvements in stroke care are best implemented on a dedicated ward. Pre-MUST scoring may not be appropriate in this vulnerable population. We advocate direct MUST with weighing on admission. Greater liaison between disciplines is warranted and involvement of medical staff in swallow screening may improve onward referral.

Current Tourniquet Practices and What Pressure Should We Use?

Afiq Slim

Aim: To compare current tourniquet practices amongst Trauma and Orthopaedic Consultants and trainees in Northern Ireland with current guidelines and determine the lowest effective tourniquet pressure.

Introduction: Pneumatic tourniquet systems form an integral part of many orthopaedic surgical procedures helping to establish a bloodless field. Complications with the use of pneumatic tourniquets are rare but significant.

Methods: (1) An online questionnaire was e-mailed to all T&O Consultants and Trainees to establish current practices. (2) We also measured the Limb Occlusion Pressure on 20 injured lower limbs to ascertain the lowest pressure required to maintain a bloodless field which was assessed by an individual surgeon.

Results: The response rate was 50%. Only 22% used contoured cuff, 10% utilized stockinette as the undersleeve, 55% set their Lower Limb Tourniquet (LLT) pressure >300mmHg. Using the limb occlusion pressure to set the tourniquet pressure there was no requirement for the pressure to be above 250mmHg.

Discussion: Current guidelines are ambiguous and clinical knowledge are poor with regards the use of pneumatic tourniquets

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

highlighting the need for unit policies. We also advocate the use of Limb Occlusion Pressure to set the tourniquet pressure.

Medical Education

Attitudes of consultants to teaching medical students in small group settings

Lynn Darragh

Introduction: The delivery of medical student education has undergone significant change recently, shifting away from didactic lectures towards small group tutorials. Anecdotally enthusiasm for teaching is waning. This study aimed to assess the attitudes of consultants to teaching medical students in small group settings.

Methods: A Likert questionnaire was distributed to all consultants working in Northern Ireland. Attitudes to teaching, financial considerations, time constraints and attitudes to students were considered.

Results: 367 responses were received. 72% of responders were actively involved in teaching. Enjoyment of teaching was evident in the majority. Financial factors and time constraints were major influences on teaching. 60% felt they were not financially remunerated for teaching, however of this group 58% continue to be involved.

Conclusion: Consultants in this Deanery are actively involved in teaching and enjoy it. The perception of lack of financial reward is not a major deterrent. Time constraints are an issue and there is a desire to have teaching included in job plans. Medical student numbers were not identified as an issue in the setting of small group tutorials. Most Consultants are complimentary about student attitudes however there is an expectation that medical students should contribute more to their own learning.

Assessment of perception of task performance

Gail Davison

Introduction: Approximately 240 4th year medical students from Queens University of Belfast (QUB) will rotate through paediatric units in N.Ireland each year. Paediatric OSCEs revealed poor performance at prescribing paediatric medication despite attendance at an Interprofessional Education Pharmacy Workshop.

Aims: The aim of this study is to assess perception of task performance, assess actual task performance and compare.

Methods: The method includes completion of a 'Paediatric Skills Survey' form and assessment of three reciprocal tasks, which include prescribing common paediatric medication, prescribing paediatric intravenous maintenance fluids and plotting growth parameters on an appropriate centile chart. 39 4th year medical students are included in the study.

Results: Both expectation and actuality were measured on 4-point ordinal scales using Kendall's tau-b. Correlation of expected and actual performance for drug prescription was 0.129 (P=0.40) while correlation of expected and actual performance for plotting growth parameters was -0.039 (P=0.80). Only 2 students gained a pass at IVF prescription despite 38 students expecting a pass of greater.

Discussion: The assumption that students are able to indicate assurances in skill performance are disproven. Lack of correlation between perception and performance would put a greater emphasis on continued assessment of medical students and doctors in training.

The European Working Time Directive (EWTD) and Surgical Training

Scott McCain

Introduction: EWTD compliance for surgical trainees poses significant challenges for patient care, training and service provision.

Aims: To examine the impact of EWTD compliance on operative experience for specialty registrars (StRs) in General Surgery and to compare mortality rates as a measure of surgical safety for compliant and non-compliant rotas.

Methods: Over an 18 month period StR operative experience in a District General Hospital was assessed when working full shift, 24-hour partial shift and on-call rotas. Mortality rates were analysed for each rota pattern.

Results: Median operative exposure increased with an on-call, compared with a full shift rota (184 vs 111, p=0.022). There was no difference in emergency or endoscopy experience. Increased experience was evident across all indicative procedures for Certificate of Completion of Training (CCT), reaching significance with regard to number of cholecystectomies (p=0.020). Significance was almost reached for inguinal hernia repair (p=0.058) and appendicectomy (p=0.055). There was no difference in mortality rates for each rota pattern.

Discussion: EWTD compliance resulted in reduced operative exposure, incompatible with achievement of CCT. Surgical safety reflected by mortality rates remained similar throughout. On-call rotas provide better training with equivalent surgical safety.

Why do OSCE Examiners vary?

Andrew Robinson

Introduction: Examiner variation can be as high as 17 % for any Objective Structured Clinical Examinations (OSCE). Some examiners have been labelled as "hawk" examiners and others as "doves". Students expect an even playing field, where the only difference between candidates is student ability and knowledge. However, examiner variation can impact on the student's final mark.

Aims: The aims of this research are to identify who are the extreme examiners and explain the factors why examiners vary.

Methods: A prospective questionnaire was administered to all Final MB OSCE examiners in February 2014. The questionnaire asked general demographic questions about the examiner. Quantitative results were analysed using SPSS.

Results: A total of 128 returned questionnaires were returned, with a response rate of 69%. No examiner within this cohort was identified as being extreme. No individual factor was statistically significant to explain examiner variation. However, there was a trend that the more junior examiners displayed "hawkish" behaviours.

Discussion: There were no examiner specific factors identified that influenced examiner variation from the cohort in this study. Examiner bias and variation is reduced by pre-exam examiner workshops and online e-learning packages on awarding a global score.

Does Video Feedback Improve CPR Performance?

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Andrew Spence

Introduction: Teaching and feedback in Advanced Life Support Cardiopulmonary Resuscitation (ALS-CPR) have been developed in QUB using high-fidelity mannequins.

Aims: Determine if video feedback is superior to verbal feedback in CPR training; Determine if video feedback is superior to verbal feedback in individual components of ALS; Determine the effectiveness of video feedback on retention of CPR skills.

Methods: 137 final year students attended the Clinical Skills Centre (QUB). Cohort A received verbal feedback on their performance and cohort B received video feedback. Video analysis (StudioCode software) was distributed to students. The study was repeated four weeks later. Performance was assessed with an OSCE tool.

Results: Video feedback students had significantly greater improvement in scores compared to those receiving verbal feedback ($p = 0.006$). Individual skills, including ventilation quality and global score were significantly better using video

feedback ($p = 0.002$ and $p < 0.001$, respectively). Video feedback showed statistically significant improvement in global score and drug administration timing.

Discussion: Use of video feedback when teaching CPR is more effective than verbal feedback and enhances skill retention. Video feedback in CPR training should be considered for all such teaching sessions.

Does Video Feedback Aid Skill Retention in Wound Suturing?

Robert Spence

Introduction: There is a lack of curricular time for both under- and post-graduates to learn and practise new skills.

Aim: This study aims to compare skill retention in medical students performing wound suturing with, and without, the use of video feedback.

Methods: Forty students were randomly allocated into verbal or video feedback groups in this cross-over study. Video feedback was given using Apple iPad (Studiocode software) giving a quantitative score. At session 1, one group received video feedback, and the other verbal feedback. Students were crossed-over, the skill repeated and scored, receiving video or verbal feedback. All completed a third session where the skill was repeated and scored.

Results: Thirty five students completed all three sessions. Receiving video feedback leads to higher skill retention than verbal feedback, with only 4.6% decrease of mean score from baseline, compared to 14.6% decrease in the verbal feedback group ($p = 0.005$). When the verbal feedback group received video feedback, their skill retention increased by 16.0% ($p = 0.005$).

Discussion: Video feedback improves undergraduate practical skills performance, allowing greater skill retention, with implications for teaching and assessment in craft specialities.

Case Reports/series

No Pain No Gain? A Case Report and Literature Review of Spinning Class-induced Rhabdomyolysis

Ashley Elliott

We present two near identical cases of exercise naive young women who had attended their first spin class and subsequently developed rhabdomyolysis. Both cases made a complete recovery in hospital without evidence of end organ damage.

Discussion: Exertional rhabdomyolysis (ER) is a rare but established clinical entity. It can present as a spectrum of illness, ranging from asymptomatic elevations in serum muscle enzymes to life-threatening electrolyte imbalances, compartment syndrome and acute kidney injury. A literature review revealed three papers reporting spin class induced rhabdomyolysis.

Our findings support the current evidence relating to risk factors for the development of ER. However, we found Creatinine Kinase (CK) levels peaked at day 5, which is later than documented in other publications, questioning the appropriate safe discharge time. As detailed our cases recovered fully, but a patient in a previous case review developed compartment syndrome, despite having similar pre-morbid characteristics. The outcome therefore can be variable and unpredictable. With the popularity of spinning classes increasing, our case report asks is it time that more information is given to those undertaking this type of training?

Uterine Arteriovenous Malformation Managed with Therapeutic Embolisation'

Catherine Malone

Case Study: A 32 year old para 1+2 required IV tranexamic acid for torrential menorrhagia one month after D+C for missed miscarriage. This procedure was complicated by massive haemorrhage despite removal of products of conception and laparotomy revealing an intact uterus. Balloon tamponade and massive blood transfusion arrested the bleeding. Histology confirmed products of conception and haematological studies ruled out any coagulation disorders. Her first pregnancy ended in D+C for miscarriage at 7 weeks, followed by an emergency caesarean section at term. She suffered a PPH intra-operatively and required two subsequent emergency laparotomies and seven units of blood for uterine angle extension and posterior uterine tears. Pelvic angiogram following second D+C showed a large AVM of the uterine blood vessels with multiple feeders. She had bilateral uterine artery embolisations, requiring three treatments before symptoms abated.

Discussion: Uterine AVMs are rare lesions with potentially catastrophic complications. They can be congenital or acquired-associated with gestational trophoblastic disease or secondary to uterine trauma. Presentation can vary from menorrhagia to life-threatening post-partum or post-instrumentation haemorrhage. Historically treatment of choice has been hysterectomy, however with interventional radiology successful embolisation of these lesions can be achieved.

Fluorine-18 Fluorodeoxyglucose Avid Oesophageal Tumour in a Fifteen Year Old Boy – A Diagnostic Dilemma

Andrew McGuigan

Introduction: A mediastinal soft tissue mass was incidentally discovered on the chest x-ray of a fifteen year old boy who presented with collapse. There was no reported dysphagia, regurgitation or weight loss. Subsequent investigations confirmed a large, solid, intramural mass in the distal oesophagus with normal overlying mucosa. Positron emission computed tomography (PET-CT) revealed the tumour to be FDG avid with an SUV max of 5.8. Given

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

the concern regarding possible malignancy raised by the PET-CT, an Ivor-Lewis oesophagectomy was performed. Histology from the resected specimen was consistent with a benign leiomyoma of the oesophagus.

Discussion: Leiomyoma is rare, but represents the most common benign oesophageal neoplasm (67-80%). Endoscopy, endoscopic ultrasound, CT and PET-CT are all useful modalities in characterising an oesophageal mass and determining the likelihood of malignancy. There have been six previously reported cases of a benign, isolated oesophageal leiomyoma showing abnormal FDG uptake on PET-CT, none of which involve an adolescent patient. Resection or eneucleation (open or minimally invasive) have both been described as valid treatment options. Oesophageal leiomyoma can cause abnormal FDG uptake in the absence of malignancy. Such lesions require careful endoscopic, radiological and intra-operative assessment to determine the diagnosis and most appropriate treatment.

PASH syndrome

Bryan Murphy

A 26 year old female presented with painful, discharging wounds in her axillae and groin. She had severe acne, suppurative hidradenitis (SH) and stable ulcerative colitis (UC) with prior subtotal colectomy and ileostomy. She denied joint problems. Despite intravenous antibiotics her wounds deteriorated warranted minimal surgical debridement and washout. Pathology demonstrated pyoderma gangrenosum (PG). She responded well to adalimumab having failed infliximab due to hypersensitivity.

Discussion: PASH syndrome is a rare, autoinflammatory condition consisting of a triad of PG, acne and SH . It is similar to PAPA syndrome (PG, acne and pyogenic arthritis) but without joint involvement, satisfying the criteria of a disease entity distinct from infection, allergy and autoimmune disorders. No genetic mutation has been found.

An association between inflammatory bowel disease and neutrophilic dermatoses is well known, however is more commonly observed in Crohn's patients. Concomitant SH and PG is so rare that a review in 2010 identified only 20 such patients; none having UC. Our review of the literature in September 2013 identified only two peer-reviewed reports describing PASH syndrome. Our patient appears to be the first case following colectomy for UC and furthermore the first to be successfully treated with adalimumab. We suggest this as a viable treatment option.

Acute Budd Chiari in previous JAK 2 Negative Patient

Rebecca O'Kane

Introduction: Budd–Chiari syndrome is an eponym for hepatic venous outflow tract obstruction, whatever the level or the mechanism of obstruction. Primary Budd–Chiari syndrome is related to thrombosis of hepatic veins or the terminal portion of the inferior vena cava. This rare disease is usually caused by multiple concurrent factors, including acquired and inherited thrombophilias.

Case: A 49 year old female admitted at the end of June 2014 with increased abdominal distension and ankle oedema. She was found to have acute Budd Chiari Syndrome, with significant ascites and underwent a TIPSS at start of July, which was unsuccessful owing to thrombus in the graft. She was therefore listed for transplant on an urgent basis, receiving an orthotopic liver transplant in August 2014. She had previously been seen by haematology in 2011 for investigation of a mild thrombocytosis, was negative for JAK 2 mutation at that time and underwent a bone marrow biopsy. They concluded that her thrombocytosis was likely reactive to her chronic sinus and chest problems (asthma, bronchiectasis). Post-transplant investigations of rising platelet count found her to be JAK 2 positive and she was started on hydroxycarbamide. Of note, her haemoglobin on admission in June was normal but with microcytic red cell indices, an elevated red cell count and thrombocytosis. She was seen again seen by haematology in September 2014 who felt that the picture is consistent with polycythaemia vera and concomitant iron deficiency. It was felt that the underlying myeloproliferative neoplasm undoubtedly contributed to the initial thrombotic event. She is currently receiving antiplatelet therapy with aspirin together with warfarin- aggressive measures with the aim of preventing further thrombotic episodes.

Traumatic Rupture of the Sternocleidomastoid Muscle following an Epileptic Seizure

Nicola Wooles

A 29 year old known epileptic, presented to A&E following a tonic-clonic seizure lasting five minutes during which he fell striking his head. He suffered a second self-limiting seizure in the department. Following these he complained of neck pain, swelling and stiffness. Otorhinolaryngology examination of his neck revealed: a tender left side with two palpable masses, reduced rotation to the right and lateral flexion to the left, and no focal neurological deficit. Ultrasound scan showed a ruptured middle third of the left sternocleidomastoid muscle. He was treated non-surgically with analgesia and intensive physiotherapy. Six weeks later there was significant functional improvement despite a palpable defect in sternocleidomastoid.

Discussion: Treatment of a ruptured sternocleidomastoid muscle is primarily conservative with early physiotherapy to reduce the torticollis risk and subsequent cosmetic and functional repercussions. Early surgical correction is advocated in patients resistant to physiotherapy.

Uncommonly sternocleidomastoid muscle rupture has been reported following high velocity trauma, but to our knowledge this is the first case described in the literature following an epileptic seizure. The case illustrates the importance of thorough examination to exclude significant pathology that may be masked by the presenting complaint and effectiveness of conservative therapy in selected traumatic ruptures.

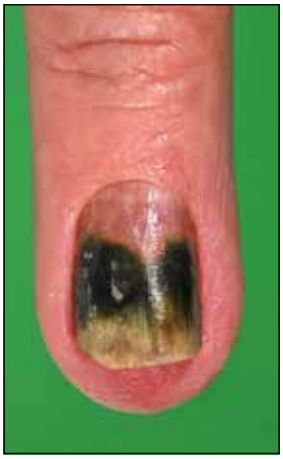
UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Ulster Med J 2016;**85(3):**219-220

Curiositas (Dermatology)

In this edition of Curiositas we have a dermatology perspective on a range of interesting clinical cases.

INTERESTING CASE



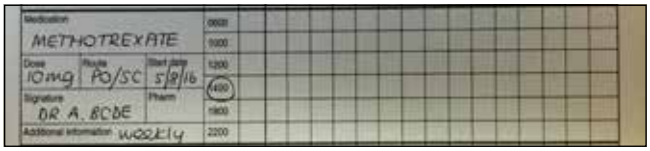
Mrs X presents with a change in the colour of her nail.

1. Describe the changes to her nail.
2. What is the underlying diagnosis?
3. What treatment options are available?
4. What alternative remedies have been used to treat this condition?

Dr Emma Mack (Specialty Doctor in Dermatology) and Dr Donal O'Kane (Consultant Dermatologist) Belfast Health and Social Care Trust.

PATIENT SAFETY

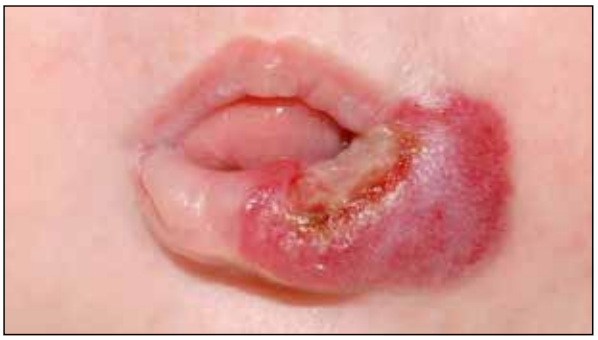
Mr X is an in-patient with psoriasis, and has been prescribed Methotrexate. Can you identify the errors in this prescription?



Dr Emma Mack (Specialty Doctor in Dermatology) and Dr Collette McCourt (Consultant Dermatologist) Belfast Health & Social Care Trust.

POSTGRADUATE QUIZ

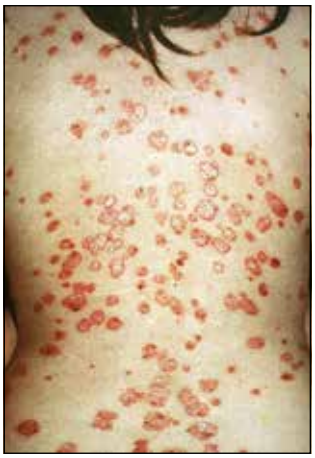
This 2 month old infant female presented with a 4 week history of a rapidly growing, ulcerated, 'strawberry pink' lesion on her lower lip.



1. What is the diagnosis?
2. In which phase of growth is this lesion currently involved?
3. What are the concerning features of this lesion?
4. How is this condition treated?

Dr Emma Mack (Specialty Doctor in Dermatology) and Dr Susannah Hoey (Consultant Dermatologist), Belfast Health and Social Care Trust.

UNDERGRADUATE QUIZ

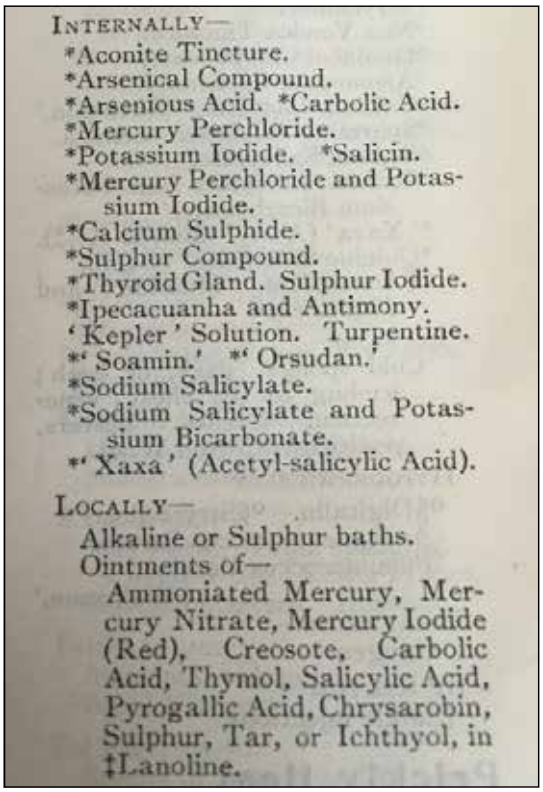


A 17 year old presents with this itchy rash approximately two weeks after being treated for tonsillitis.

1. Describe the rash.
2. What is the likely diagnosis?
3. Is there an association with the patient's recent tonsillitis?
4. What are the treatment options?

Dr Matthew Costley (Core Medical Trainee) and Dr Collette McCourt (Consultant Dermatologist) Belfast Health and Social Care Trust.

HISTORICAL CASE



INTERNALLY—
*Aconite Tincture.
*Arsenical Compound.
*Arsenious Acid. *Carbolic Acid.
*Mercury Perchloride.
*Potassium Iodide. *Salicin.
*Mercury Perchloride and Potassium Iodide.
*Calcium Sulphide.
*Sulphur Compound.
*Thyroid Gland. Sulphur Iodide.
*Ipecacuanha and Antimony.
'Kepler' Solution. Turpentine.
*'Soamin.' *'Orsudan.'
*Sodium Salicylate.
*Sodium Salicylate and Potassium Bicarbonate.
*'Xaxa' (Acetyl-salicylic Acid).

LOCALLY—
Alkaline or Sulphur baths.
Ointments of—
Ammoniated Mercury, Mercury Nitrate, Mercury Iodide (Red), Creosote, Carbolic Acid, Thymol, Salicylic Acid, Pyrogallic Acid, Chrysarobin, Sulphur, Tar, or Ichthyol, in ‡Lanoline.

This extract was taken from a 1911 physician's handbook, entitled 'Wellcome's Medical Diary'. What dermatological condition do you think this concoction of chemicals and potions was used to treat? Of course we would not recommend using these chemicals in current clinical practice!

Dr Gerry Gormley (General Practitioner, Carryduff) and Dr Emma Mack (Specialty Doctor in Dermatology) Belfast Health and Social Care Trust.

ANSWERS See overleaf

CONSIDER CONTRIBUTING TO CURIOSITAS?
Please refer to *'Curiositas: Guidelines for contributors'* http://www.ums.ac.uk/curiositas.html and email *umj@qub.ac.uk* with your ideas and submissions.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

CURIOSITAS: ANSWERS

INTERESTING CASE

1. The nail has a striking green colour and is onycholytic.
2. The green colour of the nail is classical of 'Pseudomonas Nail' or 'Green Nail Syndrome', a condition caused by the colonisation of the nail plate by Pseudomonas aeruginosa.
3. The condition is usually treated with topical or oral antibiotics, and advice should be given to avoid immersion of the hands in water.
4. Soaking the affected nail twice daily in household vinegar can help to improve the condition[3].

Dr Emma Mack (Specialty Doctor in Dermatology) and Dr Donal O'Kane (Consultant Dermatologist) Belfast Health & Social Care Trust.

POSTGRADUATE QUIZ

1. The diagnosis is of an infantile haemangioma (IH), a benign proliferation of endothelial cells.
2. This lesion is in the 'proliferative' phase, which involves rapid growth.
3. Potential complications in this case include the evidence of ulceration and the potential functional impairment from obstruction of feeding. Other important features could include bleeding, pain, compression of underlying structures or the cosmetic appearance of the lesion[1].
4. Oral propranolol is indicated in this case in order to reduce the risk of developing the above potential complications.

Dr Emma Mack (Specialty Doctor in Dermatology) and Dr Susannah Hoey (Consultant Dermatologist), Belfast Health and Social Care Trust.

PATIENT SAFETY

Methotrexate is taken weekly and the prescriber should strike out the six non-methotrexate days in the administration section. The day of planned administration should be noted in the 'special instructions' section. Methotrexate must always be taken on the same day of the week. Ideally, avoid prescribing for Mondays, as there are reports of 'Monday' being misread as 'Morning'. Routes of administration include oral tablets or liquid, and subcutaneous injection. The increased bioavailability of subcutaneous methotrexate leads to increased toxicity[2, 3]. Prescribers should therefore not write 'PO/SC.'

Dr Emma Mack (Specialty Doctor in Dermatology) and Dr Collette McCourt (Consultant Dermatologist) Belfast Health & Social Care Trust.

UNDERGRADUATE CASE

1. There are multiple well-demarcated small 'drop-like' erythematous plaques across the trunk, with evidence of scaling.
2. The diagnosis is guttate psoriasis.
3. Guttate psoriasis is associated with streptococcal infections, typically of the upper respiratory tract e.g. tonsillitis or pharyngitis.
4. Guttate psoriasis may self-resolve over weeks to months. Topical therapy with emollient, vitamin D analogue or topical steroid is commonly used. Narrowband ultraviolet B is an effective treatment for widespread plaques. Antibiotic therapy is prescribed for active streptococcal infection[4].

Dr Matthew Costley (Core Medical Trainee) and Dr Collette McCourt (Consultant Dermatologist) Belfast Health and Social Care Trust.

HISTORICAL CASE


Psoriasis

INTERNALLY—
*Aconite Tincture.
*Arsenical Compound.
*Arsenious Acid. *Carbolic Acid.
*Mercury Perchloride.
*Potassium Iodide. *Salicin.
*Mercury Perchloride and Potassium Iodide.
*Calcium Sulphide.
*Sulphur Compound.
*Thyroid Gland. Sulphur Iodide.
*Ipecacuanha and Antimony.
'Kepler' Solution. Turpentine.
*'Soamin.' *'Orsudan.'
*Sodium Salicylate.
*Sodium Salicylate and Potassium Bicarbonate.
*'Xaxa' (Acetyl-salicylic Acid).

LOCALLY—
Alkaline or Sulphur baths.
Ointments of—
Ammoniated Mercury, Mercury Nitrate, Mercury Iodide (Red), Creosote, Carbolic Acid, Thymol, Salicylic Acid, Pyrogallic Acid, Chrysarobin, Sulphur, Tar, or Ichthyol, in ‡Lanoline.

The condition was psoriasis. Curiositas was bemused to see the use of 'Arsenical compound' and 'Mercury'. Reassuringly treatment of this important condition has advanced. There are numerous guidelines resources about the treatment of Psoriasis, including NICE[5] Curiositas wonders what we might be using in the next 100 years?

Dr Gerry Gormley (General Practitioner, Carryduff) and Dr Emma Mack (Specialty Doctor in Dermatology) Belfast Health and Social Care Trust. (Extract from 'Wellcome's Medical Diary, 1911 reproduced with kind permission from the Wellcome Library, London)

REFERENCES

1. Burge S, Wallis D. 'Oxford Handbook of Medical Dermatology' First Edition, published in Oxford, Oxford University Press (2011); p 124, 550- 551; ISBN 978-0-19-955832-21.
2. McVerry, M (2014) 'Policy for the safe use of oral methotrexate in secondary care' Drugs and Therapeutics Committee, Belfast Health and Social Care Trust (Policy reference number SG 11/08)
3. NHS National Patient Safety Agency (2004) 'Towards the safer use of oral methotrexate'; www.npsa.nhs.uk (last accessed 1/8/2016)
4. Wilson JK, Al-Suwaidan SN, Krowchuk D, Feldman SR (2003) 'Treatment of psoriasis in children: is there a role for antibiotic therapy and tonsillectomy?' Paediatric Dermatology; **20**:11
5. NICE guidelines [CG153]: Psoriasis: assessment and management (2012) https://www.nice.org.uk/guidance/cg153?unlid=6915083020162141703 (Last accessed 7/8/2016)

MEDICAL STUDENT SUBEDITOR INTERNSHIP

Curiositas would like to thank our two medical student sub-editors Dr Glenn Ritchie and Dr Michael Corr for the hard work and enthusiasm that they brought to Curiositas.

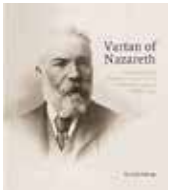
Now that Glenn and Michael are qualified doctors, we are looking for a new medical student to join the Curiositas editorial team. This internship will be, in the first instance, for 1 year. The role will involve contributing to the production of the Curiositas section. For further information on the post and the application process please email Dr Ian Bickle firbeckkona@gmail.com . Applications for this post will be accepted up until the 14th October 2016.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Book Case

Dr Shane McKee reviews 6 favourites

VARTAN OF NAZARETH



Malcolm Billings, Paul Holberton Publishing 2012

When I was a medical student in 1993, my overseas elective was in Nazareth Hospital in The Galilee, then run by the Edinburgh Medical Missionary Society (EMMS). It's the oldest continually functioning hospital in Israel, and has come a long way since 1861. Malcolm Billings' book tells the story of the Armenian tailor's son from Ottoman Constantinople who trained in Medicine in Edinburgh and, after service in the Crimean War, set up the only healthcare facility between Beirut and Jerusalem. It wasn't easy for Dr Pacradooni Kaloost Vartan and his Scottish wife Anna. Disputes with the Ottoman authorities as well as illness in the family (5 of their 10 children died) and lack of resources almost snuffed out the fledgling clinic, but through a succession of skilled directors and amid huge geopolitical turmoil, the hospital survived. Today, it is a modern (though under-resourced) facility serving much of Northern Israel – Christian, Muslim, Jewish and Druze. In November 2016, I will be returning for my second cycle ride in the region, this time to raise money for the Paediatric Unit: http://justgiving.com/shanenaz2016 . At the 150th anniversary celebrations in 2012, I was privileged to meet the current generation of the Vartan family, many of whom had come over from England, and some who had never been to Nazareth before. This is an inspiring book, lifting back the veil on 19th Century medical practice in Palestine and the people of this incredible little Arab Israeli city.

ANCIENT EGYPTIAN MEDICINE

John Nunn, British Museum Press, 1997.

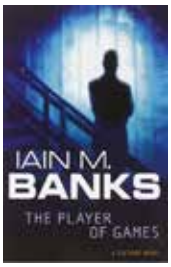
In 2016 we think we are so sophisticated, with our fancy medical diagnostics and operations. Yet we're building on a heritage that goes back before the ancient Greeks. Hippocrates credited much of his medical understanding to his Egyptian forebears. I first came across John Nunn's incredible book on a trip to Egypt in 2000. I became so fascinated with the topic that I took a 4 year Certificate in Egyptology, my dissertation being "The Medical Care of Children in Ancient Egypt". Nunn's book covers an impressively wide range of diseases and what the Egyptians thought of them, and of human physiology. He includes partial translations of some the medical papyri, which show that Egyptian *swnw* (doctors) invented the S.O.A.P. (Subjective, Objective, Assessment, Plan) structure long before we did, as well as many treatments that retain validity today. We stand on the shoulders of giant mummies.

OUR MATHEMATICAL UNIVERSE

Max Tegmark, Penguin 2015

We also live in an extraordinary Universe, larger and more complex than we ever knew before we developed Science. Yet one observation may be the most puzzling and the most profound of all. Mathematics seems to do a spectacularly good job of describing how things actually work. Moreover, the mathematical models that appear to best describe our universe imply the existence of countless other universes in an almost limitless Multiverse. And if that's not enough, the fundamental nature of this Multiverse may actually be Mathematics itself. This book unpacks these brain-melting ideas in an accessible and entertaining form, including possibly the best explanation of the physics of the Big Bang that I have ever read. The central idea in particular – that everything is Mathematics – represents a theory that is breathing new life into ideas that go back to Plato, although with a sizeable quantum twist.

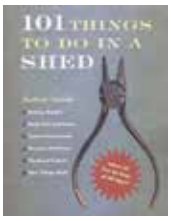
THE PLAYER OF GAMES



Iain M Banks, Orbit 1989

And speaking of universes and twists, the late (and hugely lamented) Iain M Banks was a Grand Master of this board with his sassy, engrossing, disturbing and thought-provoking series of science fiction novels based around The Culture. It is the distant future, and the Galaxy is ruled by competing civilisations with very different agendas and outlooks. Sentient spaceships, some carrying millions of people, flit in and out of hyperspace between star systems. Colossal orbitals, far larger than mere planets, retain artificial continents and oceans by centrifugal force. Humanoids and robot droids are often unwitting pawns in larger galactic games. And they do enjoy their games. Jernau Morat Gurgeh, greatest Game Player in the Galaxy (human anyway) is sent to play a high stakes game that will decide the future of an interstellar empire. But who is the player and who is being played? Banks aficionados may regard The Player Of Games as an odd choice, but its wry wit makes it my favourite of the Culture novels.

101 THINGS TO DO IN A SHED



Rob Beattie, Ebury Press, 2005

Coming back down to Earth, when I feel that Clinical Genetics doesn't let me exercise my practical side as much as I'd like, I can always head out to the garage and hammer a nail into something. It's a form of therapy. If I run out of ideas, I have "101 Things To Do In A Shed" By Rob Beattie to provide inspiration and advice. My grandfather made many of our toys when we were wee – so much so that as a kid I was convinced that he was one of Santa's elves. It's good to know that this spirit lives on amongst the Makers. Wooden games, models, science experiments, tools and techniques – this is a great little compendium for helping adults reconnect with their inner child,

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

and hopefully pass some hands-on skills and enthusiasm on to real children in the next generation.

CHICKENS: THE ESSENTIAL GUIDE TO CHOOSING AND KEEPING HAPPY, HEALTHY HENS.

Susie Baldwin, Kyle Books 2012

Stepping out of the shed and away from one form of therapy, I can turn to another. Chickens are amazing creatures, and give back so much more than they take. Provide them with food, water and shelter, and you get compost-generation, entertainment, companionship in the garden, and of course something that recycles leftover scraps into eggs. In "Chickens", Suzie Baldwin tells you pretty much everything you need to know about how to look after these remarkably low-maintenance feathered friends. And

even if you don't like eggs, someone you know is bound to. There's nothing that says "howdy neighbour" like half-a-dozen fresh free-range eggs from happy chickens. After all, promoting good physical and mental health is what we're supposed to be about.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Game Changers

THE EMERGENCY SURGICAL UNIT (EMSU) – REVOLUTIONISING UNSCHEDULED CARE IN SURGICAL PATIENTS

Dr JM Clements, Dr JD Clements, Mr WDB Clements

Emergency Surgical Unit (EmSU), Royal Victoria Hospital, Belfast, BT12 6BA

Recent recommendations[1,2] have fuelled a trend towards the segregation of elective and emergency surgical services. Belfast is no different having gone live with the EmSU in June 2013.

The "General Surgeon" in recent times has been under threat of extinction as a paradigm shift towards 'Specialist training' has compromised this identity.

The surgeons' workload encompasses four primary domains;

1. Specialist Cancer (resectional) surgery
2. Complex Specialist Elective Benign disease
3. High volume low tariff surgery, suitable for Day Case
4. General Surgical Emergencies (accounting for >60% of finished consultant episodes)

Unscheduled care, historically, has played a supporting role but never the lead. Surgery out of hours being delivered by surgeons in training with consultants 'plate spinning', spreading themselves thinly between their speciality and the general 'take-in'.

With the evolution of the EmSU 'unscheduled care' is delivered 24/7 by Consultants specialising in Upper and Lower GI surgery. Consultants see patients expediently, exercise experienced clinical judgement, implement streamlined management plans and ultimately deliver timely surgery on protected lists. These are the hallmarks of the EmSU affording the highest quality of care.

Pre EmSU <5% of all Laparoscopic Cholecystectomies were performed on the index admission, this figure has risen > 50%. Time to surgery has fallen by 50% and approximately 8000 patient/bed days are saved annually. Mortality and 'readmission rates' are also well below the National average.

We strive to improve quality and efficiency through radical changes in our working dynamic, culture and behaviour. The 'Son of EmSU' will be an Ambulatory Surgical Service with rapid access to Consultant assessment, imaging and labs with the majority of care afforded in an outpatient setting.

Long live the General Surgeon!

REFERENCES:

1. Anderson I, ASGBI on behalf of the 3 Associations and their working groups. The future of general Surgery. AUGIS 2015. Date Accessed Jan 2016. Available from: http://www.augis.org/augis-reports/
2. The Royal College of Surgeons of England. Emergency Surgery: Standards for unscheduled surgical care. RCSEng - Professional Standards and Regulation. 2011. Date accessed Jan 2016. Available from: https://www.rcseng.ac.uk/publications/docs/emergency-surgery-standards-for-unscheduled-care.

PET RESCUE

Mr. L McCadden; Mr. R Ullah

Department of ENT, Royal Victoria Hospital, Belfast, BT12 6BA

In Northern Ireland we have been fortunate to have access to PET scanning so readily. The Royal Victoria Hospital was only the fifth location in Europe to have such technology when it began operation in 2002. In Head & Neck Cancer this has been a great tool for both diagnosis and disease recurrence surveillance. PET is performed in conjunction with CT to provide detailed merged images.

Metastatic SCC of the neck is frequently seen, however occasionally the primary site is not identified. Gone are the days of the 'blanket biopsy' of tonsil, tongue base, larynx, bronchus and oesophagus. Although PET can aid in pinpointing the primary tumour location, there still exist a number of patients with a true 'unknown primary'. Part of any cancer service is follow-up, after treatment, to monitor for recurrence. This is a challenge if you don't know where it started in the first place. Indeed, these patients will invariably receive significant radiation to their head and neck.

Radiotherapy changes and tumour recurrence are not always easy to discern during follow up. False positives are possible due to inflammation, but PET has undoubtedly proved valuable.[1] Various studies have shown its strength over traditional imaging and clinical findings.[2] Its use will continue to improve care in Head & Neck Cancer.

REFERENCES:

1. Castaldi P, Leccisotti L, et al. *Role of 18F-FDG PET-CT in head and neck squamous cell carcinoma* Acta Otorhinolaryngol Ital. 2013 Feb; **33(1)**: 1–8.
2. Mak D, Corry J, et al. *Role of FDG-PET/CT in staging and follow-up of head and neck squamous cell carcinoma* Q J NUCL MED MOL IMAGING 2011;**55**:487-99

ENDO-PROSTHETIC REPLACEMENT IN THE MANAGEMENT OF COMPLEX DISTAL FEMORAL FRACTURES IN THE ELDERLY

Mr F Callachand, Mr J Barr, Mr L Cusick.

Trauma and Orthopaedic Department, Royal Victoria Hospital, Belfast. BT12 6BA.

Over recent years there have been an increasing number of elderly patients admitted to the Royal Victoria Hospital trauma unit with complex, osteoporotic fractures involving

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

the distal femur. These patients often have multiple medical comorbidities and a poor pre-injury mobility status akin to patients with fracture neck of femur. The common treatment for these fracture include locking plates, or intramedullary nails. A stable reduction is not always possible and early weight bearing is restricted. Fractures can develop non-union in 18% of cases, with subsequent implant failure[1]. These require further surgery with repeat fixation and bone grafting, with some progressing on to multiple surgeries. This carries with it increased morbidity and mortality for patients.

Endo-prosthetic replacements were initially developed for use in major bone loss associated with oncological bone disease, and have evolved significantly in recent years. They are now also being used as a salvage procedure in revision arthroplasty, non-union and infection.

Recent literature has presented evidence that endo-prosthetic replacement as a first line surgical treatment has a role in elderly patients with complex, intra-articular distal femoral fractures[2,3]. Use of these implants addresses the aims of fracture management, which are to produce a stable construct and allow early weight bearing and active mobilisation of the involved limb. This can enhance recovery and shorten hospital stays. Although not without risk, the use of endo-prosthetic replacement does offer a useful alternative to internal fixation for this group of patients.

Within our unit this is a treatment strategy that we have adopted and we are currently assessing the short to mid term outcomes for these patients.

REFERENCES:

1. Hoffman MF, Jones CB, Sietsema, DL, Tornetta III P, Koenig SJ. Clinical outcomes of locked plating of distal femoral fractures in a retrospective cohort. *JOSR*, 2013; **8(43)**
2. Appleton P, Moran M, Houshian S, Robinson CM. Distal femoral fractures treated by hinged total knee replacement in elderly patients. *JBJS*, 2006; **88-B**: 1065-70.
3. Calori GM, Colombo M, Malagoli E, Mazzola S, Bucci M, Mazza E. Megaprosthesis in post-traumatic and periprosthetic large bone defects: Issues to consider. *Injury*, 2014; *45 Suppl 6*: S105-10.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

Ulster Med J 2016;**85(3):**225-226

So You want to be an **Emergency Physician?**

Kevin Maguire

Consultant in Emergency Medicine, Ulster Hospital, Dundonald, Belfast BT16 1RH.

E-mail: kevin.maguire@setrust.hscni.net

Accepted: 10th August 2016
Provenance: invited article

I think the first thing we should try and get to the bottom of is 'What is an Emergency Physician'? We used to be Casualty and that is still the name of a popular BBC TV program. That name stems from the following definitions:

Definitions from *the Shorter Oxford Dictionary*

Casual "Occurring unpredictably; irregular"

Casualty "A chance occurrence; an accident; a mishap; a disaster. A person killed or injured in war or accident"

Accident "An event that is without apparent cause, or unexpected; an unfortunate event"

Emergency "A situation, especially of danger or conflict, which arises unexpectedly and requires urgent action"

The formation of Casualty doctors stemmed from the desire of pioneers to deliver better care to those unpredictable patients who turned up at Hospitals.

In 1972, 30 Consultant posts were established as an experimental pilot, creating a new specialty in the UK - Accident and Emergency Medicine.

In 2004, a UK Statutory Instrument formally changed the name of the specialty from A&E Medicine to Emergency Medicine (also known as Accident & Emergency Medicine), in order to keep in line with International nomenclature.

In 2008, the College of Emergency Medicine was formed with the Royal appellation coming in 2015.

That is how we moved from Casualty Surgeons to Emergency Physicians, a lot of change in a relatively short time period. That pace of change continues now.

The Royal College of Emergency Medicine has used the definition from the *International Federation for Emergency Medicine, 1991* to state that

"Emergency Medicine is a field of practice based on the knowledge and skills required for the prevention, diagnosis and management of acute and urgent aspects of illness and injury affecting patients of all age groups with a full spectrum of undifferentiated physical and behavioural disorders. It further encompasses an understanding of the development of pre-hospital and in-hospital emergency medical systems and the skills necessary for this development."

So if you've read that, then you know that we see patients whose complaints range across the entire spectrum of Medicine and, more than that, some of what we do is work to ensure that we don't see patients by creating safer systems.

It allows us to see what we believe to be the best bits of each specialty - the Emergencies.

The current training programme is a run-through training program so that you enter through a competitive Interview process at ST1 and then spend 6 years to gain a CCT in Emergency Medicine.

The interview process in Northern Ireland is run locally and focuses on clinical questions and communication skills. It is competitive as there are only 12 ST1 posts in the Emergency Medicine training program in Northern Ireland.

The first three years are part of the ACCS programme and rotate the trainee through Acute Medicine, Emergency Medicine, Anaesthetics, ICU and Paediatric Emergency Medicine thus creating a broad skill base in managing acutely unwell patients of all ages and presentation.

The last three years are spent in Emergency Medicine, utilising those skills and developing new ones to help recognise and then treat a broad spectrum of injury and illness.

Whilst working in the Emergency Department on a daily basis there is the opportunity to work in different areas. This allows you to see and assess minor injuries, children, elderly, Trauma and Resuscitation cases, patients suitable for Medical or Surgical admission, and in some departments the ability to look after patients for a short period of time using an Observation Ward model.

In the Emergency Department you work with a large and varied team with all grades of medical and nursing staff on the shop floor and allied health professionals such as Physiotherapists, Occupational Therapists, Social Workers, Psychiatric specialist staff and Pharmacists working together to achieve the best outcomes for your patients.

There is the possibility of sub-specialisation also, with recognised sub-specialty interests being Paediatric Emergency Medicine, Intensive Care Medicine and Pre-Hospital Medicine. There are other areas for developing interests and these include Academic EM, Geriatric EM, Ambulatory Care

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

and a number of other allied specialties.

Some Emergency Physicians also work as General Practitioners or have an interest in almost anything you can think of, including Toxicology, Infectious Diseases, Sexual Health, Wilderness Medicine, Retrieval Medicine... the list goes on and on!

But, still, we haven't answered the *Why* question. Being an Emergency Physician can be one of the most rewarding jobs in all of Medicine. As a person you will be constantly challenged - personally, intellectually, physically all of which will create the environment for ongoing growth and no chance of boredom.

UMJ is an open access publication of the Ulster Medical Society (http://www.ums.ac.uk).
The Ulster Medical Society grants to all users on the basis of a Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International Licence the right to alter or build upon the work non-commercially, as long as the author is credited and the new creation is licensed under identical terms.

THE ULSTER MEDICAL JOURNAL

Whitla Medical Building, 97 Lisburn Road, Belfast BT9 7BL. United Kingdom.
Contact details: T/ F: (+44) 028 9097 5780 E: umj@qub.ac.uk W: www.ums.ac.uk

NOTICE TO CONTRIBUTORS

The Ulster Medical Journal is an international general medical journal with contributions from all areas of medical and surgical specialties relevant to a general medical readership. It retains a prime focus on material relevant to the health of the Northern Ireland population. The Journal is indexed on *PubMed Central* and *Index Medicus*.

The Journal's links with the Ulster Medical Society and Queens University Belfast are reflected in regular publication of Medical History and Medical Education articles. **The front cover** of the journal usually includes an image related to an article within, but the editor is keen to consider publishing images that reflect "**Ulster medical life**" in a broader context. Please contact the editor for further details.

Papers, case reports and letters should be sent to the Editor by e-mail at editor@ums.ac.uk. The preferred format is **Microsoft Word**.

Manuscripts should be accompanied by a covering letter **signed** by all the authors agreeing to publication and stating that the work has not been published elsewhere; and stating that they have been actively involved in the preparation of the paper and outlining their contribution to the paper. Any conflict of interest should be declared.

A **PDF** copy of the printed and signed covering letter is ideal for electronic submission.

A Consultant or GP Principal (or equivalent) is required to act as guarantor of the manuscript (usually as a co-author) in case of any issues that may arise after publication.

If e-mail submission is not possible, A CD or memory stick containing the manuscript, tables, images and covering letter can be sent to the Editor at: Dr John Purvis, Consultant Cardiologist, Cardiac Unit, Altnagelvin Hospital, Londonderry, BT47 6SB, Northern Ireland.

Articles submitted for consideration should be typewritten in single spacing, with wide margins, preferably in Times (New) Roman 12pt font. They should be fully corrected and alterations in proof may be disallowed or charged to the authors.

Colour images and tables are encouraged and there is currently no charge for colour reproduction.

Images and tables should be included as separate high resolution .jpg or .tif files and NOT embedded in the Word manuscript file. Images should be appropriately annotated and labelled.

Dr Purvis will be pleased to advise on the preparation of manuscripts on request.

After editorial checks, all manuscripts are independently refereed. The editor may request revision to a manuscript before it goes to the referee, e.g., embedded images, annotation of unlabelled images or poor quality of English.

After peer review by the referee, a manuscript may either be accepted for publication, accepted with minor or major revisions requested within a deadline or rejected. The Referee's and Editor's decisions are final and not open to negotiation. A manuscript may not be re-submitted after rejection.

1. For full or short papers, the text should indicate the purpose of the paper, and should include an introduction, sections on materials and methods, results, and a discussion relevant to the findings. A brief factual summary/abstract should be provided at the beginning of the paper along with up to six key words. For case reports, these should be **novel** or particularly important cases and *not just good teaching points*, with a maximum of 10 references and appropriate patient consent for publication of photographs.
2. Letters to the editor should be less than 500 words with up to 5 references and 1 table and/or figure.
3. Audits are eligible for publication as letters to the editor but will not be considered as original papers.
4. Scientific measurements should be in SI units (DN Baron. *Units, Symbols and Abbreviations. A Guide for Medical and Scientific Authors.* 5th ed. London: Royal Society of Medicine, 1994). Blood pressure may be expressed in mmHg and haemoglobin concentration as g/dl.
5. References should be restricted to those really necessary and useful. This journal uses the "Vancouver" style. See Uniform Requirements for Manuscripts Submitted to Biomedical Journals (www.icmje.org/recommendations/) for full details and advice. Text references are numerical and each article reference should include:
    1. a list of all authors when six or less (when seven or more only the first six should be listed followed by *et al*).
    2. the title of the article.
    3. the title of the journal *in italics* (abbreviated to the form published by the National Library of Medicine, www.ncbi.nlm.nih.gov/nlmcatalog/journals).
    4. the year.
    5. volume number and issue number (in brackets) **in bold**.
    6. first and last pages.

- *Example:* Devlin LA, Price JH, Morrison PJ. Hereditary non-polyposis colon cancer. *Ulster Med J* 2005;**74(1)**: 14-21.
- Book references should give the author, title, edition, town of publication, name of publisher, year of publication, and, where appropriate, volume and page numbers.

6. Reprints can be obtained from the printers, Messrs Dorman & Sons Ltd, Unit 2, 2A Apollo Road, Boucher Road, Belfast BT12 6HP - telephone (+44) 028 9066 6700, email info@dormans-print.co.uk - who should be approached directly. For reprint information in the United States contact: International Reprint Corporation (IRC), 287 East H Street, Benecia, California, 94590 USA. Telephone (707) 746-8740, fax (707) 746-1643.
7. Fellows and Members of the Ulster Medical Society receive the journal free. Individuals may subscribe directly. Institutional subscriptions are for a calender year. The journal has three issues per year and is published in January, May and September with a circulation of 1,000 hard copies. The journal contents are covered by *Current Contents/Clinical Practice, Index Medicus, Excerpta Medica, PubMed, PubMed Central*, and *Index Copernicus*. The journal is available in 16mm and 35mm microfilm and 105mm microfiche from UMI, 300 North Zeeb Road, PO Box 1346, Ann Arbor, MI 48106-1346, USA.

The journal attempts to conform to the International Committee of Medical Journal Editors (ICMJE) and authors should consult the ICMJE website for details of policies not specifically outlined below and particularly for research on animals and other ethical considerations. In addition, the journal is a member of the Committee On Publication Ethics (COPE).

Volume 85 No. 3 **September 2016**
ISSN 0041-6193

Front cover: Primary Care for remote Alaska Native Communities: Dr Sarah Dobbs, GP in Alaska.