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# Editorial

## The Art of Motorcycle Medicine

May's edition of the journal coincides with the largest annual sporting event in Northern Ireland, the North West 200 (NW200). The event was first held as a 200 mile long race in 1929 under the auspices of the Derry and District Motor Club. At that time, it was a smaller, companion event to the well-established Ulster Grand Prix (UGP).[1]

The race relocated to its present north coast location in 1964 and has grown in stature until it is now estimated that 100,000 visitors attend the events associated with the race. Arlene Foster, Tourism Minister in 2009, calculated the direct and indirect economic benefits to the province at about £5,000,000 per year.[2]

Unlike the "Formula One" events of the motorcycle world such as FIM World Superbikes and MotoGP, motorbike events in Northern Ireland such as the NW200 and UGP occur on closed public roads and not specially-built circuits. There is no doubt that this exposes the riders to hazards that are minimised on circuits but "road racing" although seen as controversial by some,[3] remains popular with both crowds and riders.

So, how can one provide best medical care to riders capable of 200 mph+ on the longer stretches of closed road courses (a lap of the current NW200 course is 9 miles), isolated from ready access to traditional medical services?

About 25 manned first-aid posts are located at strategic points around the course with a voluntary service ambulance present at around half the posts. "On the ground" medical response is provided by a team of doctors, paramedics and nurses who are in radio contact with the chief medical officer in the pits, race control, each first-aid post and each other. Close contact is maintained with police, fire service and Northern Ireland Ambulance Service who have no ready access to the interior of the course when "bikes are on circuit". The medical response is mobile with at least two motorbike doctors and 2 rapid response vans driven by paramedics able to respond to any incident on track or within the closed area. The first-aiders use a pre-arranged coding system to relay information on number of casualties and triage information.[4] Reliable radio communication is vital and is provided by RAYNET – the Radio Amateurs Emergency Network.

The presence of a van on the course would not be welcomed by riders going at full tilt, so often the motorbike doctors are the first to respond to an incident. The doctors have been trained in race riding, wear distinctive orange helmets with full race leathers and carry a comprehensive range of equipment in orange backpacks, belts and pouches to distribute weight evenly when cornering (about 15kg of kit is carried on the person!). A reflective "slow down" marker flag covers the rear number plate. The racers and marshals are familiar with medical bikes on the circuit and don't find this disruptive. The doctors follow behind the racers for the first segment of the first lap to cover start incidents then peel off to their posts around the course.

The rapid response vans use side roads off course to get close to an incident, but will only access the course if the race is stopped (red flag) and it is safe to proceed onto the course as determined by race control and marshals.

*Fig 1.* MCUI (UC) medical team in the 1980s. From left to right; Denis Browne, Fred MacSorley, David McManus and Ian Gibson.

Prior to the modern era, things were somewhat different. Fred MacSorley recalls that the first motorbike doctor was actually a competitor – "a Dr Marty Breslin, who was a public health doctor from Lurgan. Marty was known to take some kit out on his bike to attend serious incidents on an informal basis.[5]

The concept of a mobile response was pioneered in the mid 80's by Drs Sam Tanner and David McManus, Dr. Fred MacSorley and paramedic, Mr. Denis Browne joined shortly afterwards. The mobile radio technology to support the team was introduced by Mr. Ian Gibson of RAYNET (Figure 1).

The idea of a multidisciplinary team providing trauma care was revolutionary in the 1980s and complex life-saving procedures such as roadside thoracostomy for tension pneumothorax and surgical airways were performed.

Skill in performing medical interventions at the roadside requires extensive training and although the team benefits from a wide range of disciplines amongst its membership, all are encouraged to join the British Association of Immediate Care (BASICS) and take the Pre-Hospital Emergency Care (PHEC) course which emphasises flexible team working and communication. That communication must extend to the receiving hospitals as well as emergency services operating

at the boundary of the closed circuit – The Coastguard had to be called in to assist one year at the NW200 when a rider left the course and went over a cliff between Portrush and Portstewart.

There were two major turning points in the team's history according to Dr MacSorley. The first was the incorporation of paramedics to work alongside doctors at the roadside long before that became fashionable in N.I. and the second being the pre hospital deployment of doctors skilled in anaesthesia. Motorbike doctor, Mark Sheridan, provided on-site anaesthetic services in the 90s and for the past 12 years, Dr John Hinds has fulfilled this role alongside enhanced clinical governance and education in the team structure.

As speeds get ever faster and racing technology develops, new problems emerge: the aerodynamic "speed hump" recently incorporated into the riders' leathers to improve aerodynamic profile, curves the upper spine and neck of the supine patient making it difficult to manage the airway and cervical spine. Team members have published their experience of managing this and other uniquely pre-hospital problems as part of the cycle of audit and performance improvement.[6,7]

Being a part of the Motorcycle Union of Ireland (Ulster Club) medical team offers a unique insight into the practice of medicine outside the four walls that normally constrain us. A very different environment from clinic appointments and signing off results! If you run across the team on duty, wish them; "A quiet day and good racing!"

John Purvis, Hon. Editor.

**ACKNOWLEDGEMENTS**

I am grateful to Dr Fred MacSorley, MBE for his assistance in preparing this editorial.

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*Review*

# Dementia

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## ABSTRACT

Dementia is a clinical diagnosis requiring new functional dependence on the basis of progressive cognitive decline. It is estimated that 1.3% of the entire UK population, or 7.1% of those aged 65 or over, have dementia. Applying these to 2013 population estimates gives an estimated number of 19,765 people living with dementia in Northern Ireland. The clinical syndrome of dementia can be due to a variety of underlying pathophysiological processes. The most common of these is Alzheimer's disease (50-75%) followed by vascular dementia (20%), dementia with Lewy bodies (5%) and frontotemporal lobar dementia (5%). The clinical symptoms and pathophysiological processes of these diseases overlap significantly. Biomarkers to aid diagnosis and prognosis are emerging. Acetylcholinesterase inhibitors and memantine are the only medications currently licensed for the treatment of dementia. The nature of symptoms mean people with dementia are more dependent and vulnerable, both socially and in terms of physical and mental health, presenting evolving challenges to society and to our healthcare systems.

## INTRODUCTION

Dementia is a clinical diagnosis requiring new functional dependence on the basis of progressive cognitive decline and representing, as its Latin origins suggest, a departure from previous mental functioning.

The incidence of dementia rises with age making it an increasingly common phenomenon within our aging population. The nature of symptoms mean people with dementia are more dependent and vulnerable, both socially and in terms of physical and mental health, presenting evolving challenges to society and to our healthcare systems. Despite the seemingly simple premise, the clinical diagnosis of dementia can be difficult with de novo functional impairment often obscured by physical frailty, comorbid psychiatric symptoms such as depression and a subtle but steady assuming of household responsibilities by spouses and family. Clinical and pathological criteria for the main dementia-causing diseases overlap significantly. The emergence of symptoms decades into the pathophysiological process hamper targeted disease therapy. A great number of research initiatives are underway to identify potential biomarkers of disease processes earlier. The association of both overt cognitive decline and underlying pathophysiological processes with normal aging complicate the process of identifying disease processes early within the spectrum of normal aging.

Once the diagnosis is established, prognostic measures are required, and are still lacking, as disease trajectories between individuals can vary greatly. Globally, governments are recognising these challenges. Investment and research infrastructure are beginning to reflect the scale of the need. Drugs conferring symptomatic benefit are available and memory service structures exist to diagnose dementias and guide management. The personal impact of dementia on patients and families is also being increasingly recognised, with discussion in the media surrounding famous sufferers and dramatisations in literature and film. Herein we attempt to describe the current landscape of dementia.

Table 1

*Gender specific age-related prevalence (%) of dementia in the UK (estimates from Dementia UK 2014)*

| Age in years | Female | Male | Total |
|---|---|---|---|
| 60 – 64 | 0.9 | 0.9 | 0.9 |
| 65 – 69 | 1.8 | 1.5 | 1.7 |
| 70 – 74 | 3.0 | 3.1 | 3.0 |
| 75 – 79 | 6.6 | 5.3 | 6.0 |
| 80 – 84 | 11.7 | 10.3 | 11.1 |
| 85 – 89 | 20.2 | 15.1 | 18.3 |
| 90 – 94 | 33.0 | 22.6 | 29.9 |
| 95+ | 44.2 | 28.8 | 41.1 |

## EPIDEMIOLOGY AND SOCIO-ECONOMIC IMPLICATIONS

Dementia is often arbitrarily considered early (< 65yrs) or late-onset (> 65yrs), with the vast majority (>97%) of cases being of late-onset [1]. Table 1 shows the most recent age-related prevalence estimates for dementia in the UK, which equate to 1.3% of the entire UK population or 7.1% of those aged 65 or over [2]. Applying these to 2013 population estimates gives an estimated number of 19,765 people living

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with dementia in Northern Ireland [2]. This compares to the 12,811 people registered with the Quality and Outcomes Framework for Northern Ireland (NI) with a diagnosis of dementia in 2013-2014 (http://www.dhsspsni.gov.uk/index/statistics/qof/qof-achievement/qof-lcg-13-14.htm).

The age-related incidence of dementia in the UK is falling, presumably as a result of better public health measures [3], meaning the increasing absolute numbers of people with dementia are based on the shifting population demographic, the aging population. Global estimates of a doubling in the dementia population every 20 years giving an estimated 115 million people with dementia by 2050 were revised further upwards in 2013, to take account of the likely further increases in lower and middle income countries [4].

Prognosis at the time of dementia diagnosis varies, with evidence that age at diagnosis, gender, comorbidities and disease severity can all affect life expectancy [5]. Whilst methodological variations limit the usefulness of the data available, median life expectancy from the time of diagnosis has been shown to range from 3.2 to 6.6 years, and from 3.3 to 11.7 years from dementia onset [5]. Local research has suggested a median survival of 5.9 years from diagnosis (unpublished data).

Transition into residential care as a result of the functional impairments of dementia is a prospect that worries many patients and a reality that many families face. It was estimated last year that 69% of all those living in residential care within the UK suffer from dementia [2].

It is perhaps no surprise then that dementia is expensive. The updated estimated cost to the UK economy of £26.3 billion per year published last year [2] took account of the role played by unpaid carers (£11.6 billion), social care costs were estimated at £10.3 billion and healthcare costs at £4.3 billion in comparison.

## CLINICAL DIAGNOSIS

The clinical syndrome of dementia, characterised by new functional dependence on the basis of progressive cognitive decline, can be due to a variety of underlying pathophysiological processes. The most common of these is Alzheimer's disease (AD; 50-75%) followed by vascular dementia (VaD; 20%), dementia with Lewy bodies (DLB; 5%) and frontotemporal lobar dementia (FTLD; 5%) (Figure 1). The significant clinical and pathological overlap between these processes mean their relative frequencies are estimates at best [1,6]. Less common causes (3%) include Huntingdon's disease, Creutzfeldt-Jakob disease, HIV/AIDS and multiple sclerosis. We will first consider the clinical and then the pathological properties of these diseases.

Cognitive impairments central to the diagnosis of dementia can be categorised into five main domains: memory; executive function; language; visuospatial abilities; personality and behaviour. As dementia, of any cause, progresses, cognitive impairments will broaden, involving more domains, and deepen, causing increased functional impairment. It can thus be difficult to distinguish dementias of different aetiologies in the later stages. In the early stages however the pattern of prominent symptoms can help identify the most likely

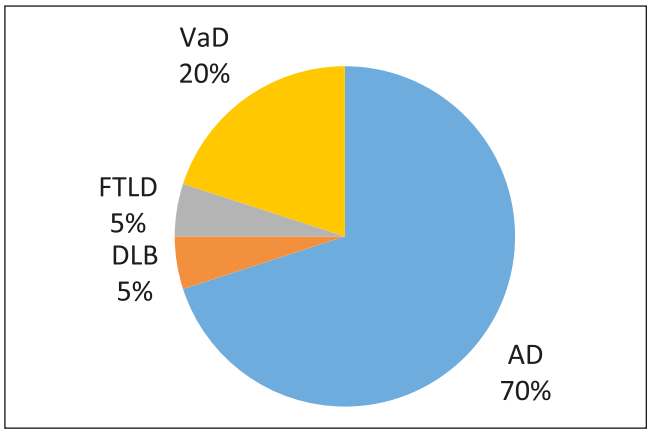


*Fig 1.* Pie chart showing estimated frequencies of dementia-causing disease processes

underlying disease process. Clinical criteria exist for all the main dementia sub-types, the main features of which are outlined in Table 2 [7-11]. All criteria require a diagnosis of dementia and include the caveats that there should not be a symptom pattern more in keeping with another of the dementias and that cognitive impairments should not be better explained by a psychiatric illness. Neuropsychiatric symptoms should be sought. Depression can be a cause or effect of cognitive impairments and often features such as hallucinations and delusions will not be volunteered unless specific enquiries are made.

AD, the most common cause of dementia, typically presents with short-term memory deficits, manifesting for example as repetitive questioning. Impairment in at least one other cognitive domain is required for a diagnosis of probable dementia due to AD (ADD). Atypical presentations of ADD include behavioural or language deficits suggesting frontal variants or prominent early visuospatial problems suggesting posterior cortical atrophy. The most relevant feature of a presentation of VaD is the temporal association of cognitive deficits with stroke and evidence of cerebrovascular disease on examination and imaging. The Lewy body diseases comprise DLB and Parkinson's disease (PD). Patients with DLB may go on to develop Parkinsonism. As a rule of thumb, if the emergence of dementia and physical PD symptoms are within one year the diagnosis is PD dementia (PDD), if cognitive symptoms predate physical symptoms and signs by more than one year the diagnosis is considered to be DLB. Early language or behavioural symptoms raise the prospect of FTLD. In the younger age groups, ie less than 65, the incidence of FTLD and ADD are almost equal, in contrast to the vastly lower incidence of FTLD in older age groups. The early symptoms of behavioural variant FTLD often raise the possibility of primary functional psychiatric diagnosis, complicating diagnosis.

It is relatively common to be presented with clinical

TABLE 2

*Clinical diagnostic criteria for dementias*

| Disease | ADD | DLB | Behavioural variant FTLD | Primary progressive aphasia (FTLD) | VaD |
|---|---|---|---|---|---|
| Authors (year) | McKhann et al (2011) | McKeith et al (2005) | Rascovsky et al (2011) | Gorno-Tempini et al (2011) | Gorelick et al (2011) |
| Required symptoms | (Typical ADD)<br>Memory deficits<br>+ deficits in at least one other cognitive domain | (Central features)<br>Attentional deficits<br>Executive dysfuction<br>Visuospatial deficits<br>(Core features, 2/3)<br>Fluctuating cognition<br>Visual hallucinations<br>Parkinsonism<br>(Suggestive features)<br>REM sleep behavior disorder<br>Neuroleptic sensitivity<br>Positive DAT scan | Behavioural disinhibition<br>Apathy or inertia<br>Loss of sympathy or empathy<br>Perseverative, stereotyped or compulsive/ritualistic behavior<br>Hyperorality and dietary changes<br>Executive dysfunction with relative sparing of episodic memory and visuospatial skills<br>(3/6 required) | Language deficit most prominent symptom and accounts for functional decline<br>No prominent memory, visuospatial or behavioural problems | Clear temporal relationship between vascular event and onset of cognitive deficits<br>Cognitive deficits independent of motor/sensory sequelae of vascular event |

scenarios that do not wholly and exclusively fulfil a single diagnostic criteria. Reflecting the concurrent accumulation of pathophysiological processes within the brain, symptoms can represent overlapping disease processes and mixed pictures can be said to occur, this is most commonly the case with ADD and VaD.

Many people present with objective cognitive symptoms that fall short of the requirements for a diagnosis of dementia. Criteria exist then for the diagnosis of mild cognitive impairment (MCI) [12,13]. Creation of this diagnostic category has facilitated focused follow up demonstrating that 5-10% per year of those with MCI will progress to fulfill the diagnostic requirements of a dementia [14]. Such symptoms can also be due to psychiatric illness, drugs known to be deleterious to cognition or may be transient and regress spontaneously. As the use of biomarkers, outlined below, evolves, identification of those more likely to be in the prodromal stages of a dementia is improving, with some arguing that patients should be identified at the MCI stage as either prodromal dementia or not [15]. For now the diagnostic bracket of MCI, whilst disputed, remains.

Other diagnostic criteria exist. In addition to the criteria set out by McKhann et al in 2011 [7] an International Working Group has proposed diagnostic criteria for ADD intended for use primarily in research [15]. The older Hachinski [16] and NINDS-AIREN [17] scales are still used to define VaD. The 5th edition of the Diagnostic and Statistical Manual of Mental Disorders published in 2013 by the American Psychiatric Association [18] has introduced the terms major and mild neurocognitive disorders, which equate to dementia and MCI. Their criteria for the various subtypes equate broadly with the pre-existing clinical criteria.

Diagnosis and differentiation of dementias requires careful history taking and examination. Both patient and collateral histories are needed to establish a new functional dependence and to explore the progressive cognitive impairments as well as neuropsychiatric symptoms. Physical examination is required to examine for focal neurological or extrapyramidal signs. Cognition will be assessed informally during the course of the consultation but formal testing is required, and facilitates longitudinal monitoring. A suggested framework for assessment of patients presenting with cognitive complaints is outlined in Table 3.

Probably the most widely recognised formal cognitive test is the Mini Mental State Examination (MMSE), first proposed in 1975 [19]. Whilst assertions of copyright have impacted on its use in recent years the MMSE has become well and widely established, and provides a common language for those fluent in its use. The Montreal Cognitive Assessment, originally developed as a test for MCI, and also marked out of 30, has expanded into the space created by MMSE apprehension (www.mocatest.org). The Addenbrooke's Cognitive Examination-III (ACE-III) provides a more thorough assessment and marks are calculated for each domain, then tallied to give a total, out of 100 (http://www.neura.edu.au/frontier/research/test-downloads/). A growing variety of scales exist, none of which is perfect. Inter and intra-rater reliability can limit use and all scales are reliant on premorbid educational abilities. The important thing is to become familiar with a scale, ensure its consistent use within a service, and use it to monitor progression.

 

Table 3

*Suggested foci of assessment of patients with cognitive symptoms*

| | | |
|---|---|---|
| History | History from patient and informant<br>Change from baseline<br>Functional decline<br>Past medical history<br>Drug history<br>Current home circumstances<br>Alcohol and smoking<br>Driving<br>Family history | Some specific examples: repetitive questioning; inability to navigate journeys and less familiar environments eg shopping centres, own children's home; difficulty recognising previously familiar people; difficulty using new equipment eg new oven; word-finding difficulties; tendency to participate less in group conversations; less attention to personal hygiene/appearance; new short-temperedness with family<br><br>Progressing to: agitation in the evening; not recognising home as own<br><br>Specific safety concerns: problems in the kitchen; problems with cigarette disposal; wandering; handling of money |
| Physical examination | Extrapyramidal signs<br>Focal neurological deficit(s)<br>Ability to follow instructions<br>Pulse<br>Chest auscultation | |
| Cognitive examination and associated scales (52,53) | Formal cognitive testing (eg MMSE/ACEIII)<br>Geriatric Depression Scale (or alternative)<br>Activities of Daily Living Scale<br>Neuropsychiatric Inventory | Neuropsychiatric Inventory includes delusions, hallucinations, agitation/aggression, apathy, disinhibition, sleep and appetite |
| Investigation | Bloods<br>CT brain (or MRI if appropriate)<br>ECG | |

## PATHOPHYSIOLOGY/ PATHOLOGICAL FEATURES

The disease processes underlying dementia are yet to be fully understood. With the (probable) exception of VaD, all involve a pathological accumulation of a native protein: in the case of AD it is the extracellular plaques of amyloid and the intracellular tangles of hyperphosphorylated tau; in DLB it is alpha-synuclein in the form of Lewy bodes; in FTLD several culprits have been identified including TDP-43 and the hallmark proteins of AD and DLB in a frontotemporal distribution. Examples of these lesions can be seen in Figures 2-5. It is important to remember that evidence of these processes is also found post-mortem in people who did not exhibit cognitive impairments prior to death, and that these patterns are not mutually exclusive, existing concurrently as they often do [20].

These pathological accumulations are associated with synapse and neuronal loss and atrophy which also demonstrate patterns in terms of distribution. Hippocampal atrophy within the medial temporal lobe for instance is associated with AD, in keeping with the early amnestic symptoms [21]

Genetic studies have contributed greatly to our knowledge of these disease processes. The observation that people with Down's syndrome (trisomy 21) almost invariably develop AD, led to the discovery of the first of three autosomal dominant genes associated with early-onset ADD [22]. Study of these genes, responsible for amyloid cleavage, have been integral to the understanding of pathological amyloid production. In contrast to the aberrant production of amyloid proteins implicated in early onset ADD, late-onset ADD (LOAD) is thought to be more to do with faulty clearance of amyloid from the brain. Apolipoprotein E [23] and, more recently, TREM-2 [24,25] alleles have been identified as risk factors for LOAD. Their pathophysiological roles remain unclear: they are implicated in amyloid processing and neuroinflammation amongst other pathways. Neither are sufficient or requisite for LOAD and are therefore not tested for in routine clinical practice. Genome wide association studies in recent years have consistently identified several genes with significant but modest associations with LOAD[26] and examination of their relevant pathways, including immune response and inflammation, cell migration and lipid transport, have enhanced the evolving understanding of the ADD disease process.

These methods are being applied across the dementia spectrum and similar pathways are implicated in DLB, FTLD and VaD [27,28]. FTLD in particular has myriad of increasingly recognized heritable components.

Animal models, often based on these predisposing genetic mutations, continue to provide basic science research opportunities. Improving chemistry techniques, such as proteomics and metabolomics are also being used to study the disease using human-derived samples such as blood and cerebrospinal fluids.

## BIOMARKERS

The search for biomarkers further informs our understanding of these disease processes and offers the opportunity to identify them prior to symptom emergence. A biomarker has

 

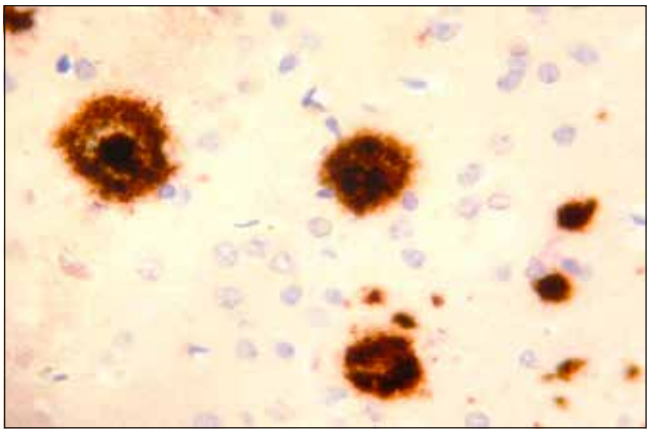

*Fig 2*. An immunohistochemical section taken through the cortex in a case of ADD. An antibody to Beta A4 amyloid is applied to the tissue and detects this antigen which in turn stains the antigen brown.
This shows a dense deposition of amyloid throughout the cortex as dense core (DC) and diffuse (D) plaques.

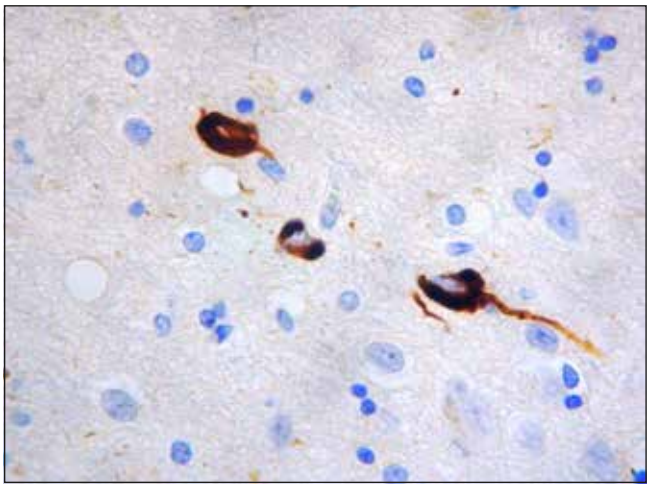

*Fig 3*. Neuronal tangles stained with an antibody to Tau (T)

been defined as a 'characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention [29]. Research into ADD is currently the main focus and biomarkers are generally considered as representing the underlying AD process (evidence of amyloid and tau accumulation) or neurodegeneration (markers of synapse/neuronal loss or atrophy) [7,15].

Low amyloid beta and high tau in cerebrospinal fluid (CSF) and high levels of intracerebral amyloid as measured by positron emission tomography (PET) scanning predict the subsequent development of ADD [30]. The downstream markers of neurodegeneration - hippocampal atrophy on MRI and decreased uptake of a radiolabelled glucose tracer (18-fluorodeoxyglucose, FDG) as measured using PET scanning (FDG-PET) have also been shown to increase diagnostic accuracy when used to supplement clinical measures [30].

The occurrence of these pathophysiological processes in cognitively normal people, especially with increasing age,

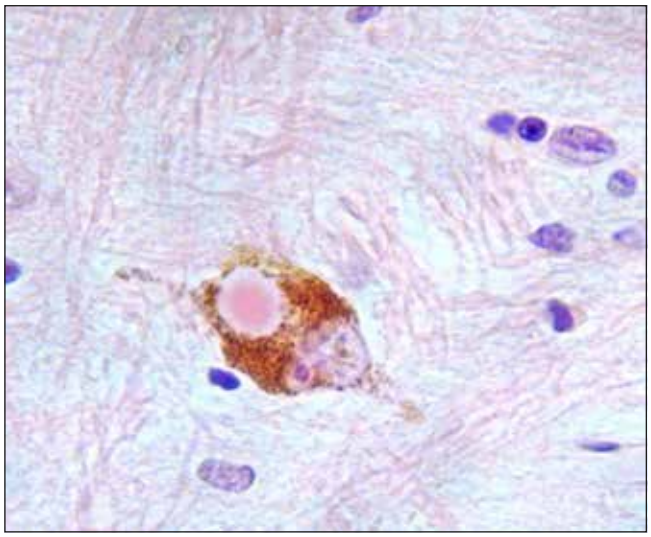

*Fig 4*. A pigmented neuron from the substantia nigra. A single Lewy Body is present. This patient also had diffuse cortical Lewy bodies characteristic of Pure Lewy Body Dementia

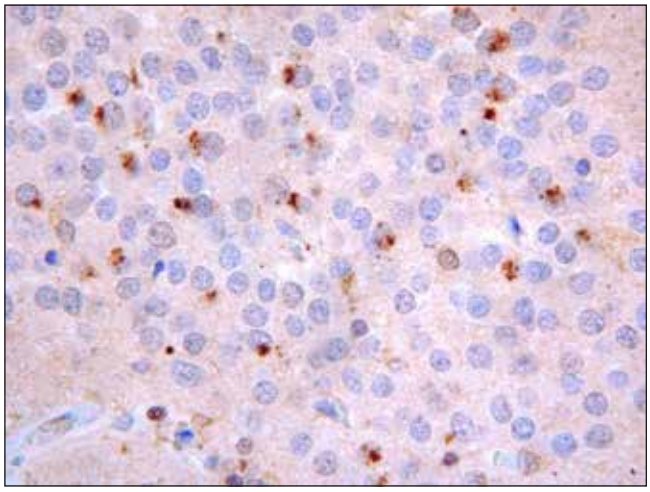

*Fig 5*. A section from the hippocampal dentate fascia showing dot like deposition of ubiquitin.
This is characteristic of Frontotemporal Lobar Dementia with Ubiquitinised inclusions (now called TDP).

complicates the interpretation of these biomarkers. Several studies of cognitively normal patients are ongoing and a recently published cross sectional study of 985 participants showed that over the age of 85 more people had biomarker changes in keeping with ADD than did not [31]. There are significant variations in neuroimaging techniques across centres and also in the sampling, handling and analysis of CSF [21,32,33]. Worldwide research collaborations, such as the Alzheimer's Disease Neuroimaging Initiative (ADNI), are in place to try and accelerate our understanding of the pathophysiological processes underlying dementia, and hence the interpretation of biomarker findings, in both cognitively normal and impaired participants. Global standardisation initiatives are also ongoing with regard to MRI and PET imaging and CSF amyloid and tau. Biomarkers are beginning to be used in clinical practice [34] but the likelihood, and benefit, of more widespread adoption is dependent on these issues being resolved.

## INVESTIGATION

Initial investigation of patients presenting with cognitive impairment centres on the exclusion of reversible causes of cognitive impairment. The National Institute of Clinical Excellence (NICE) recommends blood tests (full blood picture, urea and electrolytes, calcium, glucose, liver function tests, thyroid function tests and vitamin B12 and folate) and structural brain imaging (preferably MRI but CT will suffice) [35]. In addition to ruling out tumours, subdural haematomas, stroke and normal pressure hydrocephalus, CT, and to a greater extent MRI, can also provide information regarding chronic ischaemia, infarcts and focal atrophy. Functional imaging, such as single-photon emission computed tomography (SPECT) and FDG-PET are recommended to help differentiate between the dementia sub-types where appropriate. Figures 6&7 show normal compared to reduced uptake in keeping with ADD on FDG-PET. Dopamine transporter (DAT) scanning has shown high sensitivity and specificity for DLB and is the investigation of choice when trying to differentiate between DLB and other dementias [36].

## RISK FACTORS

In tandem with the laboratory science methods outlined above, observational studies have informed our understanding of the risk factors for dementia, as well as the natural history and prognosis of the diseases. Age is the main risk factor for dementia. Established modifiable risk factors for dementia include: depression, diabetes, (midlife) hypertension, (midlife) obesity, smoking, alcohol abuse, high cholesterol, coronary heart disease, renal dysfunction, low unsaturated fat intake and inflammation [37]. It has been argued that the decrease in age-related dementia incidence seen in the UK is due to better public health measures and thus amelioration of these factors [3]. There is in addition increased focus on recognised protective factors such as: cognitive activity, physical activity, healthy dietary pattern and low/moderate alcohol intake [37].

## MANAGEMENT – NON-PHARMACOLOGICAL

Management will be guided by the nature and severity of the symptoms and any safety concerns. Vascular risk factors should be addressed. Patients and relatives should be offered information and explanations. The Public Health Agency (www.publichealth.hscni.net ) have developed a booklet 'Communicating effectively with a person living with dementia' available via their website. The Alzheimer's Society have local offices and provide information and support (www.alzheimers.org.uk ). Patients and carers should be referred to a social worker if a carer's assessment is felt appropriate and to facilitate access to services such as Day Centres and social services care provision. As a result of the NI Dementia Strategy a navigation service for all those diagnosed with dementia is being established in all Trusts; this will ensure patients and carers have a consistent contact point throughout their journey. Moderate physical exercise should be encouraged where possible. No formal cognitive training services are currently being offered consistently though supportive evidence is emerging and may translate into service provision. Where appropriate patients can be referred to community mental health teams. Transition into residential care is influenced by social circumstances, dementia severity and the behavioural and psychological symptoms of dementia (BPSD) eg aggression. Non-pharmacological measures are recommended as first line therapy for BPSD but there is as yet no consensus regarding the most effective measures. All patients should be advised to inform the Driver & Vehicle Agency and their insurer of a diagnosis of dementia. If there are concerns regarding a patient's ability to drive they should be advised to stop driving. Where patients lack capacity to manage their own affairs and assets a referral to the Office of Care and Protection (www.courtsni.govuk/en-GB/Services/OCP/ ) may be warranted. A draft Mental Capacity Bill (NI) (working title) is due to be introduced to the NI Assembly this year having already been consulted upon. It is likely this will have significant impact on how healthcare decisions are made for people who lack capacity.

People with dementia are frequently admitted acutely to hospital, most commonly following a fall, and it is estimated that up to one quarter of in patients in UK hospitals, at any one time, have dementia [38]. This is important as caring for patients with dementia requires modification of communication, diagnostic and, at times, management approaches. Patients

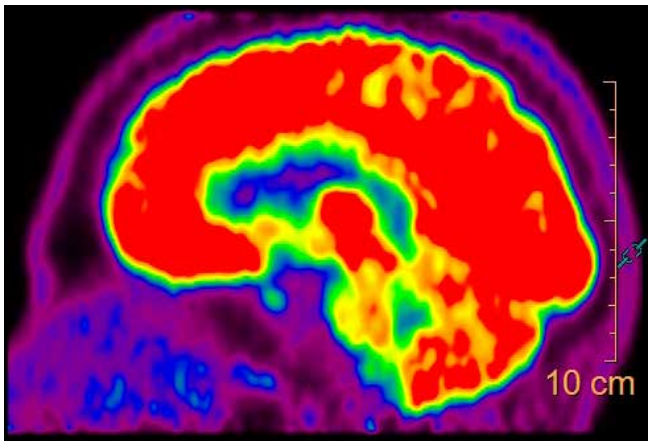


*Fig 6.*

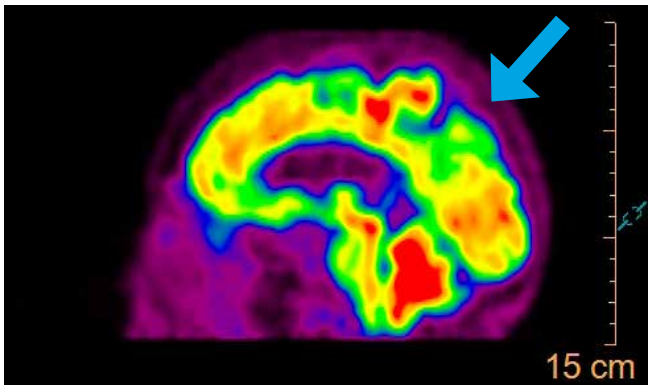


*Fig 7.*

Figures 6 and 7 show normal and reduced uptake on FDG-PET scanning respectively. The decreased uptake in the temporoparietal and precuneus (arrow) regions, typical of ADD, can be seen.

Table 4

*Acetylcholinesterase inhibitors and memantine*

| Generic name | Brand name | Dosing schedule |
|---|---|---|
| Donepezil | Aricept | 5mg od, titrated up to 10mg od after 4 weeks if tolerated |
| Galantamine | Reminyl | XL preparation available for od administration, 8mg daily initially, titrating up by 8mg after 4 weeks if tolerated to maximum of 24mg od |
| Rivastigmine<br>Rivastigmine patch | Exelon | 1.5mg bd titrating up by 1.5mg bd at intervals of at least 2 weeks; usual range 3-6mg bd<br>4.6mg/24 hours titrating up to 9.5mg/24 hours after 4 weeks if tolerated |
| Memantine | Ebixa | 5mg od, titrated up by 5mg per week to maximum dose 20mg od |

may have difficulties articulating symptoms. Constipation and acute urinary retention for example should be actively sought out. Disorientation and agitation may develop and both environmental (eg clear signage and clocks) and attitudinal (eg repeated reassurance, clear explanations, good lighting, involvement of families) approaches can ameliorate this. Dysphagia is a common occurrence as dementia progresses and patients may require dietary modification and assistance at meal times. Dyspraxia can hinder personal care, with considerate assistance required. Patients with dementia are more likely to develop delirium which can further complicate care needs [39]. Rehabilitation attempts can be hampered by cognitive impairments but dementia should not be a contraindication to rehabilitation as evidence for benefit exists. Discharge planning is required, often with inclusion of families. More than one third of patients with dementia admitted to hospital from their own homes will be discharged to an institutional setting [38]. A scheme has been introduced to increase the understanding, and identification, of dementia within hospital settings (http://butterflyscheme.org.uk ).

## MANAGEMENT – PHARMACOLOGICAL

Offending medications, in particular those with anti-cholinergic properties should be reconsidered and stopped where possible. It is important to note that even over the counter medications can affect cognition [40]. An association with benzodiazepines has been suggested by observational work and these too should be reconsidered [41].

Acetylcholinesterase inhibitors and memantine, an NMDA receptor antagonist, (Table 4) are the only medications currently licensed for the treatment of dementia. All three acetylcholinesterase inhibitors (AChEi) have a license and are recommended by NICE for the treatment of ADD with rivastigmine additionally approved for the treatment of PDD [42,43]. Memantine is approved for the treatment of moderate ADD where AChEi are contraindicated or not tolerated and as an adjunct to AChEi therapy in severe disease [43]. Evidence exists to suggest a moderate improvement in cognitive function with these drugs [44,45]. These drugs are not licensed for use in VaD. In clinical practice it can be difficult to distinguish whether there is an ADD component and these medications are often offered as a therapeutic trial. There is no evidence to support the use of AChEi or memantine in FTLD; [46,47] AChEi usually make symptoms of FTLD worse as the underlying pathological process is different to that of ADD.

Mild, moderate and severe disease severity categories are often used but are arbitrary by nature. As a rule of thumb NICE considers corresponding cut-offs by MMSE of 21-26, 10-20 and less than 10 [35] but in practice this is only a single facet of the assessment outlined in Table 3.

AChEi therapy exerts its benefit by raising pathologically low levels of the neurotransmitter acetylcholine. Potential adverse events include risk of bradycardia and syncope, potential worsening of obstructive airways disease and gastrointestinal disturbance. Assessment should therefore include an ECG and chest auscultation, with severe sinus bradycardia or evidence of a significant cardiac conduction defect or significant audible wheeze all contraindications to AChEi therapy. The possibility of reduction in the dose of beta-blocker or rate-limiting calcium channel blocker could be considered prior to initiation of an AChEi. An anti-emetic, usually domperidone, can be prescribed on an as required basis for the first few weeks to alleviate nausea. The British National Formulary recommends nocte administration of donepezil but it is acceptable to take it in the morning. The decision to continue or terminate drug therapy, in the setting of inevitable cognitive decline, can be difficult. The DOMINO-AD [48] study showed that continuation of donepezil therapy, even in severe disease, was associated with significant cognitive benefit.

Souvenaid is a food for special medical purposes with evidence for improved memory function in early ADD [49]. It is not available on prescription and requires a recommendation from a healthcare professional.

BPSD is an umbrella term for a variety of symptoms including apathy, agitation, disinhibition and sleep disturbance. These can be particularly distressing for carers and often precipitate admission to institutional care. Atypical antipsychotics are sometimes employed to combat BPSD but are associated with significant side effects including an increase in mortality and so should be carefully considered [50]. Only risperidone has a license for the treatment of BPSD and short-term treatment (<6 weeks) is recommended [42]. Depression is a common symptom (see the upcoming review in this Journal regarding diagnosis and treatment of depression).

Many pharmacological avenues are being explored in an effort to find new effective, safe drugs for dementia. Efforts

are hampered by the as yet incomplete understanding of the pathophysiological processes being targeted. Drugs targeting amyloid production and amyloid plaque clearance have failed on safety and efficacy grounds. Anti-tau agents are currently being studied. Apart from Souvenaid the much vaunted dietary supplements have yet to be supported by consistent evidence. Safety concerns are being addressed, and emerging pathophysiological insights exploited, by attempts to reposition existing drugs within the dementia field, for example metformin [51].

## CONCLUSION

Significant advances have been made in our understanding of dementia in recent decades. Dementia presents laboratory, clinical, societal and economic challenges. Diagnosis remains clinical, supplemented by improving biomarkers. Dementia causing diseases overlap in their pathophysiology and phenotypes. The only licensed drugs to date provide symptomatic benefit. Disease-modifying drug development is reliant on early identification of disease processes prior to symptom emergence, where it is currently felt best therapeutic window exists. Both biomarker and drug development depend on better understanding of underlying pathophysiological processes. The wide-reaching benefits of improved public health measures have yielded a decrease in age-related incidence but the ongoing demographic shift means efforts on all fronts must be redoubled if we are to diagnose, treat, understand and care for those of us who develop dementia. The importance of dementia as a global priority is recognised in the declarations of the G8 Dementia Summit in 2013, committing the G8 nations to the improvement in the quality of life for people with dementia and their carers and identification of disease-modifying therapies by way of a co-ordinated and funded international research framework.

## CONFLICTS OF INTEREST

ELC has received a contribution towards conference fees from Lundbeck

BMcG has received honoraria and assistance with travel from Nutricia

BH has nothing to declare

APP has received honoraria and assistance with travel from Pfizer/Eisai, Shire, J&J, Novartis, Lundbeck and Nutricia

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*Review*

# Grand Rounds: An Update on Convulsive Status Epilepticus.

Dr. Michael Kinney and Dr. John Craig

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Provenance: invited review

## ILLUSTRATIVE CASE - A COMMON SCENARIO

*A 65 year old man, with no past history of epilepsy or seizures and of weight 80kg, is admitted with sepsis. After a 5 minute generalized tonic-clonic seizure (GTCS) he is given 2mg of intravenous lorazepam. After multiple brief GTCS he is given a further 2 mg of intravenous lorazepam. He becomes obtunded. After a further 10 minutes when he has developed subtle left facial twitching, 1 g of phenytoin is infused over 30 minutes. After a further 15 minutes, by which time his GCS is 8/15, colleagues in anaesthetics are contacted with a view to transfer to the intensive care unit.*

## INTRODUCTION

Status epilepticus (SE) is the term used to describe an abnormally prolonged state of self-perpetuating and evolving seizure activity, specifically defined by time, as a 5 minute seizure or an episode of briefer seizures with reduced recovery of awareness in between seizures[1].

SE can be convulsive or non-convulsive in type. Non-convulsive seizures represent states of various levels of altered awareness, associated with electroencephalographic (EEG) seizure activity, but without outwardly observable convulsive activity[2]. An important feature of convulsive seizures is their potential for evolution into non-convulsive seizures, where the patient can appear "post ictal" but is having electrical seizures, without obvious convulsive activity[3]. Other types of status epilepticus include simple partial status (with preserved awareness), complex partial status (with impaired consciousness) and myoclonic status (often associated with coma)[4].

Records from antiquity describe SE, but it has only been in the last century that there have been major advances in its understanding and treatment[5]. Many significant questions remain about the pathophysiology and management of this medical emergency which carries a substantial morbidity and mortality. This paper will present the current understanding of SE, identifying gaps in our knowledge. The evidence base for the pharmacological management of SE will be reviewed.

## EPIDEMIOLOGY

With an incidence of 6 to 41 per 100,000[6-12] for convulsive SE, between 108 and 738 cases would be expected to occur in Northern Ireland each year. Incidence is bimodal, with peaks in infancy and in the elderly (>60). The overall case fatality rate is between 7.6 and 39%[13]. The mortality rate is higher in the elderly at 38% compared to 14% for younger adults[14].

Over half of SE patients present with de novo seizures[7] and approximately 10% will have recurrent episodes of SE[14]. Patients presenting with SE also have a higher likelihood of developing chronic epilepsy when compared to those who present with a first seizure, that does not fulfill the criteria for SE[15].

## CAUSES AND PROGNOSIS

In 50% of cases of SE no cause is identified. The common causes of SE are presented in Figure 1[6-12]. Most episodes of SE are secondary to old structural lesions (e.g. a past stroke), with acute cerebral insults including acute stroke, anoxia, toxic and metabolic causes and alcohol and drug withdrawal, accounting for a significant proportion of the remaining cases. Patients with epilepsy can develop SE for various reasons including reduced serum drug levels from poor adherence with treatment regimens, or the effects of intercurrent

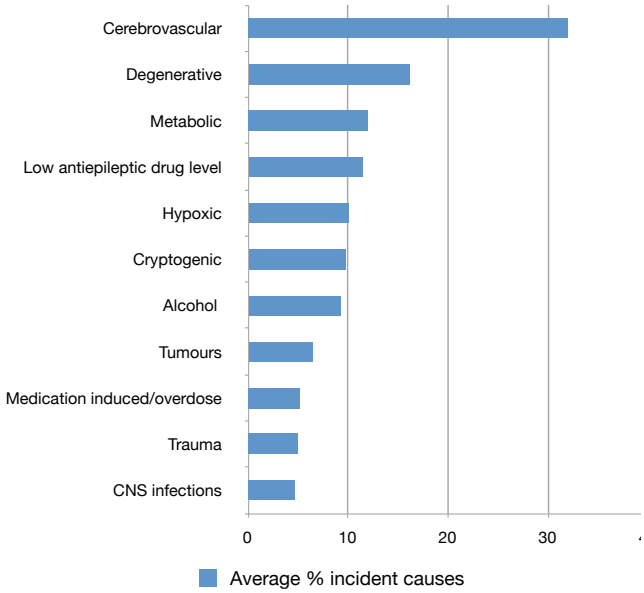


*Fig 1*. Identified aetiology of status epilepticus across major studies (6-12)

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illnesses and fever. Table 1 summarises the more uncommon causes of SE identified in a recent systematic review[16].

TABLE 1.

*The uncommon causes of status epilepticus.16*

| Category | Examples |
|---|---|
| Autoimmune disorders | Paraneoplastic disorders, Hashimotos encephalitis, anti NMDA receptor encephalitis, anti VGKC encephalitis, antibody negative limbic encephalitis, thrombotic thrombocytopenia purpura, Rasmussen encephalitis. |
| Mitochondrial disease | Alpers disease, MELAS, Leigh syndrome, MERRF, NARP, MSCAE |
| Atypical infections | HSV, bartonella, neurosyphilis, Q fever, HIV, measles, polio, CJD |
| Genetic disorders | Chromosomal abnormalities (ring chromosome 20), inborn errors of metabolism (porphyria, etc), neuro-cutaneous syndromes, malformations of cortical development, Dravet syndrome, wrinkly skin syndrome. |
| Toxic | Antimicrobial (beta lactams), antipsychotics, contrast media, cocaine, CO, ecstacy, lead, petrol sniffing, chemotherapy, acute hypo-osmolality. |
| Medical conditions | Multiple sclerosis, posterior reversible encephalopathy syndrome, Behcets disease, neuroleptic malignant syndrome, neurosurgery, electroconvulsive shock therapy. |

The outcome from SE is associated with the underlying aetiology. Anoxia is associated with a substantial mortality (72%). The lowest mortality is in patients with epilepsy who have provoked seizures, for example with low serum anti-epileptic drug levels (mortality rate 4 - 8.6%)[6] Age, duration of SE, whether there have been any prior episodes, depth of coma at presentation, and response to treatment have also been shown to be important[6, 14, 17, 18]. The main modifiable factor is the duration of SE, highlighting the importance of urgent treatment. Duration of seizure activity has been shown to be an important predictor for mortality[19], with seizures lasting less than 30 minutes having a mortality of 2.6%, compared with 19% for those lasting more than 30 minutes.

## ACUTE PATHOPHYSIOLOGY - MECHANISMS OF STATUS EPILEPTICUS

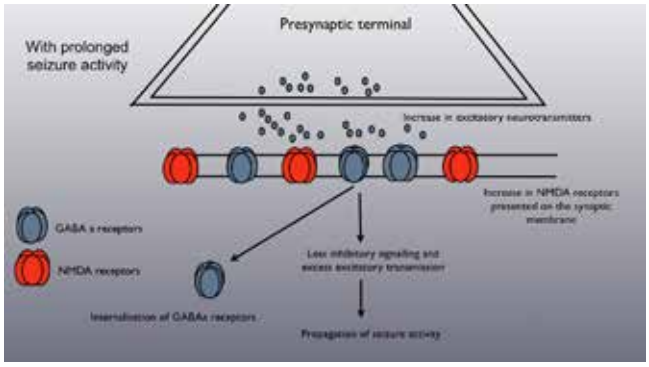


*Fig 2*. The pathophysiology of status epilepticus[21].

SE is an evolving state with changes in neuronal and synaptic chemistry and systemic physiology resulting in progressive pharmacological refractoriness. For the first 30 minutes physiological compensation occurs to meet the increased metabolic demands. Heart rate, blood pressure and serum glucose level are all elevated to minimize the risk of cerebral damage. After 30 minutes, decompensation occurs with hypotension, hypoxia, metabolic acidosis, cardiac arrhythmias and cerebral auto-regulatory failure ensuing, all of which can lead to neuronal damage. Later complications include rhabdomyolysis, renal failure, pulmonary edema, increased intracranial pressure, and electrolyte disturbance[20].

Within seconds of the development of SE alterations occur in protein phosphorylation at various synapses, ion channel function and neurotransmitter release. Within minutes, receptor expression changes in favour of excitation as a result of progressive reduction in GABA (γ-aminobutyric acid) receptors and an increase in AMPA (α-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) and NMDA (N-methyl-D-aspartic acid) receptors. (Figure 2). By one hour there is an increase in excitatory neuropeptides. The excess in excitotoxic transmission is a suggested mechanism for neuronal cell death[21].

## CLINICAL EVALUATION OF STATUS EPILEPTICUS

In evaluating the patient in SE, the ABC (Airway, Breathing, Circulation) approach to the management of any medical emergency should be employed. After airway and cardio-respiratory stability have been attained, hypoglycaemia must be excluded in all cases. Pabrinex may also be required at this stage, if the patient is at high risk of Wernicke's encephalopathy.

TABLE 2:

*Distinguishing seizure from psychogenic non epileptic attacks[22, 23, 24, 25]*

| Clinical feature | Suggestive of Epileptic Seizures (Status Epilepticus) | Suggestive of Psychogenic non epileptic attacks. (pseudostatus) |
|---|---|---|
| **Onset** | Sudden onset. May have focal seizure activity at onset. | Gradual onset potentially lasting minutes, can have a lead in of panic symptoms (which may not be recalled by the patient). At times can start with sudden onset. |
| **Motor state** | Tonic, then evolving into clonic synchronous movements. | Whole body stiffening, with some voluntary movements at times, can be flaccid largely during the ictus (ictal atonia), back arching, side to side head movements, undulating pelvic thrusting. |
| **Evolution** | A definite tonic phase, then clonic phase. As progresses the clonic movements become less pronounced, with perhaps nystagmus or subtle twitching as the only manifestation. | Varying, tonic/clonic movements. Not following specific sequence, with pauses during the ictus. Movements usually asynchronous. Subtle eye movements may occur. |
| **Vocalisation** | At onset, may have loud guttural cry as air is forced out past a tonic larynx. | May occur in the middle of a seizure, crying and shouting are possible. |
| **Eyes** | Eye closure is not typical. Eyes maybe deviated. Pupils tend to be unresponsive. | Eyes are commonly forcibly closed. (This is not always the case). Typically could be deviated away from the observer. Pupils are normal. |
| **Tongue** | Can have deep lateral tongue biting. | Typically superficial frontal tip of the tongue location. |
| **Cyanosis** | Present | Absent |
| **Responsive?** | None. No withdrawal from painful stimulus. | Variable withdrawal from painful stimulus. Limb movements may change with mild restraint. |
| **Consistency** | Usually stereotyped seizure episodes. | Variable nature to events. |
| **Recovery** | Delayed recovery after event, with amnesia. | Prompt recovery. Non-organic amnesia observed. |
| **Nocturnal seizures** | Can happen. | Not recognised. Events can occur from apparent sleep. The only way to be sure is to have EEG confirmed sleep pattern preceding the event. |
| **Ictal incontinence** | Not a distinguishing factor | Not a distinguishing factor |
| **Injuries** | Common | Common (fractures, head injuries, burns all reported) |

Pseudostatus epilepticus (prolonged non-epileptic attacks) should be considered in all patients presenting with apparent SE. Differentiating between the two on clinical grounds alone can be difficult, even for experienced practitioners. Given the limited access to EEG, when the clinical diagnosis is not established beyond reasonable doubt, it is best to err on the side of caution and treat as SE. Clinical features that can help distinguish non-epileptic and epileptic seizures are

detailed in Table 2.[22, 23, 24, 25] The importance of making an accurate diagnosis is all too obvious, to prevent medicalising a psychological condition, to prevent iatrogenic morbidity from anticonvulsant medications, and to reduce morbidity and mortality associated with intubation and ICU stay[26, 27].

Laboratory testing to include a full blood count, biochemistry, liver function tests, electrolytes, glucose, relevant serum antiepileptic drugs levels (to check compliance) and a toxicology screen are recommended as a minimum. Investigations should not delay treatment. In appropriate circumstances, where an infectious cause is suspected, lumbar puncture is necessary. SE can lead to a slightly raised cerebrospinal fluid white cell count[28]. All first presentations of SE should have emergent neuroimaging once the patient is stabilized, utilizing whatever modality is available locally. EEG is invaluable not only for confirming the diagnosis and planning treatment but in the patient who remains obtunded after a seizure, to distinguish a prolonged post ictal state from non-convulsive SE and other causes of reduced consciousness.

## STOPPING STATUS EPILEPTICUS

Delays occur at various points in the management of SE, including time to presentation and initiation of first line treatment[29]. In order to minimise these and to reduce variability in practice, SE should be managed with a protocol which provides details on appropriate doses of medications to be given in a timely manner[30]. A simple protocol for the management of SE is given in Figure 3. More detailed guidelines have been published by various groups such as NICE[31], EFNS[32], and the American Society of Neurocritical Care[33] as well as groups of international experts[34].

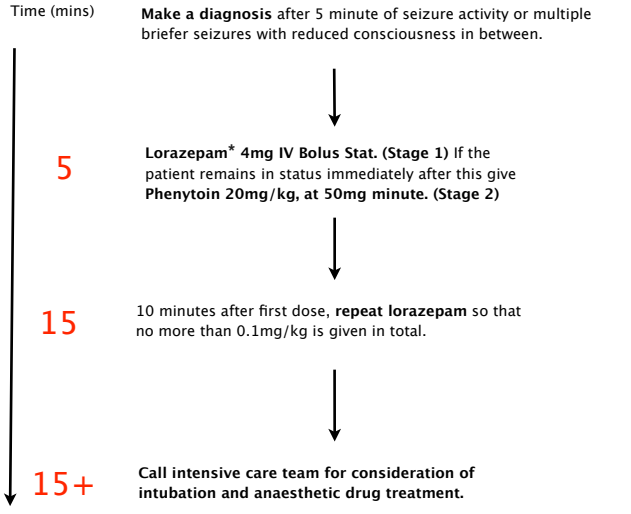


*Fig 3*. A suggested protocol for management of first and second stage of SE.

Several clinical trials guide the early management of SE[35, 36, 37, 38]. They show that early use of benzodiazepines is important for controlling SE. They work by enhancing the inhibitory GABAergic system, and at higher concentrations limit sustained repetitive neuronal firing[39]. Lorazepam, diazepam and midazolam are the most frequently used.

Diazepam achieves early high brain concentrations and therefore has a very fast onset of action. Unfortunately, it quickly redistributes to fatty tissues, limiting clinical effectiveness to 20-30 minutes and often necessitating repeated dosing which has the potential to lead to accumulation due to its long elimination half-life. While diazepam and lorazepam are equivalent at achieving seizure control[35], lorazepam is the drug of choice in early status due to its favorable pharmacokinetic profile, with a half-life of 12-24 hours. A recent prehospital study[38] compared intramuscular (IM) midazolam and intravenous (IV) lorazepam. It demonstrated that patients received treatment quicker utilizing the IM approach, and that this lead to greater cessation of SE on arrival to the emergency department. Intravenous benzodiazepines have significant side effects including respiratory depression (3-10%), hypotension (<2%), and impaired consciousness (20-60%)[39].

Second line therapies include phenytoin/fos-phenytoin, phenobarbital, valproate, levetiracetam and lacosamide. The best drug to use has not been conclusively demonstrated by a randomized controlled clinical trial.[40] Phenytoin is the most commonly used second line drug in the United Kingdom. It should be given at a dose of 20mg/kg infused at a rate of 50mg/kg. Slower infusion rates are used if cardiac arrhythmia or hypotension occurs. A loading dose can also be given if the patient is taking phenytoin. If the patient presents in SE it is likely that they have a subtherapeutic serum level of phenytoin. Maximum cerebral concentrations are achieved towards the end of the infusion. Side effects include hypotension in 28-50%, bradyarrhythmias and ectopics in <2%. It is important to monitor drug levels after loading with phenytoin, to guide further dosing. Typically maintenance dose will be started the following day at 4-5mg/kg once daily [39, 40].

Other agents used in SE (off license indication) have certain advantages over phenytoin such as faster administration rates, fewer interactions, less side effects and better pharmacokinetics[40]. The second line agents are listed in Table 3 along with their doses, mean efficacy from the results of meta-analyses, side effects and mechanisms of action.

It is presently unclear if some patients should be given one second line drug, or should be rapidly escalated to an initial polytherapy approach, given the fact that treatment of SE becomes more difficult the longer it has occurred[41]. A multi-center blinded comparative randomized control trial using an adaptive design is in the process of being set up which seeks to guide the optimal second line drug choice[42].

For those with epilepsy making sure that they get their regular AEDs in their usual doses at all times, given by whatever means possible (given by nasogastric tube or intravenously)

 

is also crucial. Maintaining therapeutic doses of any AEDs that have been commenced should also not be overlooked. Both are common reasons for failure to maintain control in those presenting with SE, where seizures have initially been successfully terminated. Treating the underlying cause whenever possible is also important if the best outcomes are to be achieved.

TABLE 3.

*Second line management of status epilepticus*[40].

| Drug | Mean Efficacy (%) | Dose | ADRs | Mode of action |
|---|---|---|---|---|
| **Phenobarbitone** | 73.6% | 20mg/kg IV up to 60mg/min | respiratory depression, hypotension, severe sedation, tolerance and the potential for drug interactions | GABA potentiation |
| **Phenytoin** | 50.2% | 20mg/kg at 50mg/minute (25mg/minute if cardiovascular instability or elderly) | cardio-respiratory risks (cardiac arrhythmia, hypotension, reduced cardiac output, the 'purple-glove' syndrome | Sodium channel modulation |
| **Valproate** | 75.7% | 30-60mg/kg IV up to 3mg/kg/min. Probably safe at 6 mg/kg/min. | Hyperammonaemia. There is a risk of hepatic and pancreatic toxicity, and valproate encephalopathy. bleeding tendency due to its effects on platelets and platelet function | Multiple. Sodium channel modulation, GABA potentiation, glutamate/NMDA inhibition. |
| **Levetiracetam** | 68.5% | 1000 and 3000 mg in young adults, or 20 mg/kg (Infuse at 500mg/minute) | Free of significant adverse-effect | Synaptic vesicle protein 2A |
| **Lacosamide** | not available | 200-400mg bolus over 5 minutes | Bradycardia, PR interval prolongation | Sodium channel modulation |

## STATUS EPILEPTICUS IN THE INTENSIVE CARE UNIT

Refractory SE is the state when first and second line therapies have failed, usually 30 minutes into the SE episode. In hospital based series it occurs in 31 - 44% of cases, and has a mortality rate between 16 - 23%[43]. It has been reviewed in several excellent recent articles[44, 45].

Anaesthetic agents used are propofol, midazolam, thiopental or phenobarbital.[46, 47, 48, 49]. These are outlined in Table 4 **in** detail. Often an antiepileptic drug is also given in a loading dose and uptitrated so that once weaning from anaesthetic agents is started there is a background effective antiepileptic agent. The choice of anaesthetic agents is based on small open trials, with no adequately powered prospective randomised controlled trial ever having been completed in this area. Decisions such as treatment duration and target of treatment (either clinical seizure suppression or EEG guided, such as suppression-burst suppression) are thus on an individual patient basis. Usually the patient will be anesthetized for 12-24 hours and then the agents weaned slowly over a period of hours. If after the first wean there are further clinical or electrographic seizures they will require further anesthesia. This situation is then termed super refractory SE[50]

With regards the anaesthetic agents used in SE a number of safety points are worth highlighting. The main clinical concern with propofol is the risk of propofol infusion syndrome (PRIS)[51]. It is characterized by metabolic acidosis, cardiac disturbances, hypertriglyceridaemia, and rhabdomyolysis. The main risk factors appear to be dosage (>83/mcg/kg/minute) and duration of therapy (>48hrs), and simultaneous vasopressor support. It carries a high mortality rate, at least in the early series, and calls for vigilance. The major limiting factors in barbiturate therapy are the risk of haemodynamic instability, immunosuppression, risk of gastrointestinal motility disturbance and nosocomial infection, particularly intestinal infection.

Oher general medical problems can befall the patient in ICU with SE. The main concerns include airway protection, aspiration related to the low GCS, cerebral hypoperfusion, and cardiac dysrhythmia. Hypertension can complicate the first 60 minutes of SE and it is worth bearing in mind that all parenteral anti-epileptic drugs will lower blood pressure, as will sedatives used for intubation. Positive pressure ventilation reduces preload and can also result in the patient ending up becoming hypotensive.

TABLE 4.

*Third line agents for status epilepticus*.[46, 47, 48]

| Drug | Loading dose | Maintenance dose | ADRs | Mode of action | T1/2 after prolonged administration |
|---|---|---|---|---|---|
| **Midazolam (midazolam paper in neurology)** | 0.1-0.3mg/kg at 4mg/minute bolus | 0.05-0.4mg/kg/hr | Hypotension, tachyphylaxis, increasing does needed with time. | GABAa agonist | 6-50h |
| **Propofol** | 2mg/kg bolus | 5-10mg/kg/hr | Propofol infusion syndrome (PRIS)<br>Hypotension. | GABAa agonist | 1-2h |
| **Pentobarbital** | 10-20mg/kg bolus at 25mg/min | 0.5-1mg/kg/hr increasing to 1-3mg/kg/hr if required | Accumulation, hypotension, and immunosuppression. | GABAa agonist | 15-22h |
| **Thiopenone** | 100-250mg bolus over 20 secs. 5-mg boluses every 2-3 minutes until seizure control. | Infusion of 2-5mg/kg/hr | | GABAa agonist | 14-36h |

Various parenteral preparations of anticonvulsants are available for use in intensive care units, namely phenytoin, fosphenytoin, valproate, levetiracetem, and lacosamide. Care should be taken in the critically ill patient to ensure that phenytoin and valproate levels are interpreted correctly as often the albumin level is low. Simple conversion tools are available online to help with administration of these drugs (http://www.mdcalc.com/phenytoin-dilantin-correction-for-albumin-or-renal-failure/ ).

Multiple anti-epileptic drugs will often be tried if patients enter a super refractory state. The duration of anesthesia, using combinations of anaesthetic agents is often prolonged and at times periods of 1 week of anesthesia are used prior to attempting weaning. At this stage attention needs to be directed towards rarer causes of SE (Table 1)[16]. One potentially very treatable group of disorders is the immune encephalopathies. If there is any concern that the cause of SE is one of these disorders a trial of immunotherapy is warranted whilst waiting for corroborative evidence such as the results of autoantibody testing or patterns of abnormalities seen on detailed neuroimaging[50].

Other novel treatments include electroconvulsive therapy (ECT), surgical lesionectomy for example in patients with

complex partial status presumed to originate from an acute structural abnormality e.g. subdural haematoma, hypothermia, and other drugs such as ketamine, lidocaine, and isoflurane. The evidence base for these treatments is currently very limited[51].

The outcome from refractory and super refractory SE is poor, with death in 35% and recovery to baseline in 35%[52]. For those surviving, neurological disability can vary considerably. In one retrospective analysis it was shown that a prolonged duration of SE did not preclude a meaningful functional and cognitive recovery[53]. It is not clear if progressive cognitive decline that can follow SE is due predominantly mainly to the underlying epileptic condition or the underlying aetiology of SE[54].

## CONCLUSION FROM ILLUSTRATIVE CASE

The management of the patient in the illustrative case would have been improved by the use of an agreed protocol. After having been diagnosed as having early SE he should have been given 4 mg of lorazepam intravenously, Weighing 80 kg, he should then have been given an infusion of 1600mg of phenytoin, to be given over 32 minutes. If ten minutes after receiving the first dose of intravenous lorazepam he was still showing any signs of seizure activity he should have had a further 4mg of lorazepam, given intravenously. Having completed the infusion of phenytoin any further seizure activity should have prompted immediate referral to ICU.

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*Clinical Paper*

# Alcohol-Related Fracture Admissions: A Retrospective Observational Study

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## ABSTRACT

**Introduction:** In April 2011 the NI public health agency estimated that alcohol misuse generates overall annual healthcare costs of £122.2m. There is currently a paucity of data regarding the burden of alcohol-related fractures on the provinces Trauma and Orthopaedic service.

**Patients and Methods:** A retrospective review of 104 patients over a 12 month period was performed. Data collected using the Fractures Outcomes and Research Database included: age, gender, smoking status, weekly alcohol intake, mechanism of injury and subsequent treatment.

**Results:** Alcohol related fractures accounted for 6.1% of all acute fractures admissions in the 12 month period. 73% were male, with a bimodal age distribution. The majority of patients were classed as social drinkers; however a significant proportion (23.1%) were alcohol dependent. 62.5% of patients were smokers at the time of admission. 95% of patients suffered a single injury which was commonly secondary to a simple mechanical fall (53.8%). The majority of patients sustained lower limb injuries, with 30.8% of these being ankle fractures.

**Conclusion:** In conclusion, our study has identified that alcohol-related trauma creates a significant financial burden on the NHS. It is likely that the incidence of alcohol related fracture is higher than documented in this study. We advocate the assessment of patients using the AUDIT-C score to assess for at risk drinking behaviour in those presenting with an alcohol related fracture.

**Keywords:** Alcohol, abuse, trauma, fracture, AUDIT-C

## INTRODUCTION

In recent years it has been acknowledged that the United Kingdom has moved to a culture of 'binge drinking', defined as more than eight units of alcohol for males and more than six units for females in one sitting[1]. The National Health Service (NHS) defines hazardous alcohol consumption as more than 21 units per week for men and more than 14 units for women[1]. Health problems associated with alcohol misuse include liver disease, reduced fertility, high blood pressure, and an increased risk of malignancy and cardiovascular disease[1].

Northern Ireland (NI), like the rest of the UK, has seen a dramatic increase in both the number of people drinking alcohol and the number of people drinking in excess of the recommended daily limit[2]. Alcohol consumption in NI has increased at a much greater pace than that of the rest of the UK [2]. Several contributory factors have been suggested, for example, easy access to cheap alcohol, changes in licensing laws and the psychological after-effects of the peace process[2].

In April 2011, the NI Public Health Agency estimated that alcohol misuse generates overall social costs of approximately £679.8m per annum. This figure includes overall annual healthcare costs of £122.2m. Specifically, acute hospitalization days cost £65.6m whilst outpatient hospital visits accounted for £5.2m of the annual expenditure. This is in contrast to the approximate figure of £400,000 spent on alcohol-related health promotion[3]. A recent survey into adult drinking patterns in NI commissioned by the Department of Health, Social Services and Public Safety[3] found that approximately 74% of adults drink alcohol and that younger adults (18 to 29 years) are more likely to binge drink than older adults (54% versus 16%). Three in every ten individuals (30%) admitted to binge drinking in the survey. The proportion of those who drank alcohol within the province varied regionally (Southern Health and Social Care Trust, 68%; Western Health and Social Care Trust, 78%) [3].

Studies have shown that patients with an elevated blood alcohol level become increasingly un-coordinated with ataxia resulting in falls[4-5]. Hingston et al have shown that blood alcohol concentrations over 1 g/l results in significant

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swaying, decreased attention, visual acuity, and adaptation to brightness and glare[6].

Whilst the socioeconomic cost of excess alcohol consumption has been well documented there is a paucity of published literature specifically dealing with alcohol-related fracture episodes and its potential cost to the health care system. We present and discuss the findings of a retrospective, observational study reviewing alcohol-related fracture admissions to our Trauma and Orthopaedic unit.

## PATIENTS AND METHODS

All patients admitted to the Trauma and Orthopaedic Unit have a detailed dataset regarding their admission entered into the Fracture Outcomes and Research Database (FORD) by a specialist nurse practitioner. Using this database we retrospectively identified those patients admitted with an

alcohol-related fracture or musculoskeletal injury to the unit over a 12month period. Patients were included if they had a documented history of alcohol ingestion at the time of injury or a raised blood alcohol level on admission.

For all those patients identified, their case notes were reviewed and the following information was recorded: age, gender, day of admission, weekly alcohol consumption, smoking status, mechanism of injury, injury or injuries sustained, open or closed injury, operative intervention, time from injury to definitive care and length of stay. On the basis of the information volunteered by the patient, drinking habit is classified on admissions as follows: alcohol-dependent, regular alcohol intake and social or occasional alcohol intake. The senior author (NWT) reviewed all of the radiographs in this study.

## RESULTS

We identified 104 patients admitted to the Trauma and Orthopaedic unit with a musculoskeletal injury related to excessive alcohol ingestion over the selected 12 month period. This figure represented 6.1% of the total number of admissions during the study period. Seventy-six patients were male (73%). Age ranged from 14 to 84 years (males, mean age 43 years; females, mean age 47 years). (Figure 1)

Seventy-two patients (69.2%) were classified as being regular alcohol drinkers and five patients (4.8%) were classified as social or occasional alcohol drinkers. Twenty-four patients (23.1%) had documented evidence of having alcohol dependence syndrome (19 males versus 5 females). In this cohort, 17 (71%) of the injuries were to the lower limb and six (25%) to the upper limb. 18 (75%) of the 24 patients sustained their fracture resulting from a simple mechanical fall. The injuries sustained within the alcohol dependent group included; nine hip fractures (37.5%), three humeral fractures (12.5%) and three tibial fractures (12.5%) including one compound injury.

86 patients (82.3%) required operative intervention. Of those not requiring surgery, four patients underwent closed reduction of a dislocated joint in the Accident and Emergency Department and were subsequently admitted for observation, this included two dislocated total hip replacements. Two patients had to be admitted as their cervical spine could not be cleared clinically due to the level of alcohol intoxication. One patient had a cervical spine fracture and was transferred to the regional spinal unit. Three patients had lumbar spine wedge fractures and four patients had ankle fractures, which were also all treated conservatively.

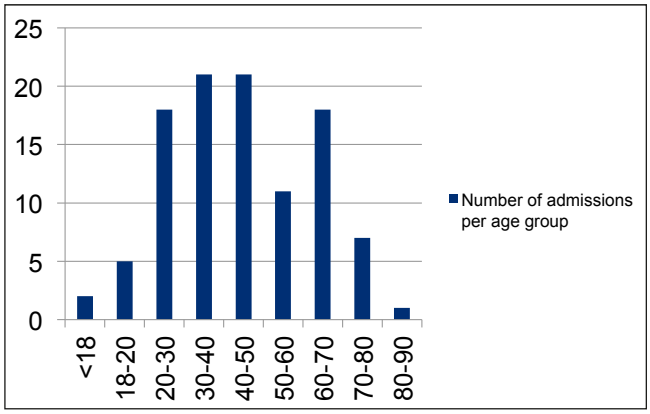


*Fig 1.* This graph illustrates the age distribution of patients admitted with alcohol related fractures.

The most common mechanism of injury was a simple mechanical fall (53.8%). Six patients (5.8%) sustained an open injury (three tibial shaft fractures, one distal humeral fracture, one olecranon fracture and one extensor tendon injury).The most common injuries were as follows: ankle fracture (30.8%), femoral neck fracture (14.4%), distal tibial fracture (7.7%), tibial shaft fracture (5.7%) and distal radial fracture (3.8%). (Figure 2)

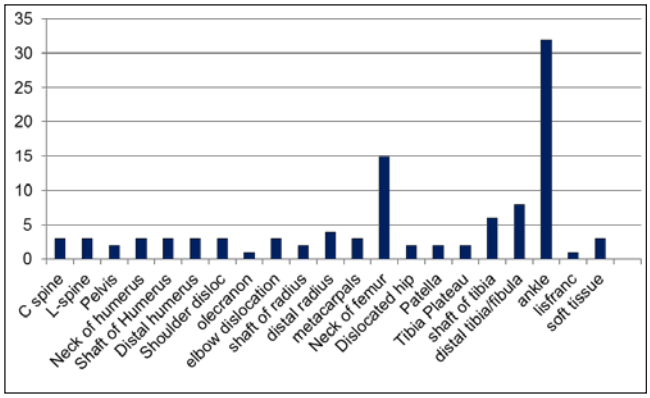


*Fig 2.* This graph shows the various levels at which an injury sustained. The lower limb was most commonly injured, especially the ankle.

Saturday and Sunday were the most common days for admission (26 admissions each day) with the weekend (Friday to Sunday) accounting for 58.6% of all admissions. Of those who were alcohol dependent 66% of the injuries were sustained midweek. (Figure 3). Length of stay ranged from one to 27 days (average, 4.5 days). The total bed cost for the 104 patients was estimated at £317,050.

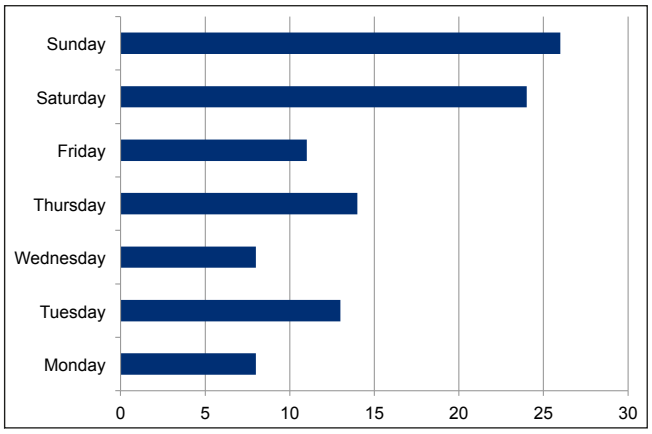


*Fig 3*. This graph highlights that alcohol related injury was more prevalent on Saturdays and Sundays in comparison with the rest of the week.

## DISCUSSION

The aim of our study was to determine the extent of orthopaedic injuries due to alcohol intake. These made up approximately 6% of admissions to the unit. Given the retrospective nature of the study and the fact that we were relying on either medical or nursing staff to document excess alcohol ingestion as a contributing factor, this figure is probably an underestimate. Furthermore, our study did not include patients whose injury was sustained as the result of another individual's drinking episode.

Adult drinking patterns surveyed in 2011 in Northern Ireland suggested there was a difference in the prevalence of binge drinking between males (35%) and females (25%) [3]. 73% of admissions in our study were male. This is significantly higher than the male cohort admitted with fractures without alcohol (55.3%).This may reflect male drinking behaviour and boisterous activity whilst under the influence of alcohol. 19 of the 24 patients with alcohol dependence were male. This is in keeping with previous studies suggesting that men are admitted more frequently with alcohol related morbidity[7]. 23% of patients admitted were alcohol dependent and in this group hip fractures were the most common injury. Several studies have shown that alcohol-related disease significantly increases the risk of hip fractures (2.33 - 2.6 times higher than that of the general population) [8,9]. Kanis et al found that alcohol intake greater than 2 units per day was associated with a significant increase in osteoporotic and hip fracture risk. We would therefore advocate that these patients should be targeted for hip fracture prevention programs as suggested in the literature[11,12].

The majority of admissions (78 patients) occurred towards the later half of the week (Thursday to Sunday), reflecting days when most people attend social events or are not working. Hospitals continue to operate with reduced staffing levels and theatre capacity at weekends which may result in increased burden on staff and resources. Patients who were admitted with alcohol related injuries had a longer mean stay than those of the general population (4.59 days vs. 3.78 days) This impacts on the total cost of the inpatient stay and discharge planning, without taking into account outpatient follow-up.

NICE guidelines recommend that NHS professionals who come into contact with patients who may be at risk of harmful alcohol intake should regularly carry out alcohol screening as an integral part of their practice. They advise the use of AUDIT (Alcohol Use Disorders Identification Test) or an abbreviated version, AUDIT-C, in order to offer intervention to the patient or make a referral to a liaison team[13]. Several large papers have shown that AUDIT-C is a quick and effective screening tool for hazardous drinking behaviour (sensitivity 51-97% specificity 70-97%) [14, 15]. We have now introduced that process into our unit.

Approximately 60% of patients sustained their injury secondary to a simple mechanical fall which likely explains why the majority of patients presented with an isolated injury (95%). This is a similar finding to previous studies[18].In our study 58.6% of patient's sustained trauma to the lower limb, most commonly affecting the ankle. This suggests stumbling, falls, and inversion injuries may be a result of alcohol suppressing basic reflexes resulting in injury. Several studies found that the lower limb is particularly vulnerable to injury in intoxicated patients[18, 19]. Johnston et al showed that injured patients with a blood alcohol level of 2–2.5g/L comprised mostly severe lower limb fractures requiring admission for open reduction internal fixation[19].

In conclusion, our study has identified that alcohol-related trauma creates a significant financial burden on the NHS. It is likely that the incidence of alcohol related fracture is higher than documented in this study and we intend to evaluate the problem in a prospective manner using blood alcohol levels, liver function tests and AUDIT-C scores. Our study highlights the need for further health promotion regarding alcohol related fractures and the risk of alcohol related osteoporosis. Medical officers need to be aware of the subtle signs of alcohol misuse and how to adequately screen for alcohol intake using tools like the AUDIT-C questionnaire.

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*Ulster Med J* 2015;**84(2):**98-101

*Clinical Paper*

# Do Regular Ultrasound Scans Reduce the Incidence of Stillbirth in Women with Apparently Normal Pregnancies?

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## ABSTRACT

**Objective:** To determine the incidence of stillbirth in women who have regular ante-natal ultrasound compared to those that have infrequent scans in a low risk population.

**Study** Design: A retrospective observational study was performed in a tertiary center with 5,700 deliveries per annum. Data on all deliveries was collected via the Northern Ireland Maternity System Database. Only women with an apparently low risk pregnancy were included. Women who had private antenatal care often had frequent scans in the third trimester. Women who did not have private antenatal care often had scans infrequently. The still birth rate was calculated for both groups of women from 2007 to 2011 and compared using a Chi-squared analysis

**Results:** Our study included 23,519 'low-risk' deliveries spanning 2007-2011. This included 2,088 (9%) patients who had frequent ultrasound surveillance and delivery at term and 21,431 (91%) patients who did not. The overall stillbirth rate was 0.34% and 0.20% respectively which was not statistically different (p=0.31).

**Conclusion:** There is no difference in the rate of stillbirth between patients who have more frequent ante-natal ultrasound surveillance compared with those who do not in a low risk population.

**Key Words:** Stillbirth; Ultrasound scan; Low risk pregnancy

## INTRODUCTION

It is recognised that intrauterine growth restriction (IUGR) is associated with stillbirth in about 40% of cases[1]. Intuitively, the solution would be to offer ultrasound scanning in the third trimester to all women[2]. There is however no evidence that routine third trimester scanning to detect IUGR for the expressed intention to prevent stillbirth, works. A systematic review from the Cochrane Collaboration of 8 studies (27,024 women) [3-9] failed to find an improvement in perinatal outcome[10]. The National Institute of Clinical Excellence (NICE) does not recommend routine third trimester scanning in apparently uncomplicated pregnancy[11]. This view is echoed by recommendations from the Royal College of Obstetricians and Gynaecologists (RCOG)[12]. Despite these guidelines, many units across Northern Ireland continue to offer third trimester ultrasound scans to women with no clinical indication.

We previously published data suggesting that for women with an apparently normal pregnancy, scanning only once in the third trimester was not associated with a higher stillbirth rate compared to women who were scanned twice[13]. We wished to study this further and determine if women who were scanned infrequently in the third trimester had a higher stillbirth rate compared to women who were scanned frequently. In Northern Ireland, we have a natural cohort of such women. Women who receive standard care in the Belfast Trust would receive one or two scans in the third trimester. Women who opt for private antenatal care would often receive up to 5 scans in the third trimester

## MATERIALS AND METHODS

The study was submitted to the local Research Governance Committee. The local Research Governance Committee advised that Ethical Approval was not required as data gathered was from an anonymous data collection system. The local audit committee for the Belfast Trust gave its approval.

For those who opt for private antenatal care (PPs) and the pregnancy is deemed to be apparently normal, the frequency of visits is at the clinician's discretion and typically involves a greater frequency of third trimester ultrasound scans to assess fetal growth. These patients would often have four to five scans in the third trimester. These patients have their antenatal care in the private sector and delivery occurs in the Royal Hospital. Typically these patients are commonly

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offered induction of labour at term (but this does not occur in all cases).

Within our unit, routine non-private patient (Non PPs) antenatal care for apparently normal pregnant women consists of shared care with the General Practioner (GP) and hospital. Patients undergo a booking visit and dating scan in addition to a fetal anatomy scan at 20 weeks. The assessment of fetal growth is performed by her GP or Midwife by palpation and symphysio-fundal height measurement, and is in line with guidance from the National Institute of Clinical Excellence. In between these visits to her GP and Midwife, she also attends the hospital at 29 and 35 weeks gestation to assess fetal growth by ultrasound. (After April 2011, the frequency of third trimester scans was reduced to only at 29 weeks). Induction of labour is typically offered ten to twelve days beyond the expected date of delivery.

For non PPs, before 2011, typically a total of 4 ultrasound scans would be performed. For non PPs, after 2011, typically a total of 3 ultrasound scans would be performed. For PPs, typically a total of 8 scans would be performed.

This study included 27,653 deliveries spanning the period 2007-2011 within a tertiary maternity unit, the Royal Jubilee Maternity Service, Belfast, which has approximately 5,700 deliveries per annum. Data was obtained from the computerized Northern Ireland Maternity System database (NIMATs).

Our primary objective was to determine the difference in stillbirth rate in apparently low risk pregnancies only in both groups. We therefore removed patients from our analysis who were deemed 'high-risk'. We removed patients that were positive for Group B streptococcal infection, women who had a multiple pregnancy, fetal congenital anomalies and women affected by medical conditions such as cardiac disease, haematological and renal conditions and diabetes, to form a 'low-risk' group. We calculated the total number of stillbirths for each year and also those that occurred in what were deemed 'low risk' pregnancies. Because we wanted to know if scanning had an impact on stillbirth, and as scanning in our unit occurred at 29 weeks gestation, we also removed deliveries before 28 weeks gestation from our final analysis (Table 1).

TABLE 1:

*Maternal characteristics for PPs and Non-PPs.*

| | PPs mean ( SD) | Non-PPs mean (SD) | P value Unpaired t test |
|---|---|---|---|
| Gestation at delivery | 38 (2.0) | 39 (1.8) | 0.0001 |
| Maternal age | 34 (4.5) | 30 (6.1) | 0.0001 |
| Parity | 1.5 (1.1) | 1.5 (1.1) | 0.1402 |
| Ethnicity | 98% Caucasian | 96% Caucasian | 0.0059 (Fisher's test) |

Statistical analysis was conducted using SPSS software® (IBM® Armonk, NY, USA). Comparison of proportions between private patient and non-private patient groups was performed using a Chi-squared test with Yates correction. All case notes of women who had a stillbirth were reviewed by hand to ensure data accuracy.

## RESULTS

When 'high-risk' pregnancies (as defined in the methods section) were omitted the total number of deliveries within this period was 23,519 with a total of 50 stillbirths giving an overall stillbirth rate of 0.21%. Of the total 'low-risk' deliveries 2,088 of these (9%) were PPs and 21,431 (91%) were non-PPs.

The maternal characteristics for PPs and non-PPs are described in Table 1. This suggests that Private patients are delivered earlier but parity is not different between groups. Maternal age was however higher for the PP group.

A breakdown of the overall stillbirth rates in low-risk pregnancies per annum are demonstrated in Table 2. There were a total of 7 stillbirths in the PP group and 43 stillbirths in the non-PP group during the 2007-2011 period, meaning that the overall stillbirth rates were 0.34% and 0.20% respectively (Table 3). Chi-squared two-tailed analysis revealed that this difference was not statistically significant (Chi-Square = 1.05 p=0.31).

The distribution of stillbirths in accordance to gestation is shown for both groups in Figure 1. This demonstrates that in the non-PP group most stillbirths occurred at an advanced gestation.

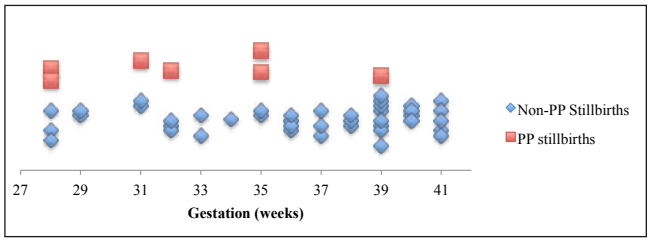


*Fig 1.* Scatterplot demonstrating the distribution of stillbirths according to gestation in Private and Non-Private patients

## DISCUSSION

This study has shown that women who have an apparently uncomplicated pregnancy are no more likely to have a stillbirth if they are scanned infrequently compared with women who are scanned frequently.

The strengths of this study are that we had a robust data collecting system and that the notes for women who had a stillbirth were reviewed by hand.

The weakness of this study is that our numbers were small. Furthermore patients that refer themselves for private care may possess different characteristics e.g. they may have had a previous poor outcome. Another weakness is that

 

TABLE 2:

*Table demonstrating the stillbirth rate from 2007-2011 in all 'low-risk' pregnancies.*

| Year | Total Deliveries n = 27,653 | Number of deliveries from 'Low-risk' women n=23,519 | Number of stillbirths (Total) n=75 | Number of stillbirths 'low-risk' n=50 | Stillbirth Rate 'low-risk' |
|---|---|---|---|---|---|
| 2007 | 5478 | 4735 | 14 | 10 | 0.21 |
| 2008 | 5521 | 4718 | 13 | 5 | 0.11 |
| 2009 | 5501 | 4667 | 16 | 13 | 0.28 |
| 2010 | 5549 | 4756 | 18 | 12 | 0.25 |
| 2011 | 5604 | 4643 | 14 | 10 | 0.22 |

TABLE 3:

*Table demonstrating stillbirth rates for Private patients (PP) and Non-Private patients (non PP) in 'low-risk pregnancies' from 2007-2011.*

| Year | Total Deliveries PP n = 2,088 | No. Stillbirths PP n = 7 | Stillbirth rate PP % (low risk) | Tot. Deliveries Non-PP n = 21,431 | No. Stillbirths non-PP n = 43 | Stillbirth rate non- PP % (low risk) |
|---|---|---|---|---|---|---|
| 2007 | 479 | 1 | 0.21 | 4256 | 9 | 0.21 |
| 2008 | 458 | 0 | 0 | 4260 | 5 | 0.12 |
| 2009 | 490 | 4 | 0.82 | 4177 | 9 | 0.22 |
| 2010 | 366 | 1 | 0.27 | 4390 | 11 | 0.25 |
| 2011 | 295 | 1 | 0.34 | 4358 | 9 | 0.21 |

this study did not remove all risk factors for stillbirths such as overweight women, women at advanced maternal age, assisted conception, preterm prelabour rupture of membranes and women that had a previous history of a small baby.

Despite these major weaknesses, we were surprised at our results. These results suggest that scanning frequently, induction at term and the benefits of greater Consultant input did not reduce the stillbirth rate.

It is clear that a randomized controlled trial of ultrasound scanning for women with no obvious complications with the expressed intention of reducing stillbirth is required. However such a trial is unlikely to be performed.

Accepting the limitations of our work, we had previously shown that scanning twice vs. scanning once in the third trimester did not reduce the stillbirth rate[13]. In the current study we have further shown that frequent scanning does not reduce the stillbirth rate. These works, taken together with a Cochrane systematic review[10], coupled with directions from NICE[11] and the RCOG[12] should suggest that we should stop offering ultrasound scanning for no clinical indication in apparently uncomplicated pregnancy.

## CONFLICT OF INTEREST

Co-author Dr S Ong has private patients

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*Clinical Paper*

# Recurrence of Phaeochromocytoma and Abdominal Paraganglioma After Initial Surgical Intervention

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## ABSTRACT

**Background:** Clinical and biochemical follow up after surgery for phaeochromocytoma is essential with long term studies demonstrating recurrence frequencies between 6% and 23%.

**Aim:** To examine the characteristics and frequency of tumour recurrence in a regional endocrine referral centre, in patients with surgical resection of phaeochromocytoma (P) and abdominal paraganglioma (AP).

**Methods:** We identified a cohort of 52 consecutive patients who attended our Regional Endocrinology & Diabetes Centre and retrospectively reviewed their clinical, biochemical and radiological data (between 2002 and 2013). After confirmation of early post-operative remission by negative biochemical testing, tumour recurrence was defined by demonstration of catecholamine excess with confirmatory imaging.

**Results:** Phaeochromocytoma was confirmed histologically in all cases (43:P, 9:AP, mean-age:53years). Open adrenalectomy was performed in 20 cases and laparoscopically in 32. Hereditary phaeochromocytoma was confirmed by genetic analysis in 12 (23%) patients. Median follow up time from initial surgery was 47 months, (range: 12 - 296 months), 49 patients had no evidence of tumour recurrence at latest follow-up. Three patients (6%) demonstrated tumour development, one in a patient with VHL which occurred in a contralateral adrenal gland, one sporadic case had local recurrence, and an adrenal tumour occurred in a patient with a SDHB gene mutation who had a previous bladder tumour. After initial surgery, the tumours occurred at 8.6, 12.0 and 17.7 years respectively.

**Conclusion:** In this study tumour development occurred in 6% of patients. Although tumour rates were low, careful and sustained clinical and biochemical follow up is advocated, as new tumour development or recurrence may occur long after the initial surgery is performed.

**Key words:** phaeochromocytoma, abdominal paraganglioma, long term follow up, tumour recurrence

## ABBREVIATIONS

CST clonidine suppression test
P phaeochromocytoma
AP abdominal paraganglioma
SDHB succinate dehydrogenase complex subunit B
SDHD succinate dehydrogenase complex subunit D
VHL von hippel-lindau
MEN multiple endocrine neoplasia
NF neurofibromatosis
SEM standard error of the mean
IVC inferior vena cava
MIBG metaiodobenzylguanidine scintigraphy
CT Computed tomography
MRI magnetic resonance imaging

## INTRODUCTION

Phaeochromocytoma is a rare catecholamine producing tumour that arises from chromaffin cells of the adrenal medulla.[1] Paragangliomas (extra-adrenal phaeochromocytoma) originate from neural crest cells and can occur in locations such as the carotid body, organ of Zuckerlandl, kidney, bladder and in the retroperitoneum.[2,3] Surgical excision of abdominal paraganglioma does not guarantee cure as local recurrence and distant metastases can occur and therefore vigilance is needed in this population.[4,5] Sustained clinical and biochemical follow up after initial surgical resection is essential, the '10 per cent rule' is often

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TABLE 1

*Baseline characteristics at presentation*

| | PHAEOCHROMOCYTOMA n = 43 | PARAGANGLIOMA n = 9 |
|---|---|---|
| Age (at diagnosis; years) | 55.2 ± 2.0 | 41.6 ± 4.9 † |
| Range | 20 – 59 | 26 – 82 |
| **Gender** | | |
| Male | 16 | 2 |
| Female | 27 | 7 |
| **Mode of Presentation** | | |
| Incidentaloma | 5 | 2 |
| Abdominal pain | 12 | 6 |
| Hypertension | 24 | 5 |
| Sweats | 15 | 2 |
| Headache | 13 | 2 |
| Palpitations | 14 | 3 |
| Flushing | 3 | 0 |
| Hypertensive crisis | 2 | 0 |
| Syndromic screening | 5 | 0 |
| Panic attack | 3 | 0 |
| **Genetics** | | |
| NF1 | 2 | 0 |
| SDHB | 1 | 4 |
| SDHD | 3 | 0 |
| VHL | 1 | 0 |
| MEN 2A | 1 | 0 |
| **Clonidine Suppression Test** | | |
| Positive | 32 | 5 |
| Negative | 3 | 3 |
| Not done | 8 | 1 |
| **MIBG** | | |
| Positive | 22 | 9 |
| Negative | 3 | 0 |
| Not done | 18 | 0 |
| **Location at Presentation** | | |
| Left Adrenal | 23 | |
| Right Adrenal | 19 | |
| Bilateral Adrenal | 1 | |
| Abdominal Paraganglioma | | 9 |

*Data presented as Mean ± SEM, †: p< 0.05*

*The following criteria were applied to constitute a positive clonidine suppression test using plasma catecholamines: baseline plasma adrenaline and noradrenaline more than 11.82 nmol/l or plasma adrenaline and noradrenaline more than 2.96 nmol/l 3 hrs after administration of clonidine and < 50% fall in noradrenaline 3hrs post clonidine*

frequently quoted with regards to phaeochromocytoma recurrence, however the reported rates of recurrence can range from 6 to 23%.[6-8] Furthermore, tumour recurrence can occur many years after the initial surgery, and in some cases can be delayed as long as 10 years to first recurrence.[9,10] Most cases of phaeochromocytoma are sporadic in origin, however in patients with hereditary phaeochromocytoma tumour recurrence is more common, in addition extra-adrenal phaeochromocytoma recur more frequently than adrenal phaeochromocytomas.[11-13]

Against this background we retrospectively examined the characteristics and rate of new tumour development or recurrence over a recent eleven year period at our centre in a cohort of 52 consecutive patients treated by surgical removal of phaeochromocytoma and abdominal paraganglioma.

## PATIENTS AND METHODS

The medical records of 52 patients who had surgical resection

of phaeochromocytoma and abdominal paraganglioma and were followed up at the Regional Centre for Endocrinology & Diabetes, Belfast were examined retrospectively between January 2002 and April 2013. Two patients had surgery performed at a different centre. The clinical characteristics of patients were collected as well as biochemical, radiological, surgical and subsequent histological data. All patients were followed up for a minimum period of 12 months after surgical removal of the tumour. Phaeochromocytoma was confirmed by catecholamine excess, confirmatory imaging (CT with contrast as the first choice for localisation, MRI if applicable and/or MIBG scintigraphy) and by subsequent histological analysis. Laparoscopic adrenalectomy as the first line procedure for removal of phaeochromocytoma was introduced at our centre in 1998.[14] After confirmation of initial post-operative negative biochemical testing, tumour recurrence was defined by demonstration of catecholamine excess with confirmatory imaging. All statistical analysis was performed using SPSS software version 20 (SPSS Inc, Chicago). Values are reported as mean ± SEM and the probability value of $p < 0.05$ was deemed significant.

## RESULTS

Phaeochromocytoma was confirmed histologically in all cases, 9 of which were abdominal paragangliomas, (male: 18, female: 34, mean age: 53 years, range: 20-82 years). Common clinical presentation included the classic symptoms of headache, palpitations, sweats and hypertension, 7/52 (13%) were discovered incidentally. Two patients with phaeochromocytoma presented with a hypertensive crisis after elective non-related surgical procedures.[15] The location at initial presentation included left adrenal: 23 (44%), right adrenal: 19 (37%), bilateral-adrenal: 1 (2%) and abdominal paraganglioma: 9 (17%). Hereditary phaeochromocytoma as illustrated in Table 1 was confirmed by the presence of classical features of NF-1 in 2 cases and by genetic analysis in a further 10 patients (SDHB: 5, SDHD: 3, VHL: 1, MEN2A: 1), the remaining patients (n=40) were considered to be sporadic in origin. For a variety of reasons four patients did not have measurement of twenty four urine catecholamines before their diagnosis of phaeochromocytoma/paraganglioma:one patient with renal failure requiring dialysis had a positive CST and MIBG scanning pre-operatively. The second patient had surgery performed at a different centre, pre-operative CST was negative. The third patient also had surgery performed at a different centre for a mass adjacent to the IVC/Liver, CST was not performed pre-operatively. The fourth patient had a nephrectomy/adrenalectomy for a renal mass, immunohistochemistry revealed a phaeochromocytoma in the adrenal gland, CST and MIBG were not performed pre-operatively. From the cohort, 27/48 (56%) had raised 24 hr urine adrenaline levels, 21/48 (44%) had raised 24 hr urine noradrenaline levels, 11/48 had both 24 hr elevations in urine noradrenaline and adrenaline levels, one patient had elevated dopamine levels. Clonidine suppression testing was performed in 43 patients, 37 (86%) of which showed a positive response, of the 6 patients with negative clonidine suppression testing we elected to proceed to surgery if urine catecholamines were elevated, and/or MIBG scanning was positive.[16] MIBG scanning was undertaken in 34 patients, 31 (91%) demonstrated positivity. Open adrenalectomy was performed in 20 cases and laparoscopic surgery in 32. The median follow up time was 47 months, (range: 12 - 296 months), 49 patients in the remaining cohort had no evidence of new tumour development or recurrence on follow up. After initial surgery, three patients (6%) demonstrated the presence of tumour development; one with Von Hippel Lindau syndrome (VHL), another with a sporadic phaeochromocytoma and one with a SDHB mutation. Contra-lateral adrenal tumour developed in one patient with VHL, in another with presumed sporadic phaeochromocytoma local tumour was present (in this patient a regional lymph node was inaccessible on initial surgery), the third patient with an SDHB mutation developed tumour growth in an adrenal gland, the original site of which was the bladder. After initial surgery tumour development occurred at 8.6, 12 and 17.7 years respectively, two of these patients were alive at most recent follow up at 19 & 25 years respectively. In the third patient with VHL syndrome, death was not related to phaeochromocytoma. Overall 46/52 patients were alive at most recent follow up, 1 death was attributable to metastatic paraganglioma, 20 months after initial surgery.

TABLE 2

*Surgical and histological data*

| | PHAEOCHROMOCYTOMA n = 43 | PARAGANGLIOMA n = 9 |
|---|---|---|
| **Surgical Procedure** | | |
| Open Adrenalectomy | 12 | 8 |
| Laparoscopic Adrenalectomy | 31 | 1 |
| Specimen Weight (grams) | 140.9 ± 47.2 | 113.6 ± 68.6 |
| Range | 8.5 - 1861 | 1.5 - 620 |
| Specimen Size Length (cm) | 4.2 ± 1.0 | 4.6 ± 0.42 |
| Range | 1.5 - 19.0 | 2.2 - 13.0 |

Data presented as Mean ± SEM

## DISCUSSION

Surgical removal of a phaeochromocytoma and abdominal paraganglioma can be difficult due in part to its anatomical location and thus surgery does not automatically confer a cure and, therefore both immediate and long-term assessments are essential.[17] In addition paragangliomas can present difficulties by appearing in unusual and surgically inaccessible locations resulting in incomplete tumour resection or tumour spillage.[18] Most centres now perform laparoscopic adrenalectomy as the preferred choice. However, tumour size and location necessitate open adrenalectomy in selected cases.[19-21] Laparoscopic resection has been deemed feasible even in patients who have a large (>6cm) phaeochromocytoma, provided there is a low suspicion for malignancy.[22] Caution should be advised, as increased rates of adrenal recurrence have been demonstrated in laparoscopic in comparison to an open procedure.[17] In our own previous series of adrenalectomies (8 of 50 for phaeochromocytoma) and in keeping with other similar studies, laparoscopic adrenalectomy in comparison to open adrenalectomy resulted in a significantly shorter hospital stay and less post-operative morbidity, although operating time was longer.[14] Some centres have reported varying degrees of success with cortical sparing adrenalectomy, more so in patients with bilateral phaeochromocytoma but it is not our current practice to perform this procedure.[23,24]

If recurrence does occur surgical removal is the first line treatment. In the current study we have demonstrated tumour development in 6% in patients in whom phaeochromocytoma and abdominal parganglioma had been surgically removed, it is arguable that genuine local recurrence in our study occurred in only one patient, in the remaining two patients who had tumour development after initial surgery; one with VHL and the other with an SDHB mutation, could possibly be explained by the increased clinical incidence of bilateral phaeochromocytomas (around 40-60%) in patients with VHL, and that patients with SDHB mutations have an increased risk of the development of multi-focal phaeochromocytomas.[25-27]

Our study numbers are comparable to previous cohorts investigating rates of recurrence in phaeochromocytoma.[3,27,28] Our current practice in Northern Ireland enables us to follow the majority of these patients long term at one centre. Previously we have reported a recurrence rate of 15% at a median interval of 5 years, a possible reason for the low recurrence rate in the current study was the relatively short follow up time,[8] we therefore presume that if patients were followed up for a longer time period, further tumour development or recurrences would possibly occur. In the current study the time to first recurrence ranged from 8.6 to 17.7 years, this demonstrates the value of prolonged follow up even in those patients who appear to have been surgically cured.

All patients with an initial surgical resection of phaeochromocytoma or abdominal paraganglioma should be followed up with careful history, examination and routine measurements of catecholamines, if the latter are raised, further imaging (initially CT with contrast) is recommended. Recent clinical practice guidelines have provided evidence for the superiority of plasma free or urinary fractionated metanephrines in comparison to measurements of catecholamines in the diagnosis of phaeochromocytoma and paraganglioma.[29] Previously published studies addressing the risk factors for recurrence demonstrate an increased risk in younger patients, larger tumours, extra-adrenal in origin and in those with genetic phaeochromocytoma.[30,31] In this regard, predicting which patients might recur in the current study was difficult, given the relatively low numbers. Current guidelines suggest that all patients with a phaeochromocytoma should be followed by for at least 10 years after surgery and in those patients with an extra-adrenal tumour or genetic phaeochromocytoma should be followed lifelong. [32]

## CONCLUSION

Although tumour development and recurrence rates were low after initial surgery, careful sustained clinical and biochemical follow up is advocated, as tumour occurrence may occur long after the initial surgery.

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*Case Report*

# Rare complications of a low lying median arcuate coeliac ligament

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## ABSTRACT

Pancreaticoduodenal artery aneurysm is a rare complication of coeliac artery stenosis secondary to a low lying median arcuate coeliac ligament. This article reports the case of a 69-year old man who presented with left arm and leg weakness, clinically in keeping with right hemisphere stroke. Initial CT brain scan was within normal limits. The patient did not receive thrombolysis as he was outside the time window. 3 hours later the patient experienced sudden onset epigastric pain and acute shock. CT aorta abdominal was diagnostic of a ruptured inferior pancreaticoduodenal artery aneurysm. Repeat CT brain the following day showed subacute infarction within the right frontal lobe. Embolisation of the aneurysm was successfully performed. It is well documented that ischaemic stroke can cause acute hypertension. This acute hypertension probably contributed to the rupture of the pancreaticoduodenal artery aneurysm. The patient was well on discharge and remains well 2 months on.

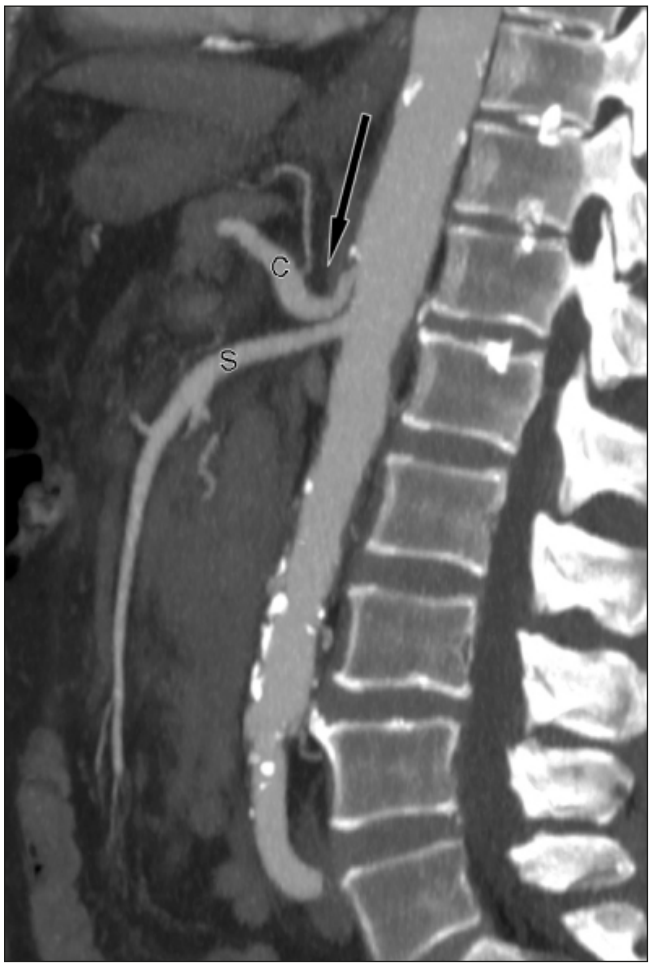


*Fig 1*. Sagittal CT reconstruction showing the coeliac axis (C) and superior mesenteric artery (S); The typical shape of the coeliac axis as it passes under the median arcuate ligament is marked by the arrow.

## CASE REPORT

A 69 year old man was admitted with left sided arm and leg weakness of 5 hours duration. He had a past medical history including ischaemic heart disease, CABG, hypertension hypercholesterolaemia and asthma. He was taking aspirin 75mg once daily. He lived with his wife and was independent for all activities of daily living.

Examination showed no cranial nerve abnormality. Medical Research Council (MRC) grading system for power scored 5/5 in the right upper and lower limbs and 4/5 in the left upper and lower limbs. Achilles tendon reflexes and deep tendon reflexes were increased on the left with a left sided upgoing plantar reflex. He was hypertensive at 206/125. The patient was not examined for the presence of an abdominal bruit.

The patient's initial full blood counts and biochemical parameters were within normal limits. Computed tomogram of the brain was also normal. The clinical picture was consistent with a diagnosis of right hemisphere lacunar stroke. As the patient was outside the thrombolysis time window, he was treated with 300mg aspirin.

3 hours after presentation, the patient developed sudden onset epigastric and back pain. He appeared cold and clammy. His blood pressure fell to 74/48 and radial pulses were not palpable. CT abdominal angiogram showed a ruptured inferior pancreaticoduodenal artery aneurysm. Coeliac axis

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stenosis with a configuration typical of a low lying median arcuate ligament was also identified. Serum amylase was normal and there was no clinical evidence of current or previous pancreatitis. The ruptured aneurysm was not embolised at this time as the patient was stable and it was felt a multidisciplinary decision should be made of the best course of action.

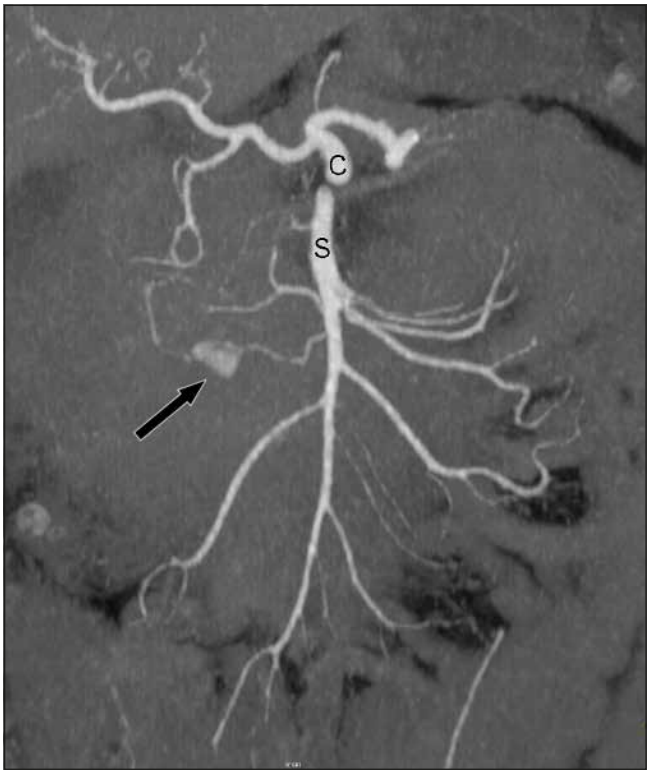


*Fig2*. Coronal CT reconstruction showing the coeliac axis (C) and superior mesenteric artery (S); the aneurysm (arrow) arises from the inferior pancreaticoduodenal artery which is a branch of the superior mesenteric artery.

The following day repeat CT brain revealed subacute infarction within the right frontal lobe, in the right anterior cerebral artery territory. After liaison between an interventional radiologist, surgeon and stroke physician, 300mg aspirin OD was continued. Echocardiogram showed mild left ventricular hypertrophy and mild dilatation of the ascending aorta. Carotid Doppler ultrasound revealed only mild (<30%) stenosis in both internal carotid arteries.

Repeat CT aortogram 3 days later showed persistence of the inferior pancreaticoduodenal artery aneurysm, again with evidence of recent rupture and haemorrhage. The patient proceeded to mesenteric catheter angiography which revealed a pancreaticoduodenal aneurysm, coeliac artery stenosis and the development of large pandreaticoduodenal territory collateral vessels supplying the coeliac vessels from the superior mesenteric artery. The pancreaticoduodenal aneurysm was successfully embolised

The patient was discharged with the support of the stroke early supported discharge rehabilitation team. At 2 month review, he has a very mild residual left sided weakness but is independent of all activities of daily living. He has not experienced any further abdominal pain.

## DISCUSSION

Compression of the coeliac axis by a low lying median arcuate ligament in asymptomatic patients has long been recognised and is a common finding on modern sagittal CT reconstructions.[1] Findings on CT include focal narrowing of the coeliac axis with poststenotic dilatation and increased collaterals from the superior mesenteric artery.

In most people, the median arcuate ligament passes superior to the origin of the coeliac artery, near the first lumbar vertebra. However 10-24% of the population may have an abnormally low ligament.[2] Complications of this anatomical variation are described and include dilatation of the pancreaticoduodenal collateral pathways and subsequent formation of a visceral aneurysm. The pancreaticoduodenal artery is a branch of the superior mesenteric artery (SMA). The superior pancreaticoduodenal artery is a branch of the gastroduodenal artery (supplied by the coeliac artery); the inferior pancreaticoduodenal artery is a branch of the SMA. These two form an arcade that allows collateral supply from the SMA to support the coeliac territory, which is undersupplied from coeliac artery due to the stenosis caused by the low lying median arcuate ligament. It is postulated that the increased flow through this collateral pathway results in the hypertrophy of the vessels and true aneurysm formation. Visceral aneurysms are a rare but potentially lethal form of vascular disease, with an incidence of 0.01% to 0.2% in routine autopsies.[3] Pancreaticoduodenal artery aneurysms are estimated as 2% of all visceral aneurysms.[4] The risk of rupture of these aneurysms is uncertain as the number of cases is too small to determine a trend.[5] Rupture is however well described and carries a 29% mortality rate.[6] Contemporary management is usually by emergency coil embolization.[3]

A less well understood complication is median arcuate ligament syndrome or Dunbar syndrome. It is the triad of abdominal pain, weight loss and abdominal bruit in patients whose only positive imaging finding is coeliac artery stenosis. The pathophysiology of this condition is contentious as mesenteric ischaemia is commonly held to only occur when at least two of the three mesenteric vessels are compromised. Our patient did not display the classical symptoms of this syndrome.

Hypertension is commonly observed in the immediate post-stroke period.[7] As described by Brainin and Heiss, 82% of patients had systolic blood pressures above 140 mmHg during the first 48 hours, 28% having a systolic blood pressure above 180 mmHg.[8] Cerebral perfusion becomes dependent upon systemic arterial BP following stroke due to impairment of cerebral autoregulation. Hypertension may sustain cerebral perfusion to the ischaemic penumbra. Very high blood pressure has been associated with poor post-stroke outcomes. Poor outcomes are said to be due to a number of factors including vascular complications and early stroke recurrence.

 

It is likely that the hypertension following our patient's stroke caused rupture of the preexisting pancreaticoduodenal artery aneurysm given the rarity of visceral artery aneurysm rupture. Administration of thrombolysis as a part of stroke management may have resulted in an adverse outcome.

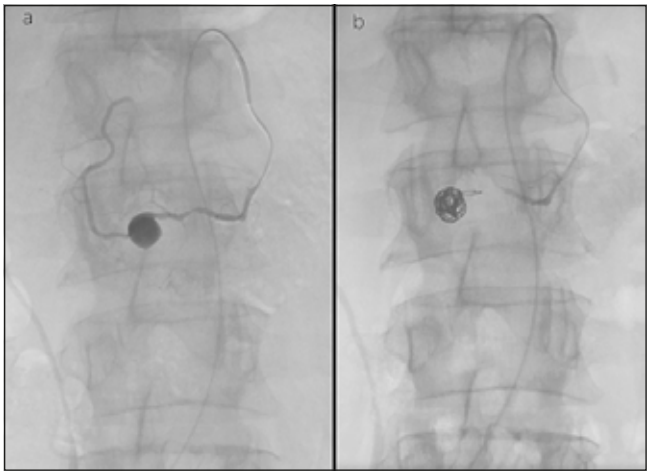


*Fig 3*. (a) catheter angiogram of the inferior pancreaticoduodenal artery demonstrates the aneurysm. (b) the aneurysm has been filled with embolization coils and there is no contrast flow into the aneurysm.

There are no previously documented cases of stroke and rupture of a pancreaticoduodenal artery aneurysm presenting together. Our case highlights the difficult management issues including thrombolysis contraindications and management of these aneurysms.

## LEARNING POINTS

1. Low lying median arcuate anatomy associated with coeliac stenosis is a common incidental finding on modern imaging, rarely associated with pancreaticoduodenal artery aneurysm.
2. Incidental diagnosis of an asymptomatic pancreaticoduodenal artery aneurysm warrants prompt evaluation and consideration of treatment.
3. Symptomatic rupture of a pancreaticoduodenal artery aneurysm is exceptionally rare.
4. Hypertension is commonly observed in the immediate post-stroke period. This has been associated with poorer outcomes.

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Treatment of deep vein thrombosis (DVT) & pulmonary embolism (PE), & prevention of recurrent DVT & PE in adults (see W&P for haemodynamically unstable PE patients). **Posology & method of administration:** *2.5 mg* – Oral *b.i.d.* dose; patients should also take a daily dose of 75 – 100 mg ASA or a daily dose of 75 – 100 mg ASA in addition to either a daily dose of 75 mg clopidogrel or a standard daily dose of ticlopidine. Start Xarelto as soon as possible after stabilisation, including revascularisation for ACS; at the earliest 24 hours after admission & at discontinuation of parenteral anticoagulation. If dose is missed take next dose, do not double the dose. *10 mg* – Oral *o.d.* dose; initial dose taken 6 to 10 hours after surgery provided haemostasis established. *15 mg/20 mg* – Take with food SPAF: 20 mg orally *o.d. DVT & PE:* 15 mg *b.i.d.* for 3 weeks followed by 20 mg *o.d.* for continued treatment & prevention of recurrent DVT & PE. *All strengths* - Refer to SmPC for full information on duration of therapy & converting to/from Vitamin K antagonists (VKA) or parenteral anticoagulants. **Special populations:** Patients undergoing cardioversion: Xarelto can be initiated or continued in patients who may require cardioversion. **Renal impairment:** mild (creatinine clearance 50-80 ml/min) - no dose adjustment; *2.5 mg/10 mg* - moderate (creatinine clearance 30-49 ml/min) – no dose adjustment. Severe (creatinine clearance 15-29 ml/min) - limited data indicate rivaroxaban concentrations are significantly increased, use with caution. *15 mg/20 mg* - moderate & severe renal impairment - limited data indicate plasma concentrations are significantly increased, use with caution – *SPAF:* reduce dose to 15 mg *o.d., DVT & PE:* 15 mg *b.i.d.* for 3 weeks, thereafter 20 mg *o.d.* Consider reduction from 20 mg to 15 mg o.d. if patient's bleeding risk outweighs risk for recurrent DVT & PE; *All strengths* - Creatinine clearance <15 ml/min - not recommended. **Hepatic impairment:** Do not use in patients with coagulopathy & clinically relevant bleeding risk including cirrhotic patients with Child Pugh B & C. **Paediatrics:** Not recommended. **Contra-indications:** Hypersensitivity to active substance or any excipient; active clinically significant bleeding; lesion or condition considered to confer a significant risk for major bleeding (refer to SmPC); concomitant treatment with any other anticoagulants except under specific circumstances of switching anticoagulant therapy or when unfractionated heparin is given at doses necessary to maintain an open central venous or arterial catheter; hepatic disease associated with coagulopathy & clinically relevant bleeding risk including cirrhotic patients with Child Pugh B & C; pregnancy & breast feeding. *2.5 mg* - concomitant treatment of ACS with antiplatelet therapy in patients with a prior stroke or transient ischaemic attack. **Warnings & precautions:** Clinical surveillance in line with anticoagulant practice is recommended throughout the treatment period. Discontinue if severe haemorrhage occurs. Increasing age may increase haemorrhagic risk. *Not recommended:* in patients with an increased bleeding risk (refer to SmPC); in patients receiving concomitant systemic treatment with strong concurrent CYP3A4- and P-gp-inhibitors, i.e. azole-antimycotics or HIV protease inhibitors; *2.5 mg* treatment in combination with antiplatelet agents other than ASA & clopidogrel/ticlopidine; *15 mg/20 mg* in patients with prosthetic heart valves; with PE who are haemodynamically unstable or may receive thrombolysis or pulmonary embolectomy. *Use with caution:* in patients with severe renal impairment or with renal impairment concomitantly receiving other medicinal products which increase rivaroxaban plasma concentrations; treated concomitantly with medicines affecting haemostasis; when neuraxial anaesthesia or spinal/epidural puncture is employed; in patients at risk of ulcerative gastrointestinal disease (prophylactic treatment may be considered); *2.5 mg* in ACS patients >75 years of age or with low body weight (<60kg). Patients on treatment with Xarelto & ASA or Xarelto & ASA plus clopidogrel/ticlopidine should only receive concomitant treatment with NSAIDs if the benefit outweighs the bleeding risk. *All strengths-* There is no need for monitoring of coagulation parameters during treatment with rivaroxaban in clinical routine, if clinically indicated rivaroxaban levels can be measured by calibrated quantitative anti-Factor Xa tests. Xarelto contains lactose. **Interactions:** Concomitant use with strong inhibitors of both CYP3A4 & P-gp not recommended as clinically relevant increased rivaroxaban plasma concentrations are observed. Avoid co-administration with dronedarone. Use with caution in patients concomitantly receiving NSAIDs, ASA or platelet aggregation inhibitors due to the increased bleeding risk. Concomitant use of strong CYP3A4 inducers should be avoided unless patient is closely observed for signs and symptoms of thrombosis. **Pregnancy & breast feeding:** Contra-indicated. **Effects on ability to drive and use machines:** syncope (uncommon) & dizziness (common) were reported. Patients experiencing these effects should not drive or use machines. **Undesirable effects:** *Common:* anaemia, dizziness, headache, eye haemorrhage, hypotension, haematoma, epistaxis, haemoptysis, gingival bleeding, GI tract haemorrhage, GI & abdominal pains, dyspepsia, nausea, constipation, diarrhoea, vomiting, pruritus, rash, ecchymosis, cutaneous & subcutaneous haemorrhage, pain in extremity, urogenital tract haemorrhage (menorrhagia *very common* in women <55 yrs treated for DVT, PE & prevention of recurrence), renal impairment, fever, peripheral oedema, decreased general strength & energy, increase in transaminases, post-procedural haemorrhage, contusion, wound secretion. *Serious: cf. CI/ Warnings and Precautions – in addition:* thrombocythemia, angioedema and allergic oedema, occult bleeding/haemorrhage from any tissue (e.g. cerebral & intracranial, haemarthrosis, muscle) which may lead to complications (incl. compartment syndrome, renal failure, fatal outcome), syncope, tachycardia, abnormal hepatic function, hyperbilirubinaemia, jaundice, vascular pseudoaneurysm following percutaneous vascular intervention. Prescribers should consult SmPC in relation to full side effect information. Overdose: No specific antidote is available. **Legal Category:** POM. **Package Quantities and Basic NHS Costs:** *2.5 mg* - 56 tablets: £58.80 & 100 tablets: £105.00. *10 mg* - 10 tablets: £21.00, 30 tablets: £63.00 and 100 tablets: £210.00. *15 mg* – 14 tablets: £29.40, 28 tablets: £58.80, 42 tablets: £88.20, 100 tablets: £210.00; *20 mg* – 28 tablets: £58.80, 100 tablets £210.00 **MA Number(s):** *2.5 mg* - EU/1/08/472/025-035. *10 mg* - EU/1/08/472/001-10, 022 *15 mg/20 mg* - EU/1/08/472/011-21, 023-024 **Further information available from:** Bayer plc, Bayer House, Strawberry Hill, Newbury, Berkshire RG141JA, U.K. Telephone: 01635563000. **Date of preparation:** March 2015.

Xarelto® is a trademark of the Bayer Group.

**Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Bayer plc. Tel.: 01635 563500, Fax.: 01635 563703, Email: phdsguk@bayer.co.uk**


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1. Patel M.R., Mahaffey K.W., Garg J. *et al. N Engl J Med.* 2011;365(10):883-91.
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[a]20 mg once daily for the prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with ≥ 1 risk factor.
AF, atrial fibrillation; PE, pulmonary embolism.



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*Medical Education*

# Medical Education: Return On Investment

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Medical education is expensive. The high cost of medical education means that there is increasing pressure on funders, providers and learners to ensure that medical education delivers return on investment.[1] There are a plethora of methods to achieve this aim; however they all work on the premise that costs must be controlled and/or returns increased. At a micro level there are arguments for doing a range of small things differently: for example more of the curriculum could be delivered in low cost environments or by means of online learning.[2,3] Or perhaps medical students could get involved in quality improvement initiatives during their attachments so that they start to deliver returns whilst they still learn.[4]

While all these initiatives are worthy and useful, they are unlikely to make a massive difference to overall education and workforce budgets. However at a macro level, if you spend hundreds of thousands of pounds educating a medical student and they leave the country where they received their education, then a great deal of loss is incurred.

In this regard the recent report by the GMC into the state of medical education and practice in the UK makes for sobering reading.[5] In the UK in 2013, 12,231 doctors stopped practising. 77% of doctors gave a reason as to why they stopped. The most common reasons were moving abroad and retiring. Unsurprisingly age had a significant effect. According to the report "81% of doctors aged 50 years and under were moving overseas and less than 1% were retiring". A proportion of these were doctors who qualified abroad and who thus were leaving the UK to go back home. Less that 4% of doctors cited revalidation as a reason for relinquishing their license to practice. Less than 3% of doctors left for maternity or paternity reasons. When doctors plan to leave the UK to work in medicine abroad, they need a certificate of good standing from the GMC. The number of UK graduates issued such a certificate has increased in recent years. Most requests for certificates of good standing were for doctors aged from 25 to 27. This is worrying because such doctors will recently have completed their undergraduate education and yet already wish to go abroad. As a caveat however it should be remembered that not all those who request such a certificate actually do go abroad.

So what does all this data mean for the economics of medical education and workforce development? At a macro level it means quite a lot. UK graduates who leave the UK in their mid 20s will have received a medical education worth hundreds of thousands of pounds and will have not have delivered much in return. They are likely to have practiced for only about two years and then under close supervision and whilst continuing to receive a substantial amount of postgraduate education.[6] The economics are stark – a great deal of input and little or no output. The amounts of funding involved dwarf any calculations with regard to small changes in curriculum delivery that might save costs. To make matters worse when graduates emigrate, the government loses the ability to pursue them for repayment of their student loans – a further loss to the exchequer.

And so if this means quite a lot, it is surely worth asking the question as to what if anything can be done about it? Some would suggest a coercive approach. Graduates could be compelled to pay for the cost of their education if they emigrate. But this wouldn't work – as there would be no effective way of following them up. Some would suggest that they should only be given a letter of good standing from UK authorities when they have worked in the UK for a set amount of time – maybe five years - but European Union laws regarding free movement of workers would render this unworkable. Alternatively graduates could have provisional registration for a longer period – thus forcing them to stay in the UK for longer – but the GMC is talking about moving the point of registration to exit from medical school – in exactly the opposite direction. In any case such a move would have deleterious effects on the international recognition of UK medical education.

If coercion will not work, the only alternative is to try to make the UK a more attractive place to work as a doctor. This will mean better training programmes, improved terms and conditions, better job prospects, and portfolio careers which might involve a blend of education, research and clinical practice.[7] State of the art facilities in medical education that satisfy learner and institutional needs can be cost effective.[8] More academic training programmes that lead to graduates who can then work in academe and clinical practice are also likely to be a good long term investment.

Some of this would cost money, but the return on investment

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would be a more contented and stable workforce that wants to stay in the UK. The alternative is continuing to pour funding into a bucket with a hole at the bottom. Cost and value in medical education can at times be a complex concept to grasp – involving models and ideas like cost utility formulae and sensitivity analyses. But sometimes it can be simplicity itself – involving the spending of funds in the reasonable expectation of returns. Retaining doctors might be a good way to start.

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*Medical History*

# The Battle of the Atlantic and American Preparations for World War II in Northern Ireland, 1940-1941 (before Pearl Harbor)

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## INTRODUCTION

In July 1940, Colonel Angus Hedley-Whyte was appointed commanding officer of the British 31st General Hospital at Musgrave Park, remaining in Belfast with his family until a month after the Hospital's handover to the U.S. The U.K. and American Officers played an important role in my[1] education, as Angus' seven-year-old son.

### 1940-41

On August 15, 1940, the Luftwaffe bombed the North and South of England and 'Wild' Bill Donovan was smuggled into the garden of 10 Downing Street. The previous month he had been to the UK, to President Franklin Delano Roosevelt's home at Hyde Park, and secretly back to London[1]. Winston Churchill later told Cecil King, Editor-in-Chief of the Daily Mirror, that August 15, 1940 was the day he knew the Allies would eventually prevail[2]. President Franklin Delano Roosevelt and Winston Churchill had been exchanging letters since September 2, 1939[3]. Bill Donovan was Roosevelt's private lawyer, a Republican and later head of the Office of Strategic Services (OSS), forerunner of the CIA. Churchill told Donovan of that day's (August 15, 1940) great successes of the RAF. During the following week Donovan was shown Government Communications Headquarters (GCHQ), Bletchley Park, the newest centimetric radar and the state of UK atomic research. This unprecedented access arranged by President Roosevelt with Winston S. Churchill followed a strictly confidential message from the President on May 17, 1940 in response to Churchill's plea for help. The archived message was annotated in Churchill's handwriting before he read it to the War Cabinet[4].

Churchill's government wanted American Armed Forces to deploy forthwith to Iceland and Ireland. Donovan suggested "yes" to Iceland, Catalina flying boats, B-24 Liberator bombers originally purchased by the then soon to be defeated French; but not delivered. Northern Ireland should be prepared for U.S. occupation. As a pre-1940 U.S. presidential election boost the swap of fifty U.S. destroyers for Canadian and Caribbean bases was agreed[5]. In Northern Ireland in 1940, the RAF had only 12 fighters and 20 light bombers[6,7], despite the strategic importance of this region to the War in the Atlantic.

## U.S. PLANNING FOR WARTIME PUBLIC HEALTH IN THE U.K.

At the outset of World War II, the U.S. Military began to address the problems of public health under war time conditions. In the fall of 1939 American observers had visited the UK to survey public health conditions. Among the first were representatives of the U.S. Navy's Bureau of Medicine and Surgery. In July 1940 Lieutenant Commander Irwin L.V. Norman and Lieutenant Simon B. Eyer established headquarters at the American Embassy in London for the collection of data on military medicine, preventive medicine and civilian public health. The British Ministry of Health issued an official invitation to the National American Red Cross and Harvard University, who then established the American Red Cross-Harvard Field Hospital Unit headquartered in London, to serve throughout the UK in preventive medicine and public health. Relocated to Salisbury, Wiltshire, they established a laboratory-equipped 100-bed hospital for the study of infectious disease, directed by John Everett Gordon, M.D., Professor of Preventive Medicine and Epidemiology at Harvard and liaison officer to the UK Ministry of Health[8].

The Office of the Surgeon General of the U.S. Army appointed U.S. Army Col. (later Brigadier General) James S. Simmons as Chief of the Preventive Medicine Subdivision. Simmons acknowledged the importance of medical intelligence for both civil affairs and the Armed Forces, and early in 1940 sent Sanitary Corps Officers to survey conditions where U.S. troops might ultimately be deployed[9].

Planning began for still neutral U.S. construction workers and U.S. Navy ensign pilots to be stationed in Ulster[10]. Max

1 All first person references in this Medical History refer to the first author.

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Leonard Rosenheim, recently recalled from the Massachusetts General Hospital[11] to be Medical Planning Officer, was to arrange for Ulster medical services for the United States civilian workers and for U.S. Navy personnel when in Londonderry or at work anywhere in Ulster. Rosenheim and Sir Alexander Hood, head RAMC, arranged for Benjamin Rycroft under DDMS Brigadier Beddows to be responsible for military and U.S. ophthalmology in Ulster[11]. Arnold Stott, paediatrician to the Royal Household, was to be on-call paediatrician[12].

Apart from the spring 1941 blitzes on Belfast, most of Beddows', Rosenheim's and Rycroft's assignments concerned RAF Coastal Command and U.S. Navy fliers, as well as the American construction workers. Max Rosenheim was impressed by Matron Mabel Huddleston (1891-1964) at Roe Valley Hospital, Limavady, "ruling strictly but with great humour and ensuring a high standard of nursing care"[13].

Wing Commander Cooper was Limavady station commander. When Limavady air-crew broke down and did not complete missions, Cooper was sympathetic and was wont to assign members of crews mentally impaired (LMF) or physically injured to Matron at Limavady Hospital, later named Roe Valley Hospital. Cooper also led Whitley VII patrols himself. He collaborated with Flying Officer Bliss and Squadron Leader Humphrey de Verde Leigh, a personnel officer, in the first trials of ASV 2 Radar-Controlled Leigh Lights W/L for illuminating U-boats. In March 1941 a Wellington was fitted with a light driven by an inboard engine which vibrated so much that the plane almost shook apart[14,15]. With the help of RN submarine H31 the perfected systems were destined to both increase morale and submerge U-boats. My father-in-law was chosen for the H31 experience because Higher Authorities would respect a Baa-Baa (Barbarian Rugby Club)[16]. As deployed, a Leigh Light was a 22 x $10^6$ candela carbon arc searchlight two feet in diameter[17].

## ULSTER AIR BASES

Number 502 (Ulster) Squadron RAF (AUX) 'A' flight moved to Limavady to be even nearer to the crucial Battle of the Atlantic from Aldergrove on December 15, 1940 followed by a full squadron move on January 27, 1941[14]. The 502's Whitley VII's were equipped with the new ASV Mark 2 radar[14,18]. 502 used the old school house at Limavady, and later the community center at Aghanloo as headquarters[15]. The officers' mess was Drenagh house, while Gorteen was for Sergeants. Early in 1941, 502 Squadron morale was poor. The Whitleys VIIs with a crew of six flew sorties of eight to ten hours north from Lough Foyle, then west to about 20 west. The last sight of land was generally Tory Island. Land was not seen again for at least five to six hours. If one engine, failed the Whitley VII crashed. The Whitleys, camouflaged with black paint, were called "flying coffins"[15]. During my future father-in-law's 500 hour flying operational tour of duty in 502 squadron, 1941 air crew mortality at Limavady and Aldergrove was 50 percent. 502 flew by astro-navigation and sun sighting at mid-day with strict radio-silence[18].

## FURTHER U.S. PLANS FOR ULSTER 1940-41

In April 1941 the U.S. War Department issued the RAINBOW-5 plan which envisioned the deployment of 30,000 U.S. troops to Northern Ireland[10,19]. On May 19, 1941, the Special Observer Group (SPOBS) was established[10,20](Fig.1). Brigadier General Joseph T. McNarney was General Chaney's chief of staff. McNarney concurrently headed the United States Joint Planning Committee of the U.S. War Plans Division[20]. He later became a four-star general and succeeded Eisenhower as U.S. Army Commander, Europe. McNarney participated with President Roosevelt and Winston S. Churchill in the ABC- 1 conversations. U.S. medical interests were represented by Major Arthur B. Welsh, a Regular Army medical officer since 1926. He was appointed in October 1939 as assistant chief of the Planning, Plans and Training Division, Office of the Surgeon General, assisting in the Army Medical Department's emergency and war planning. He was in regular contact with officers of the British Ministry of Health, the Royal Air Force and other agencies and acquired considerable expertise in medical and sanitary conditions in the U.K. Welsh's original medical plans for U.S. Army forces to be stationed in Iceland, Northern Ireland, Scotland and England were superceded after the U.S. entry into war, but the more comprehensive strategies that followed were based on his principles[20]. His U.S. appointment mirrored that of Major John Hugh Philip Gilbey, 10th Baron Vaux of Harrowden. Kay Summersby later gained fame on General Dwight D. Eisenhower's staff for her savoir faire which helped Ike gain his two-term U.S. Presidency.

*Fig 1*. The U.S. Special Observer Group (SPOBS) 1941: Front row, L to R: Case, Hinman, McClelland, Davison, McNarney, Chaney, Summers, Lyon, Bolté, Griner, Dahlquist. Middle row: Yeldham*, MacDonald*, Long, Fulford, Welsh, Middleswarat, Matejka, Coffey, Snavely, Griffiss, Louprette, J.H.P., later Lord Gilbey*; Bristol, Summersby*, Shore*, Back row: Wallace*, Casazza, Schwaiger, Paisly, Rapetti, Miller, Leland (*British personnel)[20].

On May 22, 1941, the U.S. War Department agreed coordination with the British Chiefs of Staff Committee[10,20]. On June 12, 1941, the British Government signed a contract with the U.S. G.A. Fuller and Merritt-Chapman Corporations to construct bases: the first at Londonderry for the refueling and repair of U.S. Navy destroyers and submarines and the second at Lough Erne for PBY Catalina flying boats[10]. Vice Admiral Ross T. McIntire (Fig.2) was, together with

Fleet Admiral Ernest J. King, responsible for oversight[21,22]. Because of security considerations, only the Prime Minister of Northern Ireland was initially informed, but on June 9, 1941, Sir Basil Brooke, Minister of Commerce, chaired a meeting at Stormont to discuss the "highly secret formula of additional constructions work for war purposes in Northern Ireland". This meeting was attended by U.K. naval and air commanders, the senior U.S. Naval engineer, and representatives of the U.K. Admiralty, Ministry of War Transport, Ministry of Food and the Works Branch of the Air Ministry, along with representatives of Northern Ireland executive departments including DDMS Beddows[23,24]. On June 30, 1941, more than 350 American civilians employed by Fuller and Merritt-Chapman arrived in Londonderry, another 400 arrived in July, followed by additional personnel in September and October[10,25].

*Fig 2*. Vice Admiral Ross T. McIntire. Oil-on-canvas portrait 1942 102.9 x 82.6 cm by Samuel Bookatz (1910-2009), reproduced with permission of the National Museum of Health and Medicine, Bethesda, MD.
In 1941 Admirals King and McIntire were ultimately responsible for U.S. employees in Northern Ireland and thus liaised with Brigadier Beddows[21,22,23,24].

## WARTIME EDUCATION

As a seven-year-old eldest son of the Commanding Officer at Musgrave Park 31st British General Hospital, I was mystified by us entertaining American engineers in mufti. One engineer told me that they were teaching the RAF to fly Catalinas. I thought my leg was being pulled. "Nonsense" I said to the U.S. engineer. He replied, "We found *The Bismarck* for you. Our man has been promised a George III silver salver and tea service"[26] (Fig.3). "Remarkably inappropriate". My mother joined us and decided that my brother's God-father Major Benjamin Rycroft[11,28] should keep me occupied. I was told that I should stop trying to be a spy; otherwise I might be imprisoned or even executed. Everything changed ten days after Pearl Harbor, December 6, 1941. Hitler declared war on the U.S. A fortnight later, the Yanks got uniforms and from being suspected as a "spy", I became a junior colleague in need of further education.

*Fig 3*. The *Ark Royal* (1942) by Walter Zeeden (1891-1969). Available at http://www.kbismarck.com/painting20.html and http://www.cafepress.com/kbismarck.29658895 (last accessed November 13, 2014).
The attack by Swordfish from the *Ark Royal* that crippled the Bismarck was launched in atrocious weather. Waves were the height of four-story buildings. The flight deck 62 feet up from the Atlantic was constantly drenched. The rise and fall of the *Ark Royal's* stern was 53 and 56 feet. The wind speed over the deck exceeded 50 knots. Timing of take-off was vital. Many Swordfish as they left the *Ark Royal* touched the sea. On return, three Swordfish crashed. The others took over an hour and many attempts to land safely. No monoplane could be launched[26,27].

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*Medical History*

# John Coakley Lettsome (1744-1815) Philanthropologist and physician

Caoimhghín S Breathnach

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Though they were not contemporary medical students at Leiden, John Lettsome from the Antilles and James Sims from Ireland became firm friends and collaborators when they settled into practice in London. John Coakley Lettsome was born in 1744 in the British Virgin Islands.

John and his brother were the only surviving pair of seven sets of twins born on Little Jost Van Dyke to Edward and Mary Lettsom (variant spelling was common). At the age of six, John was sent alone to England to be educated, and at school in Lancashire he came to the attention of the Quaker, Samuel Fothergill. Fothergill recommended him to his brother John, physician to St Thomas's Hospital in London, after the youth had completed an apprenticeship to a Yorkshire apothecary in 1766. However, John returned to the West Indies when his father died; he freed the family's slaves, worked hard himself and made £2,000, half of which he gave to his mother before returning to Europe to complete his medical training.

A thesis on the natural history of the tea-tree won him his MD from Leiden in 1769 and he repaired to London, took the LRCP and in 1770 founded the General Dispensary for the Sick Poor of the City in Aldergate Street. It is doubtful if many of his dispensary patients agreed with his view that long-term tea drinking was pernicious to health, causing a multitude of new diseases, leading to enervation and debility.[1]

Satellite dispensaries soon followed in the city, and members of the staff met to confer on patient care. While living laborious days, Lettsome was happy in his work, aware of the growing recognition he received from his colleagues, and in 1773 conceived the idea that a Medical Society was best suited for that purpose. Lettsome's "The Medical Society of London" has survived and continues today.[2]

James Sims, a key member of the Society, was born in county Down in 1741, graduated at Leiden in 1764, and settled in London. Some of his papers were translated into French, German and Italian. For 22 years he was president of the Medical Society of London, to which he presented his library in 1802. In 1810 he retired to Bath where he died in 1820.[3]

Originally made up of 30 physicians, 30 surgeons and 30 apothecaries, the membership of the Society was widened, to cater for a broader range of interests. Outbreaks of infectious diseases (fevers) were reported by members, case histories were analysed, instruments and new medicines were considered and medical intelligence from the provinces and from abroad was encouraged.

William Withering's (1741-1799) claim for the foxglove, digitalis in treatment of dropsy, received a stormy reception in 1785, and Lettsome was less than circumspect when commenting that his own trials of the drug 'in pulmonary consumption never cured anyone, and that its indiscriminate use had killed many' – an addendum not to be ignored [in the light of later experience].[2]

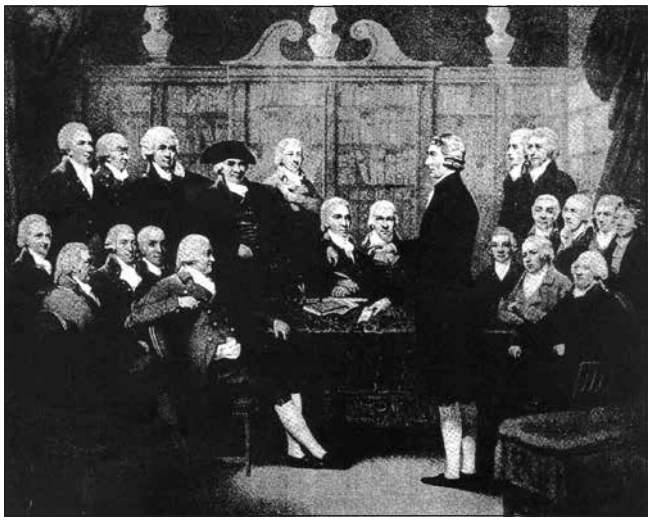

*Figure*. The meeting of the Medical Society of London when John Coakley Lettsome presented the deeds of 3 Bolt Court to the Society. The President, en chapeau, is James Sims. Reproduced from Trent's paper (p 135)[1] by kind permission of Elsevier.

The eighteenth century, in the history of culture and of science, is looked upon as the age of Enlightenment, which included (particularly by the Germans) the cultivation of the history of medicine, although it was marred by the hankering after systems tending to explain the motives or philosophy of the healing art. (pp 589, 657)[4]

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Medical practice was regarded in all circles as a matter of conscientious vocation, and not as one of the higher classes of business. Most members of the medical profession – certainly the better class, at least – also possessed, or at least strove to attain, a universal humanistic education, quite in contrast with [later] one-sided education of special branches. Hence the physicians of the eighteenth century also universally strove, with a consummate love of science, to gain for themselves an acquaintance with all the special medical and medico-technical branches of knowledge.

Upon these facts depended not only the high self-esteem of the physicians themselves, but also the general esteem which met them everywhere. (p 731)[4]

That century is widely regarded as the golden age of the medical profession, and in England, physicians far surpassed continental (especially German) counterparts in mercenary acquisition – often used, it is only fair to add, in philanthropic ways. (p 730)[4]

John Fothergill (1712-1780) bequeathed £200,000 to the poor in his will (p 764)[4], Richard Mead's (1673-1754) largest annual income was £7,000, his house with its famous museum and library at 49 Great Ormond Street became the Hospital for Sick Children[5]; and Astley Pastin Cooper (1768-1841), surgeon at Guy's Hospital, for many years earned £15,000; the highest was £21,000 (p 764)[4].

It is chastening that these huge incomes arose from 'the most profound faith in drugs' in the case of the physicians; drugs, according to the wits, were 'substances about which the physicians knew nothing, but they administered them to patients about whom they knew even less'.

Lettsome was the busiest, most philanthropic, and most successful physician of his day, earning as much as £12,000 a year, even though a large part of his practice was gratuitous, and he gave away immense sums in charitable contributions (p 652)3. He is said to be the author of

When patients sick to me apply
I physics, bleeds and sweats 'em
Sometimes they live, sometimes they die;
What's that to me? I Lettsome (p 652)[4]

The Medical Society met fortnightly to discuss current medical topics. Edward Jenner (1749-1823), who practised in his native Berkeley in Gloucestershire, became a corresponding member of Lettsome's Society in 1789. In 1800 he informed the members that in 1796, James Phipps had been protected from smallpox by inoculation of cow-pox material taken from the vesicles on the finger of a dairymaid, Sarah Nelmes; the members were suitably impressed when Jenner, in person, presented the Society with a copy of An inquiry into the causes and effects of the Variola Vaccine (July 1798). Lettsome and his fellows adopted the cause enthusiastically, spread the word widely, and struck a medal and awarded a testimonial to Jenner in March 1802.[2]

The Society was not just a talking shop. When an epidemic of influenza hit London in March 1803, a postal investigation was begun, and the Post Master General granted free postage for the 200 circulars sent to members at home and abroad.[2]

In September 1878 Lettsome presented a freehold property, 3 Bolt Court, Fleet Street, London to the Society, for meetings and space for a library; the society moved more than once over the years. The Medical Society of London, the oldest medical society in the United Kingdom, now serves the community from Chandos Street, near Cavendish Square.[2]

Lettsome disposed of his country estate at Grove Hill some time before his death, and part of his library was too large for his London residence. A philanthropist and generous patron of his many literary friends as well as learned institutions, he was forced to continue working hard late into his life, even until his death in 1815.[1]

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*Northern Ireland Medicolegal Society Lecture*

# The fortunes of the legal and medical professions during the "Troubles" - Presentation to The Northern Ireland Medicolegal Society - October 14 2014

Philip McGarry

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Provenance: externally peer-reviewed.

The seed for my presentation emerged from Mr Justice Ben Stevens' eloquent Presidential address last year. In thanking him I reflected that we have taken for granted how, after 1969, while much of civil society failed to function, lawyers and doctors maintained the highest professional and ethical standards, with many developing national and international reputations. Most crucially, law and medicine never compromised themselves by acquiescing in the divisions which have riven our community.

Against a background of incipient chaos, doctors and lawyers performed their duties with integrity and impartiality, providing a bulwark against breakdown.

## THE LEGAL PROFESSION

Unlike doctors, lawyers were directly targeted by paramilitaries.

On 11 October 1972 Resident Magistrate William Staunton (fig 1) was leaving his daughters at St Dominic's School on the Falls Road. A motorcycle drew alongside. The pillion passenger opened fire. Mr Staunton died later. This was a clear threat by the IRA to Catholic judicial figures.

*Fig 1*. RM William Staunton ©VICTOR PATTERSON

September 16 1974 was a black day for the legal profession.

At 8.30am, an IRA gunman shot dead Judge Rory Conaghan. 8 year old Deirdre witnessed her father's murder.

The IRA said: "He was collaborating with the British War Machine".

The Irish Times said: 'He restored the confidence of many members of the minority in the judicial process. He awarded damages to 16 people against the Army for mistreatment. He jailed Ian Paisley.'

At 8.50am Resident Magistrate Martin McBirney (fig 2) was at breakfast. A gumnan came round the back of his house and killed him. He was a friend of Louis McNeice and TP Flanagan, whose painting, 'Victim', is in his memory.

*Fig 2*. Police at house of RM Martin McBirney ©VICTOR PATTERSON

In October 1979, John Donaldson, 23, a Protestant solicitor was leaving Andersonstown RUC Station. A van came alongside. He was shot dead. The IRA said it was ' a mistake.'

In January 1983 Judge Billy Doyle was leaving Mass at St. Brigid's Church in Derryvolgie Avenue. A man approached and shot him dead.

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In 1978 the Economist ran an article alleging he was appointed not on merit, but because he was a Catholic. He sued and was awarded £50,000.

In December 1983 Edgar Graham, Barrister, Law Lecturer and Unionist Assembly member was shot dead in University Square.

Two former students were convicted of withholding information.

In April 1984 Resident Magistrate Tom Travers was at Mass at St Brigids. Two gunmen approached, shooting him six times. His 21 year old daughter Mary was shot dead.

Later Mr Travers recalled: 'as the man prepared to fire, I saw the hatred on his face, a face I will never forget'. At the trial a reporter wrote: 'Mr Travers broke down in the witness box, weeping openly. Hardened reporters said it was the most upsetting courtroom spectacle they had ever witnessed. The man Mr Travers identified as his daughter's killer walked free, after the judge said there was a possibility he could have been mistaken.'

In April 1987 Lord Justice Gibson and his wife were travelling across the border when a massive bomb exploded. Appointed Lord Justice of Appeal in 1975 he presided over many high profile cases including the 'shoot to kill' trial of 3 RUC officers, whom he found not guilty. He acquitted all the defendants in the Grimley Supergrass Trial. In 1985 he quashed the murder conviction of prominent republican Dominic McGlinchey.

In February 1989 Belfast solicitor Pat Finucane was shot dead at home.

He had a high profile, dealing with cases which typically involved republicans.

Much controversy has surrounded the killing. The most recent investigation in 2012, led to David Cameron acknowledging the level of State involvement had been "shocking".

In March 1999 Rosemary Nelson, a Lurgan based solicitor died when a loyalist bomb exploded under her car. She had represented a number of prominent republicans. She had alleged that she had received death threats from policemen.

There have been several investigations. The most recent in 2011 stated that RUC members had ' legitimised' her as a target and that security force members had possibly been involved in the attack.

A number of other lawyers escaped death in assassination attempts, including Lord Chief Justice Lowry on three occasions. In 1988 the Hanna family died in an explosion intended to kill Judge Eoin Higgins and his wife.

Did the legal system deliver justice?

It is accepted that some convictions were unsafe. In recent years a number have been overturned, and more cases are to come before the courts.

Professor Brice Dickson[1] wrote in 1992 of how the Emergency Provisions Act (1973) expressly altered the existing judge made rule that confessions should be excluded if obtained by 'oppression'. Despite this law, in 1975, in R v O ' Halloran, Lord Chief Justice Lowry reaffirmed that judges had the discretion to rule that any form of ill-treatment could render a confession inadmissible. Dickson added: 'This was courageous, because it contradicted the apparent intention of Parliament in deliberately excluding such discretion.'

Dickson also noted that the N.Ireland judiciary were often more progressive in their rulings than the House of Lords.

In the early 1980s nearly 600 people were charged on the evidence of 27 'Supergrasses'. The judiciary discharged almost every case.

David Bonner[2] in 'Combating Terrorism' stated: 'in executing a difficult task the NI judiciary demonstrated skill, integrity and independence of the Executive.'

'Counter- transference' describes the feelings, often unconscious, stirred up in a therapist by the patient. This is normal and universal.

*Fig 3*. Mr Derek Gordon

Judges are expected to look analytically at the evidence and weigh it up, unswayed by emotion. But judges are human, with normal emotions! And living with a death threat will affect any normal person. Judges will inevitably have a counter- transference towards defendants. Judges had to make decisions about defendants who were members of organisations which had killed some of their colleagues. They knew some defendants would have been delighted to hear that they had been assassinated at their home that night. Yet Northern Ireland did not have the debacle of the Maguire 7, the Birmingham 6, the Guildford 4 and the Winchester 3, in

 

all of which the defendants were convicted by jury. Mistakes were undoubtedly made, but on balance, during three decades of violence, we were well served by our legal system.

## THE MEDICAL PROFESSION

Prior to 1969 most doctors in Northern Ireland had rarely seen a gunshot wound. Between 1968 and 1998, there were over 3,600 deaths and 47,000 people injured, in 36,900 shootings and 16,200 bombings.

Necessity drove innovation. Across specialities, doctors rose to the unprecedented challenge not only in applying best practice, but by developing new techniques and procedures.

High velocity bullets to the head often left large skull defects. Mr Derek Gordon, (fig 3) a neurosurgeon at the Royal Victoria Hospital and Gordon Blair[3]. of the School of Dentistry developed titanium cranioplasty, in which titanium was moulded by explosives, permitting the production of a very fine, extremely strong metal. Titanium cranioplasty proved extremely effective and, following the seminal 1973 BMJ paper, was taken up worldwide.

Kenyan- born Aires Baros D'Sa[4] was appointed an RVH consultant in 1978. He achieved international recognition for his development of the shunt, which diverted blood flow around serious injuries. After this initial procedure the orthopaedic surgeons fixed the bones.

The vascular surgeons came back to construct a bypass graft. Finally, the plastic surgeons finished off. This became known as the Belfast Technique and was soon adopted internationally.

During the 1970s many trauma victims develped 'blast lung'. Bob Gray, Denis Coppell[5]. and other RVH anaesthetists developed 'Positive End Expiratory Pressure,' which kept the lungs slightly inflated at the end of the breath, preventing lung collapse and further damage. PEEP rapidly came into use worldwife.

An orthopaedics innovation was the 'Belfast Fixator', used to stabilise the leg during surgery. The original device was designed by Belfast orthopaedic surgeons and manufactured in Mackie's Foundry!

## CANDLES IN THE DARK

In 2006, former Chief Medical Officer Dr James McKenna[6] published ' Candles in the Dark'. He and two colleagues interviewed over a hundred people, health professionals, former patients - including prisoners - and family members.

In 1971 Government introduced a Statutory Order requiring the immediate reporting of all gunshot wounds to the police or army. This caused great concern. A BMA delegation led by Mr Reggie Livingstone, from the RVH and Dr Raymond Shearer, a West Belfast GP, met the Secretary of State. Agreement was reached that staff be allowed to use their discretion, and that hospitals would aggregate figures for statistical purposes.

Hospitals were not immune to the violence. In October 1976 loyalist gunmen murdered Marie Drumm, Sinn Fein Vice-President, in the Mater.

Two off duty soldiers were killed in the grounds of Altnagelvin, an ambulance man in the RVH, and an off- duty police officer in the carpark of the Mid- Ulster. A policeman guarding a patient in the Royal was shot dead in 1981.

## DOCTORS SPEAKING OUT

In 1977 the Northern Ireland Police Surgeons Association expressed concern about ill- treatment in police stations and holding centres. It issued a memorandum, describing examples of significant injuries.

The memorandum concluded: 'Doctors have to uphold their medical position as neutrals, a role which their profession demands and which doctors carry out to the letter.'

In January 1979 Dr Robert Irwin appeared on ITV's This Week'. He reported examining approximately 150 prisoners who had suffered injuries in custody. The evidence of Dr Irwin and colleagues led to a report by Amnesty International and subsequently the Bennett Inquiry.

After the programme Dr Irwin was subjected to criticism and abuse. Most shockingly the Daily Telegraph reported that official sources were trying to undermine his integrity, by briefing newspapers that he was embittered because his wife had been raped, allegedly by a soldier, and that the subsequent police investigation had been poor.

The doctors received full support from the British Police Surgeons Association, whose President came to Belfast. Bennett recommended that prisoners be seen by a doctor daily, and that closed circuit television be installed in interview rooms. The treatment of prisoners improved significantly, although the CCTV took a long time to implement.

The courageous stand taken by Dr Irwin and colleagues has had a major impact upon the treatment of prisoners ever since. These are doctors of whom the medical profession can be very proud.

## PSYCHIATRIC RESEARCH

Alec Lyons was a Consultant Psychiatrist at Purdysburn. He noted – at first sight paradoxically – that the incidence of depression fell in areas experiencing the worst violence.

I shall be immodest enough to note that in a paper I wrote with Dr Peter Curran in 1988, we found the suicide rate declined to the lowest ever level in 1972, the most violent year of the Troubles. Another Lyons paper examined individuals arrested after riots.

He wisely noted that there was little value in attributing riots merely to: 'so called riff raff, hoodlums or psychopaths', adding: 'potential riot participants are available in almost any community'. La plus ca change!

 

## IRA HUNGER STRIKE

Until the mid 1970's prisoners on hunger strike were commonly force fed.

However Government then made a decision to adhere to the World Medical Association's 1975 Declaration of Tokyo which stated: 'Where a prisoner refuses nourishment and is capable of forming an unimpaired, rational judgement concerning the consequences, he or she should not be fed artificially.'

Contrast this enlightened approach with the current disgrace in Guantanamo Bay where clinicians are colluding in long-term mass force feeding. In N. Ireland we were - and are - better than that.

Dr McKenna quotes a hunger striker: 'Dr X was the senior prison doctor. He was very professional and humane. An eye specialist, Dr F. got really involved and took his professionalism to another level. The care we got was exemplary.'

A prison doctor said: 'Dr. X was the senior doctor then. He had nursed, and I mean nursed, most of the hunger strikers. He was there when many of them died. Sometime later, one Friday afternoon at 5pm we parted company at the prison gates. At 7'clock I was phoned and told he had shot himself. It never left him. He often recounted how he felt at that time and what he had gone through, not in terms of what he had suffered, but especially the families of the hunger strikers'.

Dr McKenna states: 'The three doctors who attended the prisoners are now dead. However their memories are to be honoured as exemplars in one of the most stressful experiences imaginable for members of the medical profession.'

A final year medical student at the time, I went to bed in the Mater Hospital in the early hours of May 5th, knowing Bobby Sands was dying.

The next morning the hospital was abuzz with the presence in Intensive Care of 14 year old Desmond Guiney and his father Eric, a milkman. Following Sands' death their milk float was attacked by a crowd. It struck a lamp post. Both Guineys soon died.

During the period when 10 prisoners died on hunger strike, 25 people were killed by the organisations to which they belonged.

## TERRORISTS AREN'T (USUALLY) MENTALLY ILL

Politicians and media often describe paramilitaries as mad men, crazy, psychopaths, mindless or criminals.

It's fairly obvious most paramilitaries were not mentally ill. Relatively few were psychopaths, and to call them mindless..... is just mindless!

However it was convenient to assert that violent acts were from outside, not of us, caused by some kind of mental illness afflicting people for some unexplainable reason. In truth violence reflected the reality of a bitterly divided society in which violence has been endemic - and typically justified in retrospect - for nigh on a century.

In 1986 Alec Lyons and Helen Harbinson reviewed psychiatric reports on 106 people charged with murder. They found that politically motivated killers came from backgrounds more stable than those of 'ordinary' criminals. There was a lesser family history of personality disorder, they had better educational attainment and were much less likely to have taken alcohol.

Few paramilitaries used as a defence that they were mentally ill. The vast majority released early under the Good Friday Agreement did not re-offend; not to great surprise, because these men were different from other prisoners.

Mrs Thatcher famously - and superficially- referred to terrorists as 'common criminals'. Today that same term is often used - by republicans - to describe the current reincarnation of physical force nationalism!

## CONSULTANT SHOT

In November 1972 Mr Peter Gormley, Consultant Ophthalmologist (fig 4) was driving to work at the Mater Hospital along with three of his sons when UVF gunmen opened up on the car. Mr. Gormley was shot in the shoulder. 14 year old Rory was shot dead. Another son was hit in the arm and leg.

*Fig 4*. Mr Peter Gormley ©VICTOR PATTERSON

Three of Mr. Gormley's sons became doctors. Mark has just retired as a Physician in the Mater. He took part in a television documentary in the late 1980's. The reporter talked to him as he was driving along the Shankill Road to see a patient in their home, close to where his brother had been killed. It was a quite remarkable interview, with Dr Gormley speaking of his duties and responsibilities as a doctor. This was a testament to medicine at its very best.

Northern Ireland was not a healthy society in many ways, (nor was the Republic of Ireland). The IRA and UVF were politically motivated, and they were different from 'ordinary'

criminals. However, despite that, the killings, to use David Cameron's phrase, were unjustified and unjustifiable. It is important that our children are not given a narrative that what happened was a legitimate campaign for justice or equality, that to shoot dead a judge in front of his 8 year old daughter or a solicitor in front of his three young children was acceptable. It wasn't.

## IN CONCLUSION

I hope this evening I have given a sense of some of the significant achievements in medicine and law over the last four decades.

I look back over that period with great pride. Both professions have acted as a bulwark against breakdown and contributed to keeping our society on a level of stability. We can be proud of our achievements. I am confident that doctors and lawyers will continue to lead in our community and that in time our society will finally right itself.

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*Annual Oration*

# Medical Education in the Future: Lessons from the Past

## Royal Victoria Hospital, September 2013

Jack Crane

Accepted 24th January 2014.

ºMr Chairman can I thank you, and indeed all the members of the Medical Staff Committee for bestowing on me, a mere jobbing forensic pathologist, the honour of delivering this year's Annual Oration.

I started work as a doctor in this hospital as a pre-registration house officer in 1977 and now, in the latter years of my career, as I approach retirement, I feel very privileged indeed to be invited back to address the staff and students of this great institution. Also, can I take this opportunity to welcome so many distinguished guests, retired colleagues and friends who have so kindly honoured me by coming along to the Royal this morning to listen to my oration.

My being here at all, as a fellow member of the Medical Staff Committee of this hospital is due to the kindness, and dare I say wisdom, of a past Chairman of the Committee, the late Dr John Weaver. Following my appointment as a consultant in forensic medicine in 1985, John invited me to join the staff of the hospital. This association with the Royal, along with my appointment to the teaching staff of Queen's University, have meant more to me than all the appointments to government committees and public bodies during the past 23 years as State Pathologist for Northern Ireland.

Before I begin to talk about Medical Education – the topic I have chosen for my oration, I have an important duty, as have all distinguished orators before me, and that is to welcome the new medical students to this great hospital. And I want to emphasise the use of the term "hospital". To the patients who come through its doors, it is the Royal Victoria Hospital, the Royal or the RVH. It is **not,** and indeed never has been, the Eastern Health and Social Services Board, the North and West Belfast Trust or the Belfast Health and Social Care Trust. The welcome, ladies and gentlemen, to our new students is to the **Royal** with its longstanding tradition of excellent clinical and nursing care, compassion for the sick and outstanding clinical teaching – values which are as important today as they were when the first oration was delivered in 1826 by Dr James McDonnell in the Belfast General Hospital in Frederick Street.[1] I have no doubt that the welcome to new students then was warm and friendly despite, as one author of the time put it, medical students having "a reputation for wild fun, drinking and not doing much work".[2] Times have changed however and our students are now, at least for the most part, well behaved, sober and hard working. So the welcome to you today is no less friendly and I am delighted that you have come along this morning.

The beginning of your clinical studies is of course the start of your exposure to patients in the wards and outpatient clinics. This is an exciting and rewarding phase in your undergraduate medical career and, as Osler put it "The student begins with the patient, continues with the patient and ends his studies with the patient…".[3]

The privilege of being the Orator is the opportunity to deliver a lecture on a topic entirely of their own choosing although clearly related to medicine and, usually on a subject of relevance to the gathered audience. I was clearly conscious of the tradition of the Oration to welcome new students to the hospital and I therefore felt it appropriate to talk about some of the changes in medical education and in particular how, in my opinion, the role of the medical teacher has been downgraded and diluted over the years by changes in the medical curriculum, not just at Queen's but indeed in many medical schools in the UK.

According to Einstein "Teaching should be such that what is offered is perceived as a valuable gift and not as a hard duty".[4] That gift, I believe, at least in medicine, needs to be offered by teachers, by experts in their various specialties, by clinicians, and by enthusiastic clinical academics and not by so-called "e-learning", self directed learning or by downloading signs and symptoms on an application on your mobile phone.

The concern for the Chairman of Medical Staff and the Committee is that the Orator, having been given carte blanche for his oration, may embark on some personal crusade or vendetta causing embarrassment for all and indeed possible disgrace to the Orator himself. Such was the fate of the great physician Ignaz Semmelweiss who worked in Vienna in the 1840s and 50s and who is credited with inventing an antiseptic procedure to reduce the risk of puerperal sepsis in the maternity unit of the Vienna General Hospital. The

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medical staff of the Hospital in Vienna were so concerned about Semmelweiss's behaviour during his lectures and talks that they proposed a course of treatment for the ageing physician who was clearly suffering from organic mental illness.[5] The treatment involved blood letting, cold-water dousing and magnesium sulphate enemas. I hope that the current Medical Staff Committee do not feel it necessary to embark on such treatment for this Orator.

William Hunter, the great anatomist and obstetrician in the 1750s said that "To acquire knowledge and to communicate it to others has been the pleasure, the business and the ambition of my life".[6] He was regarded as a great teacher and this philosophy of "handing on learning", as Kenneth Calman has called it in his book on Medical Education, has also been of fundamental importance to me as a medical academic and similarly to many of my colleagues in both Queen's and the Royal.[7]

My own medical academic career began in 1979 when I was appointed University Tutor in Pathology. At that time the Professor of Pathology was Elizabeth Florence McKeown and when I suggested to her that I was quite interested in forensic pathology she replied – "Don't be silly, forensic pathology is only about sex and sudden death". Sudden death may be, but I am not so sure about the former assertion. In any event, it was under Florence's superb tutelage that my interest in pathology in general and in forensic pathology in specific developed. And therein lies the theme of my oration "Medical Education in the future …. Lessons from the past" because I believe that the foundation of a good medical education is embedded in a sound understanding of pathology, and indeed anatomy, and by the special relationship between medical teacher and student. I suspect that I may be looked on as a dinosaur by some modern medical educationists, but I remain of the view that some of the fundamentals of good medical teaching have been diluted, if not virtually lost altogether, as we modernise our undergraduate curriculum on the one hand and yet have not invested sufficiently in the recruitment and career development of enthusiastic clinical teachers on the other. Clinical teachers who can hand on learning by their skills at the bedside and in the tutorial room and not just in the research laboratory. This latter activity, a colleague of mine described, rather unkindly, as mouse molesting and rabbit raping.

Some years ago I was invited to deliver a lecture in Merton College Oxford and was privileged to dine in the College with the College Warden, College fellows and students. It was at a time when the GMC were imposing changes in the undergraduate medical curriculum on medical schools, and I asked the Warden how his College was implementing some of the radical changes being proposed by the GMC. He thought for a moment and then pointed to one of the many portraits of former College alumni. The picture was of William Harvey who was Warden of the College in 1645 and whose treatise "De Motu Cordis" or "on the motion of the heart and blood", described in detail the systemic circulation of the body.[8] The Warden said to me, "we have been teaching medicine here in the same traditional methods since William Harvey was our Warden – I don't think we need to change now. But of course he was incorrect.

All of us engaged in medical education, whether at undergraduate or postgraduate level, must embrace change and progress. Changes in the medical curriculum must reflect advances in medicine, the changes in our society and in the health of the population we serve. The General Medical Council, in their document Tomorrow's Doctors, put it like this - "we can at best strive to educate doctors capable of adaptation to change, with minds that can encompass new ideas and developments and with attitudes to learning that inspire the continuation of the educational process throughout professional life ….". [9]. However the same document also states "some of the present day art and science of medicine is fundamental to its practice and will certainly endure ….". [9] I firmly believe that pathology falls into such a category.

You may wonder why I earlier mentioned anatomy along with pathology but it is my view that they are so closely inter-linked that developing an understanding of the normal human body only serves to strengthen an understanding of disease and its effects. In the past much of the anatomical dissection was carried out on bodies ravaged by diseases such as tuberculosis and syphilis except where, when bodies were in short supply, unscrupulous body snatchers, such as Burke and Hare, saw a business opportunity in Edinburgh in the 1800s to murder inebriated victims by suffocation or "burking" and sell the bodies to the anatomist Dr Robert Knox.

One of the arguments put forward for reducing the amount of anatomy and pathology teaching in the curriculum is that much of what we learn as students is irrelevant to future medical practice and is rapidly forgotten by students as their undergraduate medical studies progress. However as Somerset Maugham the novellist, and a one-time physician at St Thomas Hospital London, said "You will have to learn many tedious things ….. which you will forget the moment you have passed your final examination, but in Anatomy it is better to have learned and lost than never to have learned at all".[10]

Maugham would not however appear to have been a fan of forensic pathology – he once said "Death is a very dull, dreary affair, and my advice to you is to have nothing whatsoever to do with it".[11] I can assure this audience that being a forensic pathologist in Northern Ireland during 30 years of the so-called "troubles" has been anything but dull.

The Medical School at Queen's has had in the past a strong tradition of pathology teaching due, in no small measure, to the influence of one man, John Henry Biggart who, in 1937, was appointed Professor of Pathology (Figure 1).

John Henry went on to become Dean of the Faculty of Medicine, an appointment he held for an unprecedented 27 years. He received a knighthood in 1967 and in 1972 was

 

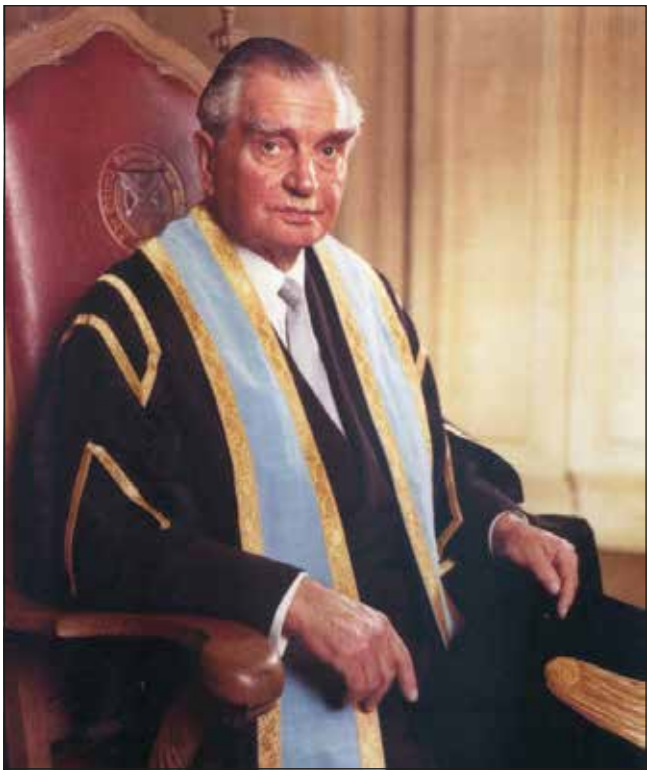

*Fig 1*. Professor Sir John Henry Biggart. A photographic copy of a portrait by Leslie Stuart, Belfast.

appointed Pro-Chancellor of the University. John Henry's influence on young doctors in training was immense. Between the 1950s and 1960s many of Ulster's most illustrious doctors spent a period of time working in the Institute of Pathology under John Henry's watchful eye.[12] In the book about his father, Denis Biggart wrote of these doctors "Each was expected to give his or her all, and more, to help achieve the high standards that he demanded. Each was proud to have been selected and imbued by his infectious enthusiasm for his subject and medicine in general. Each gave him the loyalty that his warm, personality inspired."[13]. That list of trainees included future professors of pathology, haematology, renal medicine, neuropathology, oral pathology, cardiology, dermatopathology, genetics as well as consultants in almost every branch of medicine.

John Henry was also very supportive of my own specialty of forensic medicine which, up until 1958, was part of his remit to teach to the students. When Tom Marshall was appointed the first State Pathologist for Northern Ireland in 1960 his new Department was supported and firmly embedded for many years in the Institute of Pathology and within the Medical Faculty. Links still remain, however the close relationship between the Medical School and the State Pathologist's Department has sadly been progressively lost over the years. Nevertheless it is still a great honour to have been appointed Honorary Professor of Forensic Medicine in the University in 1992 and I am indebted to all those in the University who have made this possible including successive Deans and Vice-Chancellors.

During John Henry Biggart's tenure as Professor of Pathology and indeed subsequently when Dugald Gardiner and later Florence McKeown became the Musgrave Professors of Pathology, postmortem examinations, or autopsies, were an important component of the day to day work of the Institute of Pathology. What is perhaps even more surprising is that this work was carried out, with enthusiasm, by those female doctors who Sir John had recruited into his Department, including Florence McKeown, Yvonne MacIlwaine and Ingrid Allen. However, women working in pathology is nothing new and this French engraving from the 1880s shows two female medical students or doctors about to perform an autopsy at the Medical Faculty in Paris.

At Queen's, autopsy pathology was an important component of the undergraduate curriculum. Students were expected to attend lunchtime postmortem demonstrations whereby the Professor of Medicine would present the clinical aspects of a case and the Professor of Pathology would then demonstrate the autopsy findings either confirming or refuting the clinical diagnosis. No-one who attended these lunchtime demonstrations in the old RVH mortuary with its Padua-like viewing gallery, could not have been impressed by these superb teaching experiences (Figure 2).

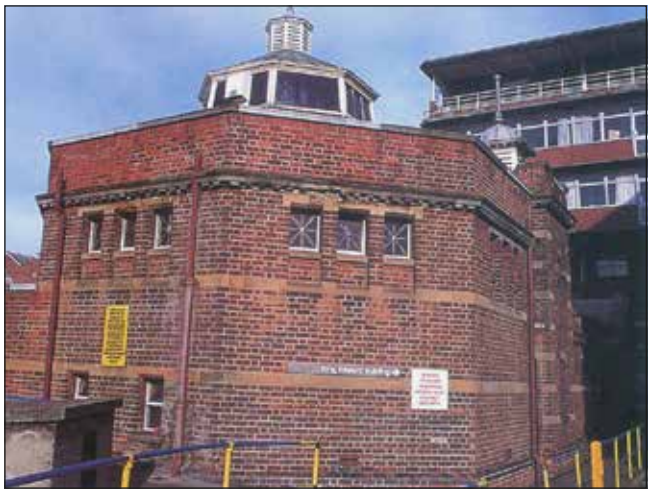

*Fig 2*. The old mortuary, Royal Victoria Hospital, Belfast.

Sadly, the consented hospital autopsy is almost extinct and only medico-legal postmortem examinations, carried out on behalf of the Coroner, take place today. The lunchtime postmortem demonstrations have also gone and for about the last 10 years, until, I am pleased to report, a couple of weeks ago, undergraduate medical students had no opportunity to ever see a postmortem. I say, until a couple of weeks ago, because with the support of the Dean and Professor Pascal McKeown and Professor Roy Spence, final year medical students are now being given the opportunity to see a postmortem examination being carried out – a lesson from the past for future medical education. But pathology has more to offer our students and young doctors **now** than ever before. Molecular pathology is a new and exciting discipline within pathology. Pathology is entering a new era that encompasses the development of molecular and genetic markers for

 

the diagnosis and classification of disease, particularly of malignancy. We are now in the realm of genome-based pathology and we must ensure that our students become enthused with these exciting developments in pathology by our research colleagues working in the Cancer Institute at Queen's.

So far I have made reference to a number of my own former colleagues and teachers who have made an impact on our Medical School, a lasting impression on our students and, perhaps above all, a healing hand on the sick so vividly depicted in the stain glass window at the end of the old main corridor. The role of the medical teacher has never been more important than it is today but it is a sad reflection on the current state of medical education that students rarely get the opportunity to spend sufficient time with gifted clinical teachers. Teachers who have so much to offer our students. Furthermore I believe that the university needs to do more to acknowledge the outstanding contribution which these clinicians make to undergraduate teaching.

Theodor Billroth, who is regarded by many as the father of modern abdominal surgery, was convinced of the importance of the personal influence of great teachers in forming the next generation of doctors. His advice to the University of Vienna in 1876 was "to secure for the universities the services of the most distinguished men of science, and to furnish them with the necessary equipment for teaching …".[14]. Our own university should seize that opportunity for the next generation of young doctors.

The GMC in its document "The Doctor as Teacher" set out a number of both professional and personal attributes of the doctor with responsibilities for clinical training and educational supervision, among these were an enthusiasm for his or her specialty, a personal commitment to teaching and learning, sensitivity and responsiveness to the educational needs of students and junior doctors, an understanding of the principles of education as applied to medicine and an understanding of research methods. [15]. But to me, personally, there is more – the good teacher must be able to inspire and motivate their students whether they be undergraduates or postgraduates.

Hero-worship might be putting it too strongly but Osler said "It helps a man immensely to be a bit of a hero-worshipper, and the stories of the lives of the masters of medicine do much to stimulate our ambition ….".[16]. This hospital has, without doubt, produced many such teachers in the past and at present and we must strive to ensure that it continues to do so in the future.

It might be invidious to single out any individuals from the many great teachers at the Royal but I feel that not to do so would be to do them, and indeed the hospital, a disservice. One physician, who had just retired when I qualified, was Frank Pantridge who was to become Honorary Professor of Cardiology at Queen's (Figure 3).

Frank Pantridge's legacy was the development of the world's first miniature defibrillator and the instigation of pre-hospital coronary care in the 1960s. It was said then, that Belfast was the safest place in the world to have a heart attack – today, we have the dubious reputation of having one of the highest incidences of ischaemic heart disease in the Western World. My personal acquaintance with Frank Pantridge was limited – as a house officer on Wards 5 and 6 on the old main corridor, Frank would call in for a cup of tea at about 11.30 pm, having spent a few hours in the Consultants' bar in the King Edward Building. On the first occasion that we met he asked me abruptly who I was and what plans I had for my career. I told him rather pompously that I wanted to become Professor of Forensic Medicine. Interestingly, he had spent some time in the Pathology Department under John Henry Biggart and he had told me that he had avoided postmortems whenever he possibly could. My last meeting with him was when he was awarded an honorary degree by Queen's University and when he saw me in the academic procession he left the company of the Vice Chancellor who was to escort him to the Whitla Hall and approached me. He then enquired whether I had managed to become Professor of Forensic Medicine. When I told him I had he shook my hand and offered me his warmest congratulations.

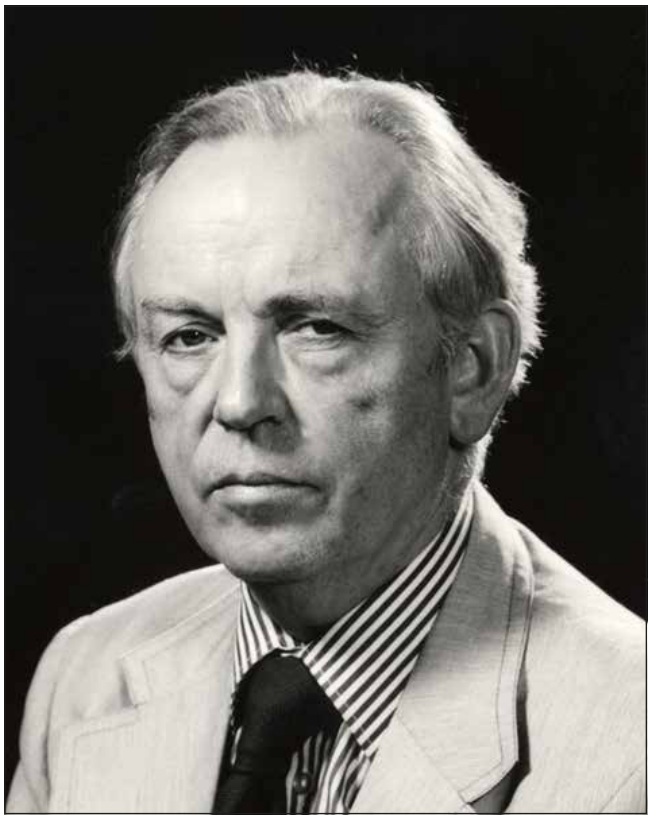

*Fig 3*. Professor J Frank Pantridge. CBE, MC.

Pantridge was only one of many great physicians and surgeons who made such an enormous contribution to the work of this hospital and who inspired several generations of students and young doctors. Others include Professor Gary Love, Professor Molly McGeown, Mr Willoughby Wilson and Professor George Johnston (Figure 4).

 

It has been a privilege to have been taught by them and to have been their colleague. All of us charged with the responsibility of teaching students and young doctors must emulate the dedication and commitment to this hospital, and indeed to Queen's, shown by these clinicians but the University also has a responsibility to acknowledge the contribution made by its clinical teachers. Whilst we have seen numerous senior academic appointments in the Medical School to develop the strong and now internationally recognised research at Queen's, on the other hand, it seems to me that there has been a progressive reduction in the appointment of clinical professors, whether in established chairs, personal or honorary appointments as well as in the dismantling of individual academic departments. We should be encouraging and rewarding academic excellence, not just in research but also in clinical teaching as it is the current and future generation of teachers who will inspire and motivate our students.

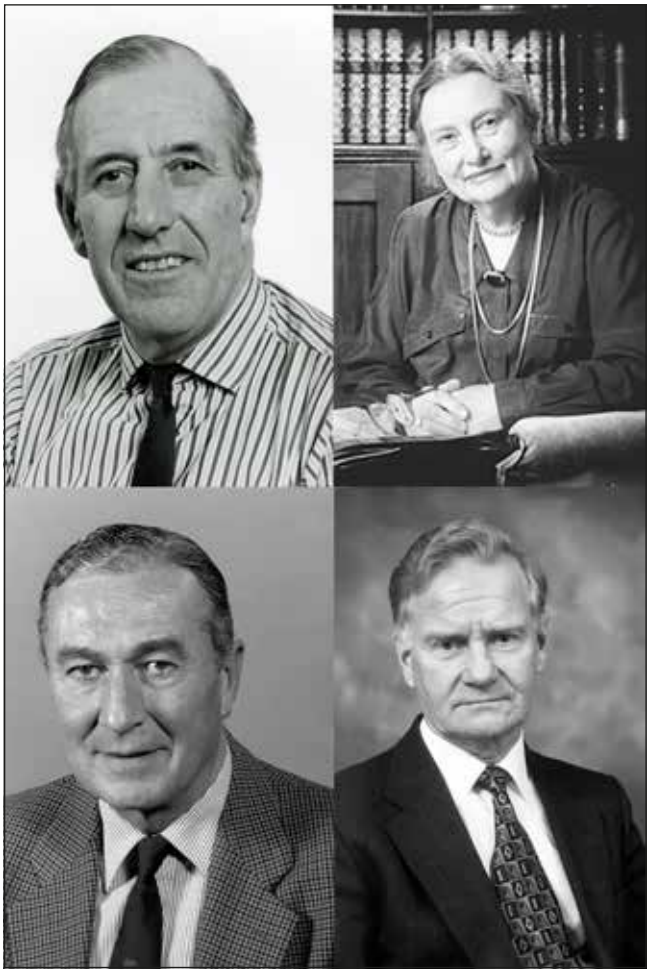

*Fig 4*. Clockwise from top left: Professor Gary Love, Professor Molly McGeown, Mr Willoughby Wilson and Professor George Johnston

No oration would be complete without reference again to Sir William Osler who is regarded by many as the Father of Modern Medicine. Born in Canada in 1849 he was instrumental in the creation of the John Hopkins School of Medicine and from 1905 until his death in 1919 he was Regius Professor of Medicine at Oxford University. To our new students who are about to embark on their first clinical clerkship, it is Osler you can thank for this privilege. He pioneered the practice of bedside teaching, making ward rounds with a handful of students. Osler said "I desire no other epitaph … than the statement that I taught medical students in the wards, as I regard this as by far the most useful and important work I have been called upon to do".[16].

Osler also had advice for clinical teachers "To have a group of cloistered clinicians away completely from the broad current of professional life would be bad for teacher and worse for student. The primary work of a professor of medicine in a medical school is in the wards, teaching his pupils to deal with patients and their diseases."[16].

Ladies and gentlemen than you so much for your indulgence this morning.

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# Letters

## TRACHEOSTOMY: WE NEED TO KNOW A HOLE LOT MORE.

Editor,

Tracheostomy is commonly performed procedure and can be a distressing prospect for both patient and surgeon. Patients undergoing tracheostomy are becoming increasingly more common. Frequently tracheostomy is performed following, or in anticipation of, a prolonged intubation for weaning purposes[1]. It is also performed to provide a conduit for airway suctioning in the infirm, for airway preservation in those with head and neck cancers and less frequently in trauma. As a result this procedure is performed by staff from a number of disciplines including ENT, Anaesthetics, Cardiothoracic and General Surgeons. Due to the multi-professional nature of this procedure these patients will often be admitted to wards without traditional airway teams during or following their acute admission. It is therefore essential that all medical and indeed nursing staff are familiar with the basic care involved in managing patients with tracheostomies, to avoid potentially life threatening complications[2].

We have provided a questionnaire survey to junior medical staff in the Northern Trust to investigate the level of knowledge and confidence in caring for patients with a tracheostomy. Eighty-seven percent of responses were from foundation trainees. Fifty-six percent of all respondents had received training in tracheostomy care with 50% being aware of the Trust's policy on the subject. Sixty-two percent commented that they were not confident with being able to change a tracheostomy tube and few were comfortable with airway management in general. Despite this the same percentage had looked after a patient with a tracheostomy. Most of the respondents understood the wide variety of indications for tracheostomy but had very limited understanding of the types of tube available and the rationale for their use. All respondents thought that further teaching on the subject was needed and the majority felt that this would be beneficial upon starting a foundation program, with nearly 20% feeling that training was required immediately. The respondents felt that tracheostomy care is poorly taught at undergraduate level and that a simple troubleshooting algorithm on the front of patient notes to deal with common tracheostomy problems would be beneficial.

Patients with temporary or long-term tracheostomies are frequently seen in our hospitals for a variety of reasons. It is likely that their presence on general wards may become increasingly common and therefore reliance on traditional airway teams is unlikely to be sustainable for non-emergencies. Adequate teaching from an early stage should provide a baseline knowledge that will allow doctors to more confidently handle problems that may arise from this particular patient group enabling a more efficient clinical course. Recent publications suggest that a regional teaching scheme should be implemented for F0 doctors with workshops in airway management. In the interim, the authors recommend that each trust provides a tracheostomy teaching session to its new doctors at induction, and that an individualised care pathway is available in the front of the notes for each patient following tracheostomy[3,4].

The authors have no conflict of interest.

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## ENDOSCOPIC SELF-EXPANDING METAL STENTS FOR MALIGNANT COLONIC BOWEL OBSTRUCTION

Editor,

Colon cancer presents as acute bowel obstruction in approximately 20% of patients[1]. A common treatment for a patient presenting with acute malignant bowel obstruction is resection and colostomy. Emergency surgery for acute obstruction is associated with a mortality rate of 2.8- 3.5% after elective surgery and 8-10% after an emergency operation with resection, with a complication rate of 24% and 38% respectively [2]. Instead of emergency surgery, an alternative option is placement of a self-expanding metal stent (SEMS).

Recently published guidelines show variation in recommendations with regards to SEMS usage. NICE guidelines for management of colon cancer have advised that if the cancer appears potentially curable on scans, medics should explain to the patient and their family that acute bowel obstruction can initially be managed either with emergency surgery or a colonic stent, and that there is no clear evidence that one treatment is better than the other. If the cancer appears non-curative then a SEMS should be considered as a palliative measure[3]. However ESGE guidelines (endorsed by AGSE) do not recommend SEMS as a bridge to surgery as standard treatment and should only be considered as an alternative to emergency surgery in those who have an increased risk of postoperative mortality. They do however

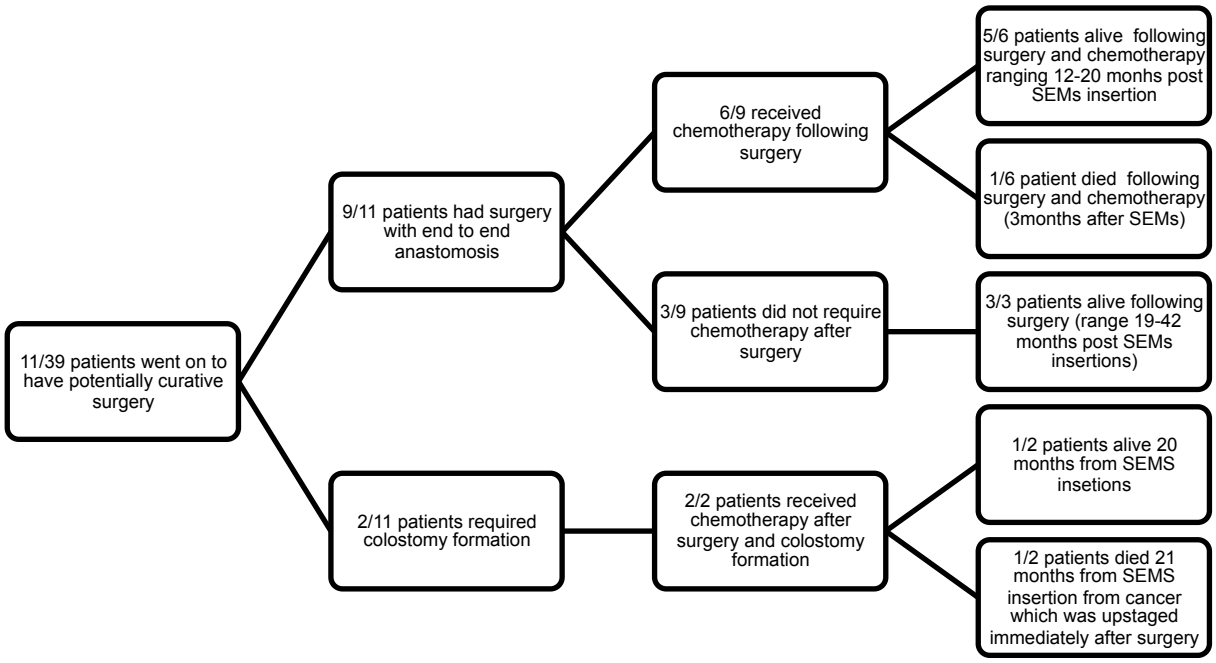


*Fig 1*

state that SEMS is first line treatment for palliative patients[4].

The purpose of this study carried out in a teaching hospital in Belfast was to assess our patient outcomes. We felt this was necessary given the variation between the ASGE guidelines and the NICE guidelines. Also, we felt our outcomes differed from those of some studies considered for the guidelines.

All patients who had a SEMS inserted between October 2009 and January 2011 were included. Data regarding the patients' age, sex and co-morbidities were recorded. With respect to the SEMS insertion, data recorded included time to stent from admission, histology and staging, time to surgery (if applicable), location of tumour and outcome (including complications and failure).

59 patients were recorded as having SEMS insertion attempted between these dates. 49 of the patients who were stented had malignant obstruction whilst the remainder had benign causes, (7 diverticular strictures, 1 extrinsic compression, and 2 anastomotic strictures). Out of the 49 patients with malignant obstruction there were 10 failures at the time of insertion. Of the remaining 39 patients SEMS were inserted at a median of 2 days from admission (range 0-26 days). 11 of the 39 patients went on to have curative surgery following SEMS insertion. 9 of 11 patients received primary anastomosis. 9 of these 11 patients who had SEMS as a bridge to surgery were alive at the time of data collection (Figure 1).

In our experience there is a positive outcome for patients receiving SEMS both for palliative purposes and also as a bridge to surgery. Low complication rates for these patients and high rates of primary anastomosis are encouraging.

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## A SEVERE CASE OF ADULT ONSET STILLS DISEASE WITH MYOPERICARDITIS, RESISTANT TO TREATMENT WITH TOCILIZUMAB BUT RESPONSIVE TO ANAKINRA.

Editor,

A 26 year old male presented with high-grade pyrexia, sore throat, joint pain and a distinctive evanescent rash on his hands and legs. Within 24 hours of hospital admission he developed severe central chest pain (requiring opiate analgesia) and shortness of breath. On examination, he had a mildly congested oropharynx, pyrexia of 39ºC, sinus

 

tachycardia (>120bpm) and muffled heart sounds. He developed acute synovitis of his wrists, knees and ankles. ECG showed widespread ST elevation across limb and chest leads. CXR showed bilateral moderate pleural effusion. Abnormal blood results included: raised cardiac troponin 661 ng/L(<14ng/L), WBC 25x$10^9$ cells/L(4-10x$10^9$ cells/L), 90% neutrophils, CRP 376 mg/L(1-5mg/L), ESR 68mm/hr, Hb 10.7 g/dl(13-18g/dl), ferritin 4427 ug/L(30-400ug/l), rheumatoid factor (RF) weakly positive at 23 (0-14 IU/mL). Anti-cyclic citrullinated peptide (Anti-CCP), antinuclear antibody (ANA) and vasculitic screen were negative. Extensive infection screen (including serial blood cultures, viral/fungal myocarditis screen and HIV) was negative.

| Major criteria | Minor Criteria |
|---|---|
| Fever of at least 39ºC lasting at least one week | Sore throat |
| Arthralgia or arthritis lasting two weeks or longer | Lymphadenopathy |
| Characteristic skin rash (nonpruritic macular or maculopapular salmon-colour) over the trunk or extremities during febrile episodes | Hepatomegaly or splenomegaly |
| Leucocytosis (10,000/mL or greater) with at least 80% granulocytes | Elevation in liver enzymes concentrations - ALT, AST, LDH |
| | RF and ANA negative |

*Fig 1*. Yamaguchi criteria (1): In the presence of five features with at least two being major diagnostic criteria yields 96% sensitivity and 92% specificity for AOSD

A trans-thoracic ECHO showed pericardial effusion with mildly impaired left ventricular systolic function (LVEF 50%). CT imaging confirmed bilateral pleural effusion and moderate pericardial effusion (Figure 1). In the absence of confirmed infection and based on characteristic features (high grade fever, rash, arthritis, hyperferritinaemia, and neutrophilia) a working diagnosis of AOSD[1] presenting with myopericarditis and pleuritis, was made. (Figure 2)

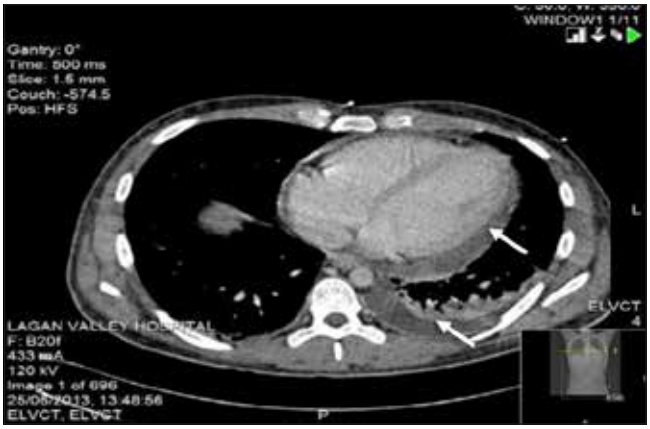


*Fig 2*. CT chest showing pericardial and plural effusions (white arrows).

Initial treatment was with pulses of high dose intravenous methyl prednisolone (500mgs) over three days. There was an immediate response with resolution of pyrexia, chest pain and improved cardiac function. However symptoms recurred after switching to oral prednisolone 40mgs/day. Subsequent cardiovascular deterioration prompted further treatment with biologic therapy - the interleukin 6 inhibitor-Tocilizumab (8mgs/kg IV). Although there was a brief period of favourable response, clinical deterioration re-occurred within 48 hours with high grade pyrexia, marked increase in central chest pain and short runs of ventricular tachycardia. Of note, there was a marked rise in ferritin level (3313 $\mu$g/L pre-treatment to 60626 $\mu$g/L post-treatment) and liver enzymes (AST 435 U/L, ALT 411 U/L,GGT 462 U/L, ALP222U/L).

Tocilizumab was discontinued and the IL-1 inhibitor, Anakinra (100mgs sc/day) was commenced. Within 24 hours, there was a marked clinical improvement with rapid normalisation of blood parameters. Following his sustained favourable response, oral steroids were gradually tapered down. Cardiac MRI, 4 weeks post-presentation, showed contrast enhancement of pericardium and some sub-pericardial left ventricular lateral wall, confirming recent myopericarditis. More than a year later, our patient is stable on Anakinra 100mg (daily) with low dose methotrexate, prednisolone 5mg/day, ramipril and bisoprolol. 18 month follow-up cardiac MRI demonstrated undilated ventricles and no evidence of pericardial constriction.

AOSD can be a difficult diagnosis to make and myocarditis is a rare complication[2,3]. Our patient presented with myopericarditis at disease onset following a rapidly progressive clinical course. This warranted prompt treatment with high dose systemic steroid and biologic therapies. Successful treatment of severe AOSD has been reported with anti-TNF drugs, Tocilizumab and Anakinra[4]. It is difficult to ascertain if this patient's deterioration with apparent worsening of Ferritin and LFTs after starting Tocilizumab was due to drug (5) or worsening disease activity. The response of our patient to IL-1 blockade but not to IL-6 blockade may suggest that AOSD is a heterogeneous disease driven by a different cytokine mix in different individuals.

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## A MULTIVARIATE ANALYSIS OF FACTORS AFFECTING DID NOT ATTEND (DNA) RATES IN A PAEDIATRIC EYE CLINIC: DO WEATHER AND SCHOOL HOLIDAYS AFFECT ATTENDANCE AT PAEDIATRIC EYE CLINIC?

Editor,

Every paediatric ophthalmic unit has myths to explain variable Did Not Attend (DNA) rates; with the commonest related to weather and school holidays. The author has however found little data to support these claims. A study of colorectal clinic attendances did not show a relationship between weather and the DNA rate[1], neither did a study of genitourinary clinic attendees[2]. With regard to holidays, increased DNA rates amongst Islamic patients during the festival of Ramadan[3] and Jews during Jewish religious holidays in Israel[4] have been demonstrated but no link shown thus far between DNA rate and school holidays amongst the UK population.

The theory most commonly mentioned in paediatric ophthalmology clinics involved an increased DNA rate during school holidays and good weather. With increasing demands on clinic capacity, we determined to find out if there was indeed a predictable relationship between weather, school holidays and the DNA rate.

A database of paediatric ophthalmology clinic attendance for Singleton Hospital Eye Clinic was accessed for the period of January 2013 to June 2014, a total of 357 clinic days and 7322 patient appointments. Of all the published studies to look into this issue, this is so far the largest. School holiday information was provided by Swansea City Council and the weather for the dates in question was accessed via the Met Office website with information obtained from weather station 405687, located in nearby Llanelli. Low average air temperature, low pressure, high windspeed and high average rainfall rates were determined to be factors representing bad weather. Multivariate analysis of the results was performed using ANOVA.

Of the 7322 paediatric eye clinic appointments analysed the DNA rate was found to be 23.74% for new patients (n=1306) and 22.47% for follow ups (n=6016). The presence or absence of school holidays was not found to be statistically significant in predicting DNA rate variability. Weather indicators tended towards higher DNA rates during worse weather, although only increased rainfall rate was found to be statistically significant ($p<0.01$). This relationship was found to be dose dependent with average rainfall rates of <0.01mm/hr (n=217) resulting in a DNA rate of 22.33%, 0.01-0.04mm/hr (n=76) resulting in a DNA rate of 24.81% and above 0.04mm/hr (n=64) resulting in a DNA rate of 28.93%. This was the opposite result to that which was predicted, and although it was statistically significant, the $R^2$ was 0.035 and thus only explained a small portion of DNA rate variability.

This is the first study to demonstrate a relationship between increased rainfall rates and increased DNA rates in paediatric ophthalmology clinics and to disprove a link between school holidays and DNA rates.

Although interesting, it is important to determine what factors influence DNA rates to utilise limited clinic capacity to its fullest. An ideal solution would be to minimise DNA rates as much as possible, but in a public health system such as the NHS, non-attendance is always going to be a fact of life. Very little effort seems to have been made in understanding the causes of missed appointments and in order to make the most of our limited resources, this issue requires further exploration.

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## NO PAIN NO GAIN? TWO CASES OF SPIN CLASS INDUCED RHABDOMYOLYSIS.

Editor,

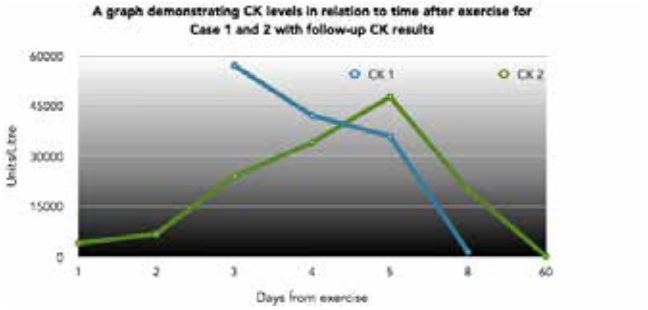
We present two near identical cases of exercise naive young women taking up spin classes for the first time and then subsequently being diagnosed with rhabdomyolysis in 2014.

Case Report 1

A 21 year old female attended a 40 minute spin class 2 days prior to hospital admission. She was 4 months post partum and this was her first return to strenuous exercise. She complained of progressive pain, stiffness and swelling in her legs, particularly on the left side and increased thirst. She was otherwise healthy and was on the combined oral contraceptive pill. On examination there was tenderness on palpation of both legs. The left and right legs measured 49cm and 47cm respectively, at a point 10cm superior to the apex of the patella. Clinical exam was otherwise normal and blood tests

revealed a Creatinine Kinase (CK) level of 57,115 units/litre. White cell count was raised at 15 x 109/L along with a low calcium at 2.08mg/dl. Aspartate aminotransferase and Alanine aminotransferase were raised at 810 U/L and 336 U/L respectively and the remaining bloods were all normal (Figure 1).




Intravenous fluid resuscitation was commenced and after a peak in AST and ALT 2 days after admission the patient improved clinically and was discharged home at day 3.

Case Report 2

A 17 year old female attended her first spin class lasting 45 minutes the day before admission. She had awoke with severe pain in her right thigh and was unable to straighten her leg. She was also healthy but did not participate in regular exercise. Examination was normal apart from tenderness at the right thigh. When measured at the same landmark to case 1, the patient's right leg measured 47cm and left leg 43cm, again highlighting a discrepancy in size between both legs in keeping with the patient's symptoms. Serum CK was 6745 U/L but other blood tests were normal. The patient was commenced on intravenous fluid resuscitation. The patient noted a worsening of her symptoms, with tenderness in both legs from day 4 and the CK level peaked at a maximum of 47,738 U/L on day 5. At day 6 the patient was well improved clinically and had no evidence of liver or renal impairment (Figure 1).

Key Points

Normal physical exertion can lead to subclinical elevations in serum CK without complication as documented in studies looking at marathon runners[1] and military training[2] . At the other end of the spectrum, exertional rhabdomyolysis (ER), an established clinical entity with an incidence of 26,000 people in the United States alone[3] can lead to serious complications including electrolyte imbalances, compartment syndrome and acute kidney injury (Table 1). Key diagnostic tests include a CK level five times the upper limit of normal and a positive urine dipstick for blood, in the absence of red blood cells on microscopy, suggesting myoglobinuria

| Risk factors for Massive Rhabdomyolysis following exertion (Table 1) [4] |
|---|
| A physically untrained individual |
| Concurrent viral illness |
| Concurrent history of dehydration (including recent alcohol use) or shock |
| Hot and humid training conditions |
| Medications (e.g anticholinergics) or equipment impeding normal heat loss through sweating |
| Other medications including NSAIDs and Statins |
| Sickle cell trait |
| Hypokalaemia |

ER may still occur in a physically fit patient and therefore advice to prevent rhabdomyolysis when training includes

- Perform sub-maximal training over a longer period of time instead of short bursts of high intensity and limit exercise in hot conditions
- Consume a high carbohydrate load, hydrate well and space out rest periods to optimise glycogen repletion

Dr Ashley Elliott (CT2), Dr Rachel Burke (FY2) and Dr Nathaniel Liggett (Consultant Rheumatologist) Daisy Hill Hospital, Newry.

Correspondence to Dr Ashley Elliot.

E-mail; aelliott09@doctors.org.uk

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# Book Reviews

## PRACTICE ACCOUNTS MADE EASY


Ann Tudor, 10 Chapters, 112 pages, ISBN-13: 9781907904172 Scion Publishing, First, Edition, 30th September 2013. RRP: £15.99

The business and accounting aspects of General Practice are integral to daily practice. In addition, recently there have been radical changes in the world of General Practice (GP). While formal post graduate GP training in the UK is thorough and practice accounts are included in the MRCGP syllabus, many GP registrars struggle with the subject and there is obviously less emphasis on this than the clinical aspects of the profession. This book helps to address that deficiency and would be invaluable to all those confused by accounting terminology, including GP registrars, locums and principals. This text would also prove practical for new practice managers.

'Practice Accounts Made Easy' is a concise guide on the fundamentals and often confusing world of practice accounts. The book assumes a basic knowledge but is written in a clear jargon-free way, with detailed examples given throughout. The author is an accountant with a specialist interest in medical accounting and thus a wealth of knowledge in this very specialised field. The book sets out to define almost every term associated with General Practice accounts and the minefield that is taxation. It provides a breakdown of the now ubiquitous Quality & Outcomes Framework (QOF). The text sets out an example balance sheet from a practice and all the various items that would be included in this. Other important aspects of business are covered, including, the make-up of payments for a practice medical services contract, joining and leaving a practice and superannuation. It also provides information for the individual GP on how to pay their tax, tax deductible expenses and the differences on being employed and self-employed for tax purposes.

In summary, I would recommend this book to anyone entering the world of General Practice or indeed interested in consolidating their knowledge. Each section of the book is easy to follow and as a result it can be used as a quick reference guide. Alternatively, it would lend itself to being read 'cover to cover'. The book reflects efficient and patient-friendly practice. The continuing evolution of the NHS reforms are presented in clear, comprehensive and concise terms, from which the reader will derive confidence and understanding, whether they use the book for background reading in the practice, or as a stand alone textbook on this important and evolving subject.

Gillian Johnston
General Practitioner

## RHEUMATOLOGY: A CLINICAL HANDBOOK FOR MEDICAL STUDENTS AND JUNIOR DOCTORS.


Al-Sukaini A, Azam M Samanta A. First edition, 168 pages. Publisher: Scion Publishing Limited 2014. ISBN-13: 978-1907904264 RRP: £ 18.99

This is a specifically designed textbook to aid medical students who often find rheumatology a bewildering specialty and to serve as a quick reference guide to those in their early postgraduate careers. The book is broken down into four main sections: specific conditions, investigations, pharmacology and approach to OSCE examinations with a useful breakdown to take a history or examine a patient with a musculoskeletal problem. Each condition is presented in a logical manner covering pathophysiology, epidemiology, clinical features, differential diagnoses, diagnostic investigations and management with useful diagrams and tables. A good range of rheumatological conditions are covered and as well as up to date information including NICE guidelines where available. Each chapter ends with self assessment questions to reinforce learning points.

Although the different conditions are laid out in a logical fashion, the main sections of the book could have been ordered better. Instead of diving straight into the different rheumatological conditions, it would have been better to start with history taking and examination of a patient with musculoskeletal problems. This section itself could also be expanded upon, since this is a rheumatology textbook it should cover all joint examinations instead of just focusing on the GALS screen and hand and wrist examination. It does provide though a link to a site to access demonstration videos of joint examinations however this did not work. Having the investigations and management chapters before the specific conditions section would make this section easier to follow without having to flick back and forth various chapters.

There are a few details that are incorrect. Firstly, IL-1 inhibitors are not licensed for the treatment of rheumatoid arthritis and are not part of NICE guidance. Secondly, following an EMA alert in 2014, strontium ranelate is only recommended in the management of post menopausal osteoporosis only if all other treatments have failed due to its cardiovascular risk, therefore it should not be included in the list of treatments. Lastly, there are no classification criteria for rheumatoid arthritis either the old 1987 ACR criteria or the newer 2010 ACR/EULAR criteria which is a shame as the faults of the old criteria could be explained and would then introduce the importance of early diagnosis and the need for updated classification criteria and the use of newer tests such as anti-CCP and musculoskeletal ultrasound.

The authors admit that this clinical text does not replace a more weighty textbook, but it is by and large a well presented book and although the flow of the book could be better the

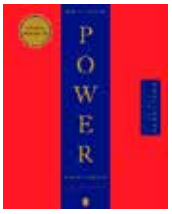
information is presented in a clear and concise manner. As a clinical handbook for medical students, it should have focussed more on clinical aspects by expanding more on taking a musculoskeletal history, joint examinations and formulating a diagnosis but it is up to date and information is laid out in such a fashion with bullet points and tables, along with self assessment questions. It would serve as a highly recommended revision aid for medical students but is probably pitched too low for those who are postgraduates.

Wing Hoi Yau
Consultant Rheumatologist

# Book Case

Professor Patrick Morrison humorously considers six books that exemplify medical management and fighting through red tape to get towards the top of the Medical tree.

## THE 48 LAWS OF POWER




Robert Green (Viking, 1998)

I've worked for at least eight A+ merit award holders. Good to know the modus operandi of the boss, although all of them seem to have got there by sheer hard work (genius is 1% inspiration and 99% perspiration, as Thomas Edison once said). My favourite is law 30 – 'make your accomplishments seem effortless' which is a very hard slog (although if you are too successful at this one, it looks like you are actually doing nothing so use with care). Most applicable for career progression is probably Law one – 'never outshine the master'

## GO ADD VALUE SOME PLACE ELSE: A DILBERT BOOK.


Scott Adams (Andrews McMeel, November 2014)

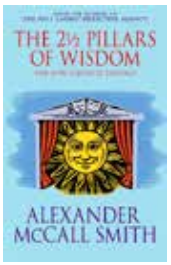
Never go on a management course (one of my A+ bosses, now deceased, once declined a time management course as he 'hadn't the time to go'). Read this book (or any Dilbert book) instead. You know that bit where trainees are encouraged to 'reach for the stars'? Dilbert comments that 'if you did manage to grasp one, it would burn your hand clean off…'. Enough said, going forward. You'll score highly on management bingo after reading this.

## BRITISH NATIONAL FORMULARY (BNF 68)


Joint Formulary Committee (Pharmaceutical press, September 2014)

What not to like? The correct dose is there, side effects, and a little about the drug action so you can tell at this stage of your career if your antidepressants are working properly or not. Handy for writing accurate prescriptions for patients too. I facilitated the recent introduction of the BNF phone app into the NHS through NICE which has reduced prescribing errors although the irony is my NHS hospital blackberry can't actually access it! We need better hospital phones with access to the electronic patient record - that would reduce many more errors (health minister please note).

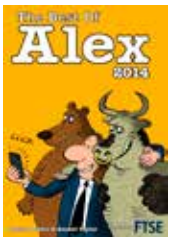
## THE 2½ PILLARS OF WISDOM.




Alexander McCall-Smith (Abacus, November 2004)

A handy guide to the idiosyncrasies of the academic Professoriate (usually omitted in the above books). Hilariously funny. Giving a lecture on a subject the professor knows nothing about with roaring success, academic jealousy and bickering over such small pay stakes. All accurate. Having worked with Sandy and been presented with a signed copy hot off the press in 2004, I suspect I may feature in the book. I've narrowed myself down to four of the characters.…

## BEST OF ALEX 2014




Charles Peattie, Russell Taylor (Prion books, October 2014)

A must for the aspiring clinical or medical director. Want to know how your subordinates are fiddling their expense claims? Away on a 'course' (yes a 'golf course') etc. Bankers are the classic profession for managing to do OK whether in a bull market or a bear one. Every trick in the book, but now you're on the case and in the know. Want to demotivate and unsettle people to get them to move jobs whilst keeping your fingerprints off the file? It's all there for the poacher turned gamekeeper manual.

## DK EYE WITNESS SPAIN TRAVEL GUIDE

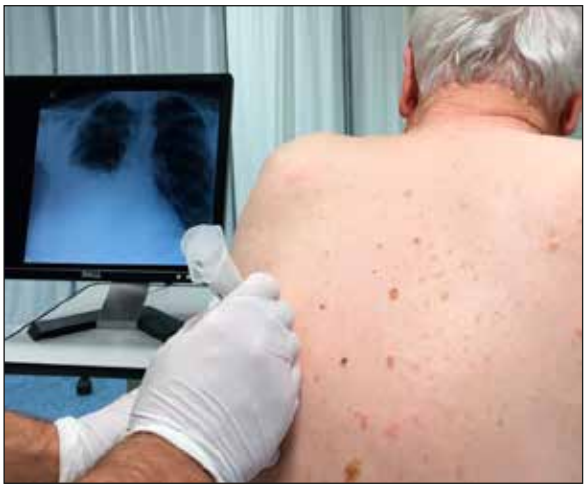

Collectif (Dorling Kindersley, April 2014)

Having got this far, you'll now need a well-deserved holiday. This guide to southern Spain was handy when I went to Andalusia in October. Not sure why it's taken me 51 years to master cheap direct flights off season to a sunny place – possibly getting children through school in term time is the reason. Didn't realise the Moroccans ruled southern Spain for 1000 years until Queen Isabella kicked them out in ~1500 A.D. A few good tips then on how to get rid of awkward colleagues hogging the place for too long from someone at the top of her (Royal) game. The excellent tapas, fresh figs and pressed olives are a bonus as you relax in the sunshine beside the pool.

# Curiositas

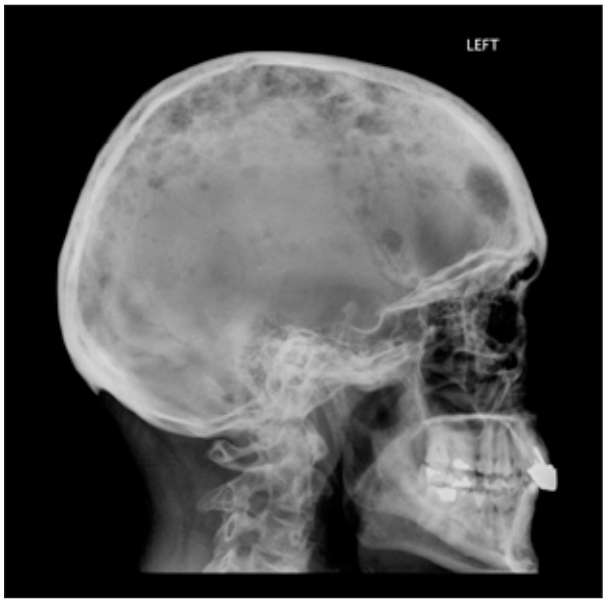
## PATIENT SAFETY

The following patient is undergoing thoracentesis. What is the most obvious patient-safety error? Why, sometimes, does this sort of error occur in clinical practice?



*Dr Gerry Gormley (Senior Academic General Practitioner, Queen's University Belfast) and Glenn Ritchie (Medical Student, Queen's University Belfast)*

## MEDICAL STUDENT QUIZ




1. What is the name of this classical radiological sign?
2. What disease processes can cause these appearances?

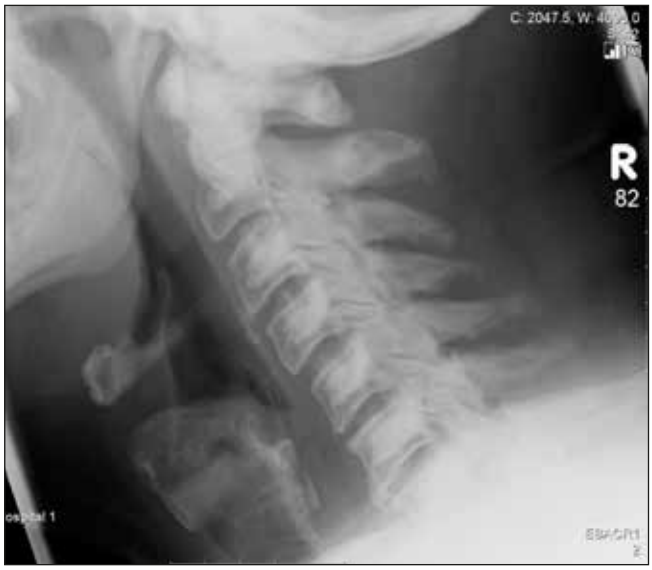
*Michael Corr (Medical Student, Queen's University Belfast) and Dr Ian Bickle (Consultant Radiologist, Raja Isteri Penigran Anak Saleha Hospital, Bandar seri Begawan, Brunei Darussalam)*

**ANSWERS** See overleaf

**CONSIDER CONTRIBUTING TO CURIOSITAS?**
Please refer to '*Curiositas: Guidelines for contributors*' http://www.ums.ac.uk/curiositas.html and email *curiositas@ums.ac.uk* with your ideas and submissions.

## POSTGRADUATE QUIZ

This is the cervical spine radiograph of a 58 year old man referred to the metabolic bone clinic.




1. What are the possible causes for the striking abnormality shown?
2. The diagnosis is supported when his dual-energy x-ray absorptiometry (DXA) results reveal extremely high T scores in both the hip and spine. What is the likely natural history of his condition?
3. What is the literal translation of the name of his condition?

*Dr Paul Hamilton (Specialty Registrar, Chemical Pathology, Belfast Health and Social Care Trust) and Dr Tim Beringer (Consultant Geriatrician, Belfast Health and Social Care Trust)*

## HISTORICAL QUIZ

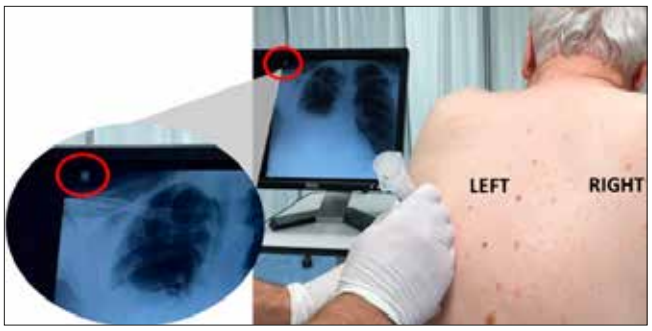
1. What is the name of this small silver Victorian medical device?
2. What purpose would this early Victorian medical device have been used for?

*Dr Mark Frazer, Retired General Practitioner, Tonbridge, Kent.*

# Curiositas: Answers

## PATIENT SAFETY

The patient is having a thoracentesis on the **wrong side** of their chest.




Some of the most catastrophic errors in medicine have occurred when an operation was performed on the wrong side, for example removal of the wrong kidney. However, such wrong-sided errors are not restricted to the operating theatre. Miller *et al* performed a Root Cause Analysis of wrong-sided thoracenteses *(performed in ambulatory clinics and hospital units other than the operating room)* that were captured in a National Patient Safety database.[1] As ever, such laterality errors are often multifactorial in origin, but often human error can be a major contributory factor. The authors provided guidance as to how we might best minimise such laterality errors occurring in clinical practice. Using and adhering, to 'check lists' should not be restricted to the operating theatre. Training, education and 'patient assessment for early detection of complications' are also recommended. Time-outs provide opportunities to detect errors early and, if possible, allow action to take place to minimise the impact of such errors on patients. Furthermore real time ultrasound guided thoracentesis also reduced error rates.[2]

On a daily basis we make numerous right-left decisions, often without a second thought. However, for a significant proportion of the population, correctly discriminating right from left is a challenging and demanding task. In healthcare we also have an extra challenge. When a doctor or nurse faces a patient, their right-side is on the patient's left-side. So correctly distinguishing right from left in a patient also involves the visuo-spatial function of mental rotation. So the next time you have to check the correct side of a patient, make sure to double check you actually have the correct side.

1) *Miller KE et al. Wrong-Side Thoracentesis Lessons Learned From Root Cause Analysis. JAMA Surg. 2014;149(8):774-779.*

2) *Jones PW et al. Ultrasound-Guided Thoracentesis: Is It a Safer Method? Chest 2003;123(2):418-423.*

*Dr Gerry Gormley, (Senior Academic General Practitioner, Queen's University Belfast) and Glenn Ritchie (Medical Student, Queen's University Belfast). Thank you to the simulated patient portrayed in this picture who kindly gave consent for this image to be published)*

## MEDICAL STUDENT QUIZ

This is a 'Pepperpot Skull' which is most commonly identified in multiple myeloma. The key differentials are skull vault metastases and hyperparathyroidism. The image shows a granular or mottled calvarium with numerous punched out radiolucent lesions throughout the skull. The lucent rounded lesions represent the numerous holes in the top of a pepper pot (shaker). In myeloma the osteolytic lesions are due to malignant plasma cell proliferation invading the bone marrow and even the bone itself with rapid immunoglobulin production.

*Michael Corr (Medical Student, Queen's University Belfast) and Dr Ian Bickle (Consultant Radiologist, Raja Isteri Penigran Anak Saleha Hospital, Bandar seri Begawan, Brunei Darussalam)*

## POSTGRADUATE QUESTION

The cervical radiograph shows osteosclerosis of the cervical spine vertebral bodies. These have a very characteristic 'bone within bone' appearance. The radiological differential diagnosis includes; hypoparathyroidism, Paget's disease of bone, hypervitaminosis D, sickle cell disease, thalassaemia, acromegaly, exposure to various chemicals and osteopetrosis.

Most causes of 'bone within bone' might be expected to reduce bone mineral density. In osteopetrosis however, bone mineral density is usually increased. In this case, the patient had markedly elevated T-scores (for example, +14.2 in the L2 vertebral body), making osteopetrosis the most likely diagnosis. Although bone mineral density is elevated, patients are at a higher risk of fracture compared to those with normal bone density.

Osteopetrosis literally means 'stone bone'. A sub-type is sometimes referred to as 'marble bone disease.'

*Dr Paul Hamilton (Specialty Registrar, Chemical Pathology, Belfast Health and Social Care Trust) and Dr Tim Beringer (Consultant Geriatrician, Belfast Health and Social Care Trust)*

## HISTORICAL QUIZ

This is a 'Personal Respiratory Device'. In the words of the Patent granted to Thomas Wroughton on 26th August 1846 it is "an apparatus or instrument to be used for respiration. It consists of a flat rectangular case, containing sponge, and perforated on its inner and outer faces with numerous small holes. It is curved to fit the space between the lips and gums so that it may be held there by the mere compression of the lips and be externally invisible - or nearly so - when in use".

It seems probable that the sponge (or wadding) would have been soaked in Menthol and the '*Therapeutic Vapours*(!)' inhaled by the patient.

Perhaps Wroughton's Patent Respirator can be regarded as the forerunner of the advanced inhalers of today!

*Dr Mark Frazer, Retired General Practitioner, Tonbridge, Kent. Curiositas would like to thank Dr Frazer who kind gave provided permission to publish these images.*

# Game Changers

## ULTRASOUND AS A DISEASE ASSESSMENT TOOL FOR INFLAMMATORY POLYARTHROPATHY

Dr. Stephen McDonald & Dr. Stephanie Walker
Craigavon Area Hospital, Portadown, BT63 5QQ

The evolution of musculoskeletal ultrasound as a tool in the daily practice of the rheumatologist has been astounding. Its benefits include relative lack of expense and the capability to carry out dynamic joint assessment [1]. Whereas plain radiographs demonstrate established bony damage, ultrasound can highlight ongoing synovial inflammation, non-radiographic bony erosion and soft tissue pathology. This has augmented the assessment of inflammatory polyarthropathies and aided in clinical decision-making.

Whilst limitations in intra-operator variability and reproducibility have been cited, education through both practical and on-line musculoskeletal ultrasound courses is helping to address these caveats[2]. With tailored standardised training, incorporated into the rheumatology curriculum, confidence in point of care scanning will increase.

What does this mean for the future? Working groups such as the OMERACT ultrasound group are evaluating its role as an outcome measure[3]. Issues remain in cases where there is clinical disease remission but ongoing ultrasonographic evidence of active synovitis. Ultrasound based synovitis has been suggested to predict radiographic damage. Will this mean the need to escalate treatment in a case of clinical remission? Furthermore, will outcome measures such as the DAS28 joint score require enhancement or even replacement with ultrasound based scores? Some clinical trial data to date has shown no significant difference at primary outcome points but this is in need of further evaluation[4]. We guess time will tell.

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## TRANSFUSION FOR ACUTE UPPER GASTROINTESTINAL BLEEDING – IS LESS BETTER THAN MORE?

Dr. Andrew Spence & Dr. Tony Tham
Ulster Hospital, Dundonald, Belfast, BT16 1RH

Acute upper gastrointestinal bleeding (UGIB) is a common presentation to emergency departments and is associated with significant morbidity and mortality (5-10%). While blood transfusion may be part of the management, the most effective red cell transfusion strategy is debatable.

A 6-year European prospective randomised trial of 889 patients presenting with upper GI bleeding showed a restrictive transfusion strategy was associated with significantly better outcomes when compared to liberal transfusion. Outcomes, including rebleeding (10% v 16%) and adverse events (40% v 48%), were significantly better with a transfusion haemoglobin (Hb) threshold of 7g/dL when compared to 9g/dL. Survival was also improved in peptic ulcer and cirrhotic Child-Pugh A & B patients.[1]

In addition to UGIB, a meta-analysis has shown in patients with a critical illness and a GI bleed, that cardiac events, infections and overall mortality are reduced when a restrictive blood transfusion approach is implemented.[2]

A restrictive transfusion strategy should be considered in the management of patients with acute UGIB. We suggest transfusing only when Hb is less than 7 g/dL, and aiming for a target of 7 – 9 g/dl. The exception when Hb threshold for transfusion may be higher may be the haemodynamically unstable patient and those with recent symptomatic cardiovascular disease. The ongoing TRIGGER trial will assess the feasibility of implementing a restrictive vs liberal red blood cell transfusion policy for adult patients with UGIB in the UK.

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## MATRIX-ASSISTED LASER DESORPTION/ IONIZATION- TIME OF FLIGHT (MALDI-TOF) SPEEDS UP CLINICAL MICROBIOLOGY

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There's a saying in medicine that sums up traditional clinical microbiology:

> *The physician knows everything and does nothing.*
> *The surgeon knows nothing and does everything.*
> *The psychiatrist knows nothing and does nothing.*
> *The microbiologist knows everything, but tells you a week later.*

Historically, clinical microbiology has been wedded to conventional culture techniques, which have not fundamentally changed since the days of Koch and Pasteur. Turnaround times of microbiological cultures have been aided somewhat with the arrival of the digital age, but "digitalisation" has not radically altered turnaround times nor the microbiologist's attempt to culture pathogenic

bacteria from clinical specimens *in vitro*, for isolation and identification purposes.

That's all about to change. The arrival and adoption of matrix-assisted laser desorption/ionization - Time of flight (MALDI-TOF) is a technology that will revolutionise the identification of bacterial and fungal pathogens within service level clinical microbiology, in a way that molecular (PCR) methods never managed. This technique works by allowing software to match spectral profiles of bacteria, which are generated by bombarding the bacterial culture with a laser, resulting in the sublimation and ionisation of the bacteria. Resulting ions are separated as determined by their mass-to-charge ratio on exit of a time-of-flight tube. In practical terms, the instrument can identify several hundred bacterial/fungal isolates simultaneously in less than 20 minutes and is relatively cheap to run.

To date in Northern Ireland, Antrim Area Hospital and Belfast Trust hospitals are employing MALDI-TOF technology. Adoption of MALDI-TOF technology will help speed up time to result in clinical microbiology laboratories and go some way in debunking the traditional view of the slowness of this pathology discipline.

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# So you want to be a **Radiologist?**

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Clinical Radiology is undoubtedly the speciality that has undergone a transformation in recent times. In the last twenty years the advent of computed tomography and magnetic resonance imaging in conjunction with advances in ultrasound technology has revolutionised the diagnosis of patients in modern healthcare systems. Radiology is now at the fulcrum of any hospital and is intrinsically embedded in the management of almost all specialities. In tandem, the emergence of interventional radiology has opened a wide variety of previously unavailable methods for treating patients in a minimally invasive manner. Interventional radiology continues to expand as evermore new techniques evolve in conjunction with technical innovations.

Radiology is now truly a clinical speciality with increased patient interaction. The speciality has had to evolve into true a 24/7 speciality and provision of emergency radiology services at all times is now expected as a basic standard of modern medical care.

Technological advances have resulted in multislice CT, diffusion MR and PET imaging becoming standard diagnostic tools in modern clinical practice. This has undoubtedly lead to huge benefits for patients in terms of accurate non-invasive diagnosis and staging of disease processes.

Percutaneous angioplasty and stenting have revolutionised the treatment of peripheral vascular disease. Endovascular aortic stent graft insertion has transformed the management of patients with aneurysm disease. Liver interventions have allowed for both curative and palliative treatment for a wide variety of both benign and malignant conditions.

The ability to arrest haemorrhage via percutaneous fluoroscopically guided techniques has enhanced modern surgical and critical care treatment and indeed the management of traumatic haemorrhage has been enhanced by interventional radiologists

As a result, clinical radiology is now a broad exciting speciality with numerous sub-speciality interests open to those training as radiologists. Entry to radiology training programmes has thus become very competitive particularly given the run through nature of the training and the career opportunities thereafter. This is particularly the case in Northern Ireland where a combination of locality and an excellent training programme have resulted in extremely competitive entry at specialist trainee level (ST1). Entry to training can occur following foundation training or after a period of core training. Approximately 40% of our local trainees enter clinical radiology training directly after completing their F2 year.

Clinical radiologists undergo a five to six year run through training programme. There is now a separate sub- speciality of interventional radiology which requires six years of training. Sub-speciality training in radionuclide radiology, musculo-skeletal radiology and neuroradiology along with paediatric, breast and cardiothoracic radiology is available within most UK training scheme including Northern Ireland. Trainees undertake the examinations for the fellowship of the Royal College of Radiologist during the first four years of their training. These examinations are challenging and compliment the intensive daily training which forms the other arm of their training. There are opportunities to undertake further training both with the UK and internationally at completion of specialist training and attainment of the certificate of completion of training (CCT).

The constant increased demand and advances in diagnostic and interventional techniques has resulted in a world – wide shortage of radiologist. As such consultant career opportunities are varied and plentiful at this time.

A consultant radiologist's working pattern can vary widely between doctors. Most consultants will have core commitments of plain film, ultrasound, CT and MR lists, but these usually have a degree of sub-speciality bias. Many consultants will have commitments to interventional radiology, radionuclide or breast radiology, for example, in addition. The breadth of the specialty is now difficult at times to comprehend as clinical radiologists interact extensively with all other branches of medicine.

Any young doctor should therefore consider this dynamic, fascinating and innovative branch of medicine when deciding on their future career.

# THE ULSTER MEDICAL JOURNAL

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