

Selected abstracts from the RCPE St Andrew's Day Festival Symposium

Held on 3–4 December 2009 at the Royal College of Physicians of Edinburgh

THERAPEUTIC ADVANCES IN THE MANAGEMENT OF AORTIC STENOSIS

Dr Michael Mullen, Consultant Cardiologist & Senior Lecturer, Royal Brompton & Harefield NHS Trust, London

Aortic stenosis is a common condition, whose prevalence is increasing in line with the increasingly aged population. In symptomatic patients, median survival, without surgery, is between two and four years. Until recently treatment of aortic stenosis has been entirely within the domain of the surgeon. It is, however, widely recognised that many patients with aortic stenosis are not referred or considered suitable for surgical intervention due to high risks of morbidity and mortality related to their advanced age or co-morbidities.

The introduction of transcatheter techniques for treating aortic stenosis has already had a major impact on the management of this common condition. While initially targeted at patients who otherwise would not be considered for surgical intervention it is likely that the real benefit of these new techniques will be in patients who, although considered operable, are at medium to high risk of complications. For this to be successful the technology will need to evolve and provide reliable relief of aortic stenosis in the form of a durable valve with low rates of paraprosthesis leak and procedural complications. As transcatheter aortic valve implantation becomes a wider reality its use will need to be tested in randomised control trials against the surgical goal standard, and plans for these trials are currently under way.

HEART FAILURE: NO LONGER A DEATH SENTENCE?

Professor Martin Cowie, Professor of Cardiology, Royal Brompton & Harefield NHS Trust, London

Heart failure is a complex syndrome that can result from any structural or functional disorder of the heart. In the UK, the single most important aetiology remains coronary artery disease, often with a past history of hypertension. Without adequate treatment the symptoms are severe and life expectancy is markedly reduced. The evidence base for diagnosis and management has enlarged dramatically in the past decade as a result of many randomised controlled trials. In addition to lifestyle measures, proper treatment with neurohormonal antagonists (such as angiotensin-converting enzyme

inhibitors, beta-blockers and aldosterone antagonists) is essential. Electrical device therapy has also improved the outlook for many patients with severe symptoms. The evidence base has been codified in several guidelines, including those from the Scottish Intercollegiate Guidelines Network and the National Institute for Health and Clinical Excellence, with clear identification of the priorities for implementation. Better adherence by physicians to such guidelines translates into improved outcomes for patients. Modern treatment includes a multidisciplinary approach across primary and secondary care, often facilitated by increasingly expert patients and home-based monitoring. Data will be shown that strongly suggest a marked improvement in outcome in the past 10 years. The challenge remains that of implementing high-quality care for all patients with heart failure, not just those seen in specialist centres.

THE RE-EMERGENCE OF AN OLD FOE: SYPHILIS FOR THE ACUTE PHYSICIAN

Dr Gordon Scott, Consultant in Genito-Urinary Medicine, Royal Infirmary of Edinburgh

The importance of syphilis has waxed and waned throughout the centuries, but the advent of effective antimicrobial therapy was expected to ensure its lasting demise. However, globalisation and migration has led to a resurgence in the number of cases of syphilis in the UK. At first, this was largely restricted to men who have sex with men (MSM), with many cases transmitted via oral sex due to the understanding that this sexual practice carries little risk of human immunodeficiency virus (HIV) acquisition/transmission. However, cases of syphilis are now being diagnosed in other populations.

Primary syphilis presents with a genital ulcer that should alert physicians to its likely origin, but symptoms of secondary syphilis include rash, alopecia, oral lesions, lymphadenopathy, arthralgia, hepatitis, nephrotic syndrome, uveitis/iritis, periostitis, parotitis, meningism, deafness and lethargy/malaise. Serological tests for syphilis should be undertaken in any patient presenting with any of these features. Tertiary syphilis is, as yet, unlikely to be seen. As syphilis spreads into the wider heterosexual population, there is an increasing worry of infection during pregnancy with its potential outcomes of miscarriage, stillbirth and congenital stigmata.

Syphilis remains sensitive to penicillin. Partner notification is an essential part of case management, and testing for

other sexually transmitted infections, including HIV, should also be undertaken.

HOW TO RECOGNISE AND MANAGE FUNCTIONAL DISORDERS

Dr Jon Stone, Consultant Neurologist, Western General Hospital, Edinburgh

Symptoms and syndromes that are not associated with an underlying organic disease such as irritable bowel syndrome and atypical chest pain are very common throughout medicine, accounting for 30–50% of patients seen in most hospital medical clinics.

In neurology, patients present commonly with symptoms such as weakness, sensory disturbance, movement disorder and seizure-like episodes. These have been called non-organic, psychogenic, functional, conversion, dissociative and hysterical symptoms. A positive diagnosis of a functional disorder can be made by finding evidence of internal inconsistency or a typical presentation. Such diagnoses are, however, often overlooked by general physicians, a typical scenario being the patient with dissociative seizures who is treated mistakenly for status.

The assessment of patients with functional disorders requires a knowledge of relevant features in the history, such as other functional somatic symptoms, illness beliefs and a willingness to 'tread carefully' around possible psychological factors. Ultimately, in neurology we have the luxury of being able to make the diagnosis on the basis of positive features on examination or a typical description of an attack.

Our model of why some people get functional symptoms and how they happen in the brain is in need of updating. Issues such as feigning and misdiagnosis will be discussed.

I will argue that the 'functional' model, already prevalent for irritable bowel syndrome, is applicable and practical in patients with more dramatic functional neurological symptoms. A positive diagnosis that makes sense to the patient and makes them feel believed is a key starting point for treatment. Further treatment with modalities such as physiotherapy, graded exercise, psychotherapy, hypnosis or sedation is often much more rewarding than conventional teaching suggests.

Further reading

- www.neurosymbols.org – a self-help website for patients produced by the author to assist in the management of these disorders
- Stone J. Functional symptoms in neurology: the bare essentials. *Pract Neurol* 2009; 9:179–89.

THE FOUR-HOUR TARGET: IS IT GOOD FOR PATIENT CARE AND CAN IT BE MAINTAINED?

Professor Derek Bell, Professor of Acute Medicine, Chelsea & Westminster Hospital, London

The delivery of unscheduled care is an international problem. The UK has adopted a proactive approach and in England, Scotland and Wales there is a four-hour target.

The four-hour emergency access standard in Scotland states 'patients will wait no longer than 4 hours between arriving at the units and admission, discharge or transfer, unless there are stated clinical reasons for keeping the patient in the unit. The maximum wait will also apply to other emergency care in minor injury units or areas of assessment units where trolleys are used.' It is aimed to improve patient and carer experience and satisfaction. The target is similar in England.

To successfully achieve four-hour emergency care throughput in hospital requires a focused approach to managing unscheduled care; hence delivery requires a whole system approach. Indeed, primary care and the ambulance services have a key role in supporting sustainable solutions.

It is known that patients who wait the longest in emergency departments usually require an inpatient bed, and vulnerable patient groups are usually over-represented (mental health and the elderly) in terms of longer wait times. Acutely unwell medical patients represent the largest single group requiring hospital care and physicians are key to ensuring sustainable systems of acute medical care.

Outcomes will be discussed in relation to:

- Patients and carers
- Staff
- Hospitals

Peer-reviewed evidence and narrative will be used to illustrate current understanding in a UK and an international context.

Data show that in addition to concerns about communication, patients report concerns over waits and delays in emergency departments. Treatment delays contribute to poor patient outcomes and poor organisation of both acute care and elective care pathways can have a detrimental impact on patient care.

Currently in the UK the vast majority of hospitals deliver sustainable high-quality emergency access. Models of care developed in the UK are now being adopted elsewhere.

HYPERTENSION: DO WE KNOW WHAT WE ARE DOING?

Professor Paul Padfield, Consultant Physician, Western General Hospital, Edinburgh

The simple answer is that we may not!

Background The World Health Organization recognises hypertension as the major determinant of mortality throughout the world, and the evidence base for intervention with medication is compelling. Despite this knowledge many individuals with raised blood pressure (BP) remain undetected and, arguably of more concern, doctors do not deliver effective therapy to those who might benefit, even when BP is known to be elevated. The 'rule of halves' appears to be alive and well! Why there remains such therapeutic inertia is unclear. Blood pressure control may well be better in the UK since the introduction of the new GP contract in 2004 where the Quality Outcomes Framework (QOF) awards points (money) for reaching certain targets. The most recently published data have suggested that ~76% of patients in primary care are treated to the QOF target of 150/90 mm Hg.

Issues for individual patients When faced with individual patients we make judgements that are based upon an ill-defined combination of factors, which might include whether an individual corresponds to those in outcome trials, whether they are likely to take medication, whether they are at sufficient risk to warrant drug treatment at all and whether we, using the art of medicine, believe that they should have treatment. At the end of the day, however, it is the level of BP that informs a decision as to whether we start or modify drug therapy and it is in this area that we are at risk of the largest of potential errors.

The measurement of blood pressure All doctors have been taught to measure BP and this is one of the most common procedures carried out in clinical practice. It may not, however, be readily appreciated just how imprecise even an accurate recording of BP might be when used to describe an individual's 'usual BP'.

Blood pressure is inherently variable, from day to day, hour to hour and even minute to minute, and information gleaned from so called 'out of office' recordings can easily demonstrate this. In an attempt to correct for BP variability all guidelines stress the importance of making 'several' readings over time before taking a decision (it is generally assumed that the higher the BP the shorter the time period for observation). The implied argument is that, over time, it will become clear on which side of the intervention threshold an individual will lie and thus appropriate management can follow.

Such a view is simply not borne out by the evidence. Blood pressure categorisation (normotension/hypertension) is not reproducible even within the confines of a research study, and even with careful attention to detail in a hospital setting the difference between BP on sequential visits can vary by far more than the effect of a drug and can easily result in erroneous judgements being made. It seems unlikely that in the hurly burly of routine clinical practice the situation will be better.

At a population level this variability may matter less, but for our patients it is arguable that we simply delude ourselves when we embark on the diagnosis and management of hypertension.

Blood pressure variability decreases when more measurements are taken (and averaged) and it is likely that the reason both ambulatory and self-monitored BP are better predictors of morbidity and mortality is no more complicated than that the measure itself is more reproducible. An optimum number of readings necessary for reasonable reproducibility is 20–25 and this may not be practicable in a GP surgery.

If it is accepted that it is unlikely that we will improve the way clinic or surgery BP is used, we need a cost-effective way of delivering multiple measurements of BP in order to better inform both the diagnosis and ongoing management of patients who might be offered BP-lowering drugs.

In the USA and Japan 65% and 85% respectively of hypertensive patients own a home BP device, and the figure in the UK is 30% and rising. We need to ensure that we understand how to use the information patients will obtain and direct them as necessary to the most appropriate way of collecting the readings.

The management of elevated blood pressure needs a radical rethink if we are to apply the evidence to our patients!

NEW STRATEGIES IN THE NEW MANAGEMENT OF BARRETT'S OESOPHAGUS AND OESOPHAGEAL CANCER

Dr Ian Penman, Consultant Gastroenterologist, Western General Hospital, Edinburgh

The incidence of oesophageal adenocarcinoma is rising rapidly but, despite advances in treatment, five-year survival is only 13%. More than 90% arise on a background of Barrett's oesophagus – the major known risk factor. Barrett's has a population prevalence of about 1.6% and a cancer incidence of 0.5–1.0%. Screening for Barrett's is currently not possible as most reflux patients do not have Barrett's, many Barrett's patient have no history of reflux and endoscopy is expensive, invasive and lacks an evidence

base. Similarly, surveillance of Barrett's remains controversial and lacks a strong evidence base. This has recently been challenged by studies showing a survival benefit of surveillance-detected cancers compared to patients presenting with symptoms. New endoscopic imaging techniques, such as magnification, autofluorescence, narrow band imaging and confocal endomicroscopy, allow better detection of dysplasia and early cancer than standard white light endoscopy.

New techniques are also emerging for the endoscopic management of early lesions, including endoscopic mucosal resection (EMR), submucosal dissection (ESD) and, perhaps most promising, radiofrequency ablation (RFA). When combined, EMR and RFA offer the possibility of comprehensive endoscopic therapy for removal and ablation of early neoplasia in Barrett's. Early results are promising and randomised trials comparing endotherapy to surgery are awaited. In summary, much progress has been made in understanding the epidemiology, molecular biology, diagnosis and minimally invasive management of early Barrett's neoplasia. Challenges remain, however, in developing workable screening strategies to find patients with Barrett's and in targeting surveillance to those with the highest risk of cancer.

MATERNAL MEDICINE: WHAT THE GENERAL MEDIC NEEDS TO KNOW

Dr Catherine Calderwood, Consultant Obstetrician & Gynaecologist, Royal Infirmary, Edinburgh

Saving mothers' lives is the longest running report of its kind in the world. In the UK the leading causes of maternal mortality are venous thromboembolism and cardiac disease. Maternal mortality is, of course, only the tip of the iceberg and there is also long lasting morbidity, the true extent of which is not known.

Despite key recommendations from each triennial report a frequent comment is of substandard care. Symptoms and signs are not taken seriously and risk factors are ignored. Senior advice is not sought and team-work and communication are poor.

This lecture outlines the main findings of the most recent report covering the years 2003–05.¹ The physiological adaptations of the coagulation and cardiovascular systems in pregnancy are discussed in detail. The diagnosis and subsequent treatment of venous thromboembolic disease in pregnancy will be reviewed. The most common cardiac causes of maternal death and how these may present in the pregnant woman will be discussed.

References

- 1 Confidential Enquiry into Maternal and Child Health (CEMACH). *Saving mothers' lives: reviewing maternal deaths to make motherhood safer – 2003–2005*. London: CEMACH; 2007.

PALLIATIVE CARE: HOW TO MANAGE DYING WELL

Dr Kirsty Boyd, Consultant in Palliative Medicine, Royal Infirmary of Edinburgh

In 2008, both the Department of Health and the Scottish Government published major new policies on end-of-life care. These aim to ensure that all patients with a life-limiting illness receive better co-ordinated care in the last year of life. Implementation programmes are already under way and will affect health professionals working in all settings and most medical specialties, given that hospital is still the place where the majority of people in the UK die and about 30% of all bed days are taken up by people in the last year of life. The focus is on improving the care provided by primary care teams and hospital teams.

Support from specialist palliative care services is important, but most of the care will continue to be delivered by the patient's existing healthcare team. Ensuring that people have more choice about place of care at the end of life and enhanced primary care services are important elements of the new policies. General practitioner palliative care registers are being set up and will link to an electronic palliative care summary that is transferred to NHS 24 so that unscheduled care services have good handover information about palliative care patients in the community.

We will review the current policy developments and tools including the Liverpool Care Pathway, for the last days of life and look at how we might improve hospital care for people who are dying by identifying people with palliative care needs, diagnosing dying and planning care, including good symptom control and effective communication with patient and family.

Resources

- SE Scotland Palliative Care guidelines project: <http://www.palliativecareguidelines.scot.nhs.uk>
- Living & Dying Well: <http://www.scotland.gov.uk/Topics/Health/NHS-Scotland/LivingandDyingWell>
- Office of the Public Guardian: <http://www.publicguardian-scotland.gov.uk/index.asp>
- NHS end-of-life programme: <http://www.endoflifecare.nhs.uk>

STEM CELL THERAPY FOR CHRONIC LIVER DISEASE

Professor Stuart Forbes, MRC/University of Edinburgh Centre for Inflammation Research, The Queen's Medical Research Institute, Edinburgh

It is estimated that over the next six to ten years there will be a 500% increase in the need for liver transplantation in the UK. Techniques that promote liver regeneration are urgently required. Liver cell mass is usually restored

primarily through the division of mature hepatocytes and not via a dedicated stem cell population. However, following severe or chronic liver damage these hepatocytes lose their ability to divide and regeneration then occurs via a second cell compartment. These hepatic progenitor cells regenerate the liver and can give rise to both hepatocytic and biliary lineages. Promising recent data from both pre-clinical and early clinical studies has shown that this form of liver regeneration can be influenced therapeutically.

Stem cells from various sources are being tested as a source of hepatocyte-like cells (HLCs). The use of HLCs in extracorporeal bioreactors ('liver machines') could potentially allow more time for endogenous regeneration or for a suitable organ to become available for transplantation following acute liver injury.

The bone marrow strongly influences liver fibrosis and regeneration. Human trials of autologous cell therapy for cirrhosis have mainly employed bone marrow fractions enriched for haematopoietic stem cells. To date, the published data have been generally suggestive of a positive effect. However, the small numbers of patients, variable trial design and uncontrolled nature of the work do not permit firm conclusions.

ACUTE AND SCARY INTERSTITIAL LUNG DISEASE: HOW TO RECOGNISE AND HOW TO TREAT

Dr Nikhil Hirani, Senior Lecturer in Respiratory Medicine, Royal Infirmary, Edinburgh

Acute respiratory failure presenting with diffuse radiographic infiltrates is a common clinical scenario. Distinguishing the common conditions of infective pneumonia and pulmonary oedema from the uncommon interstitial lung diseases (ILD) is often challenging. The specific interstitial lung diseases most frequently present in this way are acute exacerbation of idiopathic pulmonary fibrosis (IPF), cryptogenic organising pneumonia (COP) and acute interstitial pneumonia (AIP). Drug-induced pneumonitis and rare syndromes such as eosinophilic pneumonia are also important diagnoses not to be missed. Often there are 'clinical clues', including computed tomography (CT) imaging, that favour interstitial lung disease, but usually the exclusion of pulmonary infection, often with bronchoalveolar lavage, is a critical component of the diagnostic pathway. A definitive diagnosis usually requires a surgical lung biopsy with associated risk in a compromised patient.

Some key learning points for diagnosing and managing ILD with acute respiratory failure:

1. High resolution CT scanning can be informative, especially if performed early in the course of disease.

Some conditions (e.g. IPF, lymphangitis carcinomatosa, eosinophilic pneumonia) can have highly characteristic CT appearances.

2. Bronchoalveolar lavage is a relatively safe procedure in experienced hands in an intensive care/high dependency unit setting and is a requirement for excluding infection.
3. Some ILDs, particularly COP, eosinophilic pneumonia and hypersensitivity pneumonitis respond rapidly to corticosteroids.
4. Acute exacerbation of IPF has a >90% mortality regardless of treatment.

Recommended reading

- Bradley B, Branley HM, Egan JJ et al. Interstitial lung disease guideline: the British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. *Thorax* 2008; 63 (Suppl 5):v1–58.

TOXICOLOGY FROM ACROSS THE POND

Dr Bob Hoffman, Director, New York City Poison Control Center, USA

Current trends in poison epidemiology demonstrate that lethal poisoning continues to fall in children, but increases dramatically in adults. Deaths from substance abuse, suicidality and adverse drug effects are likely causes. This lecture will focus on three areas of severe poisoning where new approaches to therapy may improve the outcome of poisoned patients.

Most substance abuse deaths result from opioids. Recent data demonstrate that opioids are used in groups, with fatalities occurring in the presence of living drug users. Harm reduction programmes in the USA teach opioid users rescue breathing and basic cardiopulmonary resuscitation, and dispense naloxone for bystander rescue. Multiple successes are reported.¹

Current trends in paracetamol overdose reveal a striking number of patients who have massive concentrations that are either sustained or result from multiple peaks. The most rational explanations include ingestions that far exceed paracetamol solubility or combinations with drugs that delay gastric emptying such as diphenhydramine. Some of the patients develop severe hepatotoxicity despite seemingly adequate treatment with n-acetylcysteine.² Current research is attempting to evaluate the mismatch between n-acetylcysteine kinetics and paracetamol kinetics in these growing numbers of atypical overdoses. Practice changes include doubling of the third maintenance dose of n-acetylcysteine, and/or reloading followed by doubling the maintenance dose.

Intravenous fat emulsion (IFE) reverses cardiotoxic drugs by either creating a lipid sink that removes drug from end-organs or by improving cardiovascular energy dynamics. Experimental models support rescue therapy

with IFE for calcium channel blockers, beta adrenergic antagonists and many psychiatric medications. Human experience confirms this basic research.³

References

- 1 Doe-Simkins M, Walley AY, Epstein A et al. Saved by the nose: bystander-administered intranasal naloxone hydrochloride for opioid overdose. *Am J Public Health* 2009; 99:788–91.
- 2 Smith SW, Howland MA, Hoffman RS et al. Acetaminophen overdose with altered acetaminophen pharmacokinetics and hepatotoxicity associated with premature cessation of intravenous N-acetylcysteine therapy. *Ann Pharmacother* 2008; 42:1333–9.
- 3 Sirianni AJ, Osterhoudt KC, Calello DP et al. Use of lipid emulsion in the resuscitation of a patient with prolonged cardiovascular collapse after overdose of bupropion and lamotrigine. *Ann Emerg Med* 2008; 51:412–5.

NEW HORIZONS IN ANTICOAGULATION

Dr Henry Watson, Consultant Haematologist, Aberdeen Royal Infirmary

The need for better anticoagulant drugs has never been greater. In Northern Europe, Canada and the USA 1–1.5% of the population require anticoagulant treatment to prevent thromboembolic events. Long-term anticoagulation is mostly prescribed for the prevention of cardio-embolic stroke in patients with atrial fibrillation. As the age of the population increases the number of patients with degenerative vascular disease likely to benefit from anticoagulation does likewise. In addition, effective short-term antithrombotic therapy is required to prevent thrombosis during and after extremely prothrombotic periods such as those following the insertion of coronary artery stents. In these clinical circumstances a combination of anti-platelet therapy and anticoagulants is required to prevent vessel occlusion. Finally, huge numbers of elective orthopaedic joint replacements, which are associated with a high risk of perioperative deep vein thrombosis (DVT) and pulmonary embolism, are performed every year.

Until very recently the majority of patients requiring anticoagulation received either warfarin or a heparin. While there have been improvements in the available low molecular weight heparins, the management of anticoagulation with warfarin remains a significant challenge. In both the perioperative period and in individuals requiring long-term anticoagulation there are significant benefits in providing an oral anticoagulant which has a predictable dose effect, rapid onset of action, minimal drug interactions and which does not require monitoring of anticoagulant effect. Several candidate drugs which will be discussed have recently been subjected to clinical trials in the prevention of perisurgical venous thromboembolism (VTE), the management of acute VTE and the prevention of cardioembolic stroke in patients with atrial fibrillation.

WHAT IS WRONG WITH TRAINING?

Professor Sir Neil Douglas, President, Royal College of Physicians of Edinburgh

Historically medical training in the UK was deemed to be excellent but in reality involved exhaustive and exhausting hours of osmosis in conjunction with years wasted in service grades without any teaching. The attempt to focus training with Modernising Medical Careers started disastrously due to the Medical Training Application Service fiasco. We are left with a variant, uncoupled process with flaws that need remedying. These flaws include:

- Inadequate priority for training – financial targets to maximise the quantity of clinical care delivered by doctors have resulted in an increasing difficulty to create time to train. The Colleges are leading a drive to ensure that quality of care and quality of training become clear and rewarded targets.
- Poor selection processes – selection needs to be fair, transparent and to reward excellence.
- Poor matching of numbers of applicants to posts – The taxpayers subsidise undergraduate and postgraduate training but the universities have financial incentives to maximise medical student numbers, while the Department of Health wishes to match trainee numbers to likely vacancies, hence a real risk of mismatch. There needs to be joined-up planning and a tracking system for trainees to allow improved planning.
- Rigidity – it is very difficult to change from one specialty to another. The profession has to realise that those changing direction often bring additional skills and should be welcomed not shunned.
- Tick-box assessment – workplace assessment should be formative only, to help the trainee, and followed by summative assessment of a sample of competencies towards the end of attachments.
- Using junior doctors as rota fodder – while service delivery is an important component of training, employers must provide trainees with coherent training, not rota them to cover service gaps in uncivilised ways or in disconnected specialties.
- Treatment of trainees – they rarely feel valued or empowered and seldom work in a stable enough team to cultivate mentors. Consideration should be given to slowing down rotations and ensuring geographic stability.