

## Warfarin dosing based on genotype more effective

The effectiveness of warfarin can be improved if genotype testing is carried out before the dose is decided, according to the findings of a study presented at the American Heart Association meeting and published in the *New England Journal of Medicine* (Pirmohamed et al, 2013).

This research tested the effect of warfarin when it was prescribed in a standard dose and when it was prescribed based on genotype testing of patients.

Warfarin doses have to be constantly monitored, but variations in genetic makeup, age and size can cause either too small or too big an effect from the treatment.

Genotyping patients to help calculate the dose is not cur-

rently recommended but variation in the genes that are involved in the vitamin K cycle and the metabolism of the drug can make a difference between patients. To test this difference, Professor Pirmohamed and his team studied 455 patients in a

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trial undertaken in the UK and Sweden, with patients recruited in the UK by the Royal Liverpool University Hospital.

Half of the patients were prescribed warfarin based on their genotype test results, while the other half were prescribed the standard dose. The researchers were looking for the amount of time patients spent within the international normalized ratio range of two and three.

Patients who were on the genotype-based dose spent 67% of their time in the ideal range – 7% more than the group on the standard dose. The first group also had far fewer instances of an international normalized ratio of four or higher, which can lead to an increased risk of bleeding. It also took less time for the medicine to become effective – 21 days in the genotyped group, compared to 29 in the standard dose group.

Professor Pirmohamed, Director of the University of

Liverpool's Wolfson Centre for Personalised Medicines, and Liverpool Health Partners' Clinical Academic Programme Lead for Drugs, said: 'Warfarin is extremely useful but difficult to prescribe in the most efficient way.

'We have been able to show that personalizing the dose to the patient, based on their genes, age and body weight, can help set the right dose and reduce both risk and the time it takes for the medicine to become effective, when compared with the standard doses used in the UK and Sweden.'

He concluded: 'This could have major implications for the use of a drug that is taken by millions of people with serious conditions every year.'

Pirmohamed M, Burnside G, Eriksson N et al, for the EU-PACT Group (2013) A Randomized Trial of Genotype-Guided Dosing of Warfarin. *N Engl J Med* November 19 (epub before press) doi: 10.1056/NEJMoa1311386

### Improving bone density in patients on antiepileptic drugs

Calcium and vitamin D supplementation improved bone density in a group of male veterans with epilepsy who were treated chronically with anti-epileptic drugs, shows a new study (Lazzari et al, 2013). The results suggest that risedronate may help to prevent new vertebral fractures when taken with calcium and vitamin D supplementation.

The antiepileptic drug and osteoporosis prevention trial (ADOPT) was a prospective 2-year randomized, double-blind, placebo-controlled phase IV clinical trial of 80 male veterans with epilepsy who were treated with an antiepileptic drug for a minimum of 2 years. All participants received calcium and vitamin D supplements, and

were randomized to risedronate or placebo. Total body, hip and spine bone density was assessed at baseline, 1 year and 2 years after study enrollment.

Baseline characteristics of subjects were similar and 53 patients completed the study. Significant improvement in bone density compared to baseline was seen in 69% and 70% of patients in the placebo and active drug groups respectively. Patients taking risedronate had a significant increase in bone density at the lumbar spine compared to subjects in the placebo group.

Lazzari AA, Dussault PM, Thakore-James M, Gagnon D, Baker E, Davis SA, Houranieh AM (2013) Prevention of bone loss and vertebral fractures in patients with chronic epilepsy—Antiepileptic drug and osteoporosis prevention trial. *Epilepsia* 54(11): 1997–2004 (doi: 10.1111/epi.12351)

### Headaches in lupus patients not linked to disease activity

Headache is common among patients with system lupus erythematosus according to new research (Hanly et al, 2013). The study found that 18% of lupus patients experienced headache at the onset of disease, increasing to 58% after 10 years.

While headaches were linked to a lower health-related quality of life, these episodes resolved over time independent of treatment specific to lupus and were not associated with disease activity or specific lupus autoantibodies.

Researchers found no association between headache and

specific lupus autoantibodies or lupus medications. 'While lupus patients with headaches reported lower quality of life, the majority of cases resolved on their own without lupus-specific therapies,' concluded lead author, Dr John Hanly from Dalhousie University and the Queen Elizabeth II Health Sciences Centre, Halifax, Nova Scotia, Canada.

Hanly JG, Urowitz MB, O'Keefe AG et al (2013) Headache in Systemic Lupus Erythematosus: Results from a Prospective, International, Inception Cohort Study. *Arthritis Rheum* October 28 (epub before press) (doi: 10.1002/art.38106)

## Institutional support lacking for surgeons affected by surgical complications

Many surgeons are seriously affected on an emotional level by major surgical complications, and they often feel that institutional support is inadequate.

These findings from a small study (Pinto et al, 2013) provide valuable insights into the factors that affect surgeons' reactions to surgical complications and how surgeons could be better supported in their aftermath.

To explore the impact of complications on surgeons, Dr Anna Pinto, of the Imperial College London St Mary's Campus, and her colleagues examined how surgeons are affected by such incidents on personal and professional levels, which factors affect their reactions, how they cope with

their consequences, and how they perceive support at their institutions.

The researchers conducted individual interviews with 27 general and vascular surgeons from two large NHS organizations in London. The interviews revealed that surgeons are seriously affected by major surgical complications, particularly those for which they feel responsible.

All participants referred to at least one case in their practice where a complication affected them significantly on personal and professional levels.

Factors that determined their reactions included the complication's preventability, surgeons' personalities and experience, patients' outcomes and

reactions, colleagues' reactions, and the institution's culture.

Dr Pinto commented: 'Given the potential impact on patients as well as on surgeons, additional support and mentoring should be seriously considered by the surgical community and by those involved in the management of surgical services. Further research is needed on how to implement support structures that meet the needs of the small number of surgeons who are affected to the point that personal life and clinical practice deteriorate.'

Pinto A, Faiz O, Bicknell C, Vincent C (2013) Surgical complications and their implications for surgeons' well-being. *Br J Surg* November 14 (epub before press) (doi: 10.1002/bjs.9308)

### Revised standards for inflammatory bowel disease

Revised UK inflammatory bowel disease standards have been launched. The standards seek to inform NHS managers and commissioning organizations of the essential components of a quality inflammatory bowel disease service.

### Linagliptin allows safer control of blood glucose in older patients

Research published in the *Lancet* shows that linagliptin could be used safely to lower blood glucose levels in older people. The drug only works when levels are rising or high – its actions 'switch off' when blood glucose levels fall and normalize.

### Rapid flu diagnosis allows more appropriate care

When patients in the emergency department are diagnosed with influenza by means of a rapid test, they get fewer unnecessary antibiotics, are prescribed antiviral medications more frequently and have fewer additional lab tests compared to patients diagnosed with influenza without testing, according to a new study published in the *Journal of the Pediatrics Infectious Diseases Society*.

## Hospital treatment for patients who self-harm in England is 'as variable as ever'

Hospital management of patients who self-harm in England has barely changed in the past 10 years despite the introduction of clinical guidelines, shows a study by Cooper et al (2013).

Researchers from The University of Manchester found 40% of those attending hospital after an overdose or other self-injury did not get a specialist psychosocial assessment.

The treatment patients received also varied according to where they lived – suggesting that a postcode lot-

tery was still in operation.

The researchers looked at 6442 individuals who presented at 32 hospitals with 7689 episodes of self-harm over a 3-month period and investigated how people were treated and followed up. They also measured the quality of self-harm services using a 21-item measure. The team compared its results with an earlier survey that was carried out in 2001.

'Hospitals varied markedly in their management of self-harm,' commented Dr Jayne Cooper from the

University's Centre for Suicide Prevention, who led the study. She added: 'The proportion of episodes that received a psychosocial assessment in line with national guidance varied from 22% in some hospitals to 88% in others. Overall we found the level of assessment had remained more or less static over the last 10 years.'

However, the study did show some evidence that the quality of health services for patients who self-harmed may have improved, she added.

Cooper J, Steeg S, Bennewith O et al (2013) Are hospital services for self-harm getting better? An observational study examining management, service provision and temporal trends in England. *BMJ Open* 3: e003444 (doi:10.1136/bmjopen-2013-003444)

**Dr Jayne Cooper, Senior Research Fellow, Centre for Suicide Prevention, University of Manchester, Manchester**



## 9TH CONGRESS OF THE EUROPEAN UNION GERIATRIC MEDICINE SOCIETY; VENICE, ITALY, 2–4 OCTOBER

### Review reveals predisposing factors for bacteraemia in older patients

Most elderly patients with bacteraemia in hospital have clear predisposing factors that hospitals can often prevent, according to a hospital-wide review.

A group at the Royal Berkshire NHS Foundation Trust, Reading, retrospectively analysed all bacteraemia in patients aged 65 years and older in September and October 2012. They obtained data on first isolates for each patient from microbiology laboratory systems, hospital patient administration and medical notes.

They identified a total of 110 blood cultures in 99 patients; 33 were excluded because patient notes were unavailable. *Escherichia coli* was the commonest isolate, and this increased in older age groups with more than three-quarters occurring in patients over 75 years.

Nearly two-thirds (62%) of patients had a predisposing factor for sepsis. A recent surgical procedure had the highest association with bacteraemia; 24% of patients had a urinary catheter.

‘Most elderly patients had a preventable factor as a cause for infection,’ concluded the researchers. ‘Hospitals should avoid unnecessary procedures or catheters to reduce this risk.’

**Susan Mayor**

### Monitoring and compression halve VTE rates in patients with fractured neck of femur

The rate of venous thromboembolism (VTE) in patients with fractured neck of femur halved in a UK hospital after introducing electronic monitoring of VTE prophylaxis, regular use of intermittent pneumatic compression stockings and CQUIN incentives, according to results reported at the congress.

Researchers identified all patients presenting to the Royal Berkshire Hospital, Reading, with fractured neck of femur in 2010 using the National Hip Fracture Database. They then reviewed all of those investigated for VTE within 6 months after their fractures. This process was then repeated for patients presenting between 1 June and 1 December 2012, after the hospital had intro-

duced CQUIN incentives, regular use of intermittent pneumatic compression stockings and electronic monitoring of VTE prophylaxis.

Results showed that nine (1.93%) of the 467 patients presenting with fractured neck of femur in 2010 suffered VTE; five patients had pulmonary embolism and four had a deep vein thrombosis. These VTE rates halved for the 2012 cohort of 226 patients, with only two (0.88%) having VTE (one pulmonary embolism and one deep vein thrombosis).

The researchers, from the Department of Elderly Care at the Royal Berkshire Hospital, warned: ‘VTE is a potentially fatal complication after a fractured neck of femur.’ They

noted that the national incidence of clinically detected and radiologically confirmed deep vein thrombosis in these patients is 3% and pulmonary embolism is 1%.

The incidence of VTE in patients at the hospital was already lower than the national average in 2010, partly because it has a comprehensive orthogeriatric service, multi-disciplinary team assessment and a clear VTE prophylaxis protocol requiring administration of low molecular weight heparin to all patients with fractured neck of femur. ‘But the addition of mechanical, electronic, and financial measures halved the VTE rate further in 2012,’ the researchers concluded.

**Susan Mayor**

### Congress keynote focuses on valve implants

The spotlight of this year’s congress fell on Europe’s ageing population and on how to improve health-care outcomes of older patients. Transcatheter aortic valve implantation, a rapidly evolving, minimally-invasive heart valve replacement procedure for elderly patients with severe symptomatic aortic stenosis, was chosen as the best example of this health-care improvement.

Focusing on this innovation, the keynote speech at the European Union Geriatric Medicine Society congress was delivered by Professor Alain Cribier, Professor of Medicine,

University of Rouen, France, who developed and performed with his team the first transcatheter aortic valve implantation in 2002.

‘Transcatheter aortic valve implantation is a prime example of a new procedure that brings quality of life improvements specifically to elderly patients,’ he said. ‘Since the first case over 10 years ago, and despite initial resistance, over 80 000 patients have now benefitted from transcatheter aortic valve implantation.’

Professor Cribier noted that at 85 years of age, around 8%

of today’s population can expect to have aortic stenosis, a condition characterized by the calcification and stiffening of the aortic valve.

‘Given the increasing proportion of elderly individuals in the population, aortic stenosis will become a significant burden,’ he commented. ‘Considering that disease-modifying pharmaceutical therapies are not available, and that many patients are inoperable or at high risk of open heart surgery, transcatheter aortic valve implantation has been a very significant development.’

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### Prospective study reveals impact of long-term shingles

One in five people aged 50 years and over suffer prolonged postherpetic neuralgia 3 months after contracting shingles despite prompt antiviral treatment after rash onset. This is the warning from a prospective study, which also showed that one in ten people still have postherpetic neuralgia at 6 months.

The Italian multicentre study followed up 413 patients aged 50 years and older (mean age  $67.9 \pm 10.7$  years) with a new episode of herpes zoster between March 2009 and July 2010. All patients (100%) presented with a rash at their initial visit with shingles, most commonly localized in the tho-

racic dermatome (59.1%). Nearly 90% of patients had herpes zoster-related pain at their initial visit, with an average severity of 5.8/10 on a visual analogue scale. Most of the patients (91.5%) were treated with oral antivirals soon after

**Dr Robert Johnson, Senior Research Fellow, University of Bristol, Bristol**



the onset of their rash; 9.4% received topical antivirals.

After 3 months, 20.6% of patients had postherpetic neuralgia, with a higher incidence in older patients (24.5% in those over 70 years of age). Postherpetic neuralgia was still present in 9.2% of the patients at 6 months, with severity remaining above the threshold of 3. The researchers noted that the pain had a major impact on people's quality of life and need for further GP and hospital treatment.

Dr Robert Johnson, senior research fellow and herpes zoster specialist, University of Bristol, commented: 'There is a clear age-related increase in

both incidence and severity of shingles over the age of 50 years because of immunosenescence and comorbidities.'

He noted that postherpetic neuralgia is the commonest complication of the infection: 'The pain can be very severe and greatly impact on daily activities and functional ability, so preventing shingles infection and postherpetic neuralgia is highly desirable.'

Clinical trials with the herpes zoster vaccine Zostavax have shown a 51% reduction in overall incidence of herpes zoster in people aged 60 years old and over and a 67% reduction in the incidence of postherpetic neuralgia. Real-life experience with vaccination in the USA confirmed the efficacy seen in clinical trials, with a 55% reduction in incidence of herpes zoster. 'The recent UK recommendation to vaccinate all people aged 70 years, with a catch-up programme for those aged 79 years, is a huge advance,' Dr Johnson concluded.

Dr Jean-Paul Kress, president of Sanofi Pasteur MSD, the company that has developed Zostavax, added: 'This vaccine represents a really strong scientific advance in meeting previously unmet medical need. For the first time, we can prevent a virus that can reactivate and cause painful and debilitating symptoms for which there has been no effective treatment.'

**Susan Mayor**

*Susan Mayor's attendance at the Congress of the European Union Geriatric Medicine Society was supported financially by Sanofi Pasteur MSD.*

### Rapid access and consultant evaluation unit reduces length of hospital stay in older patients

Introducing a dedicated Rapid Access and Consultant Evaluation (RACE) unit significantly reduced length of hospital stay in results reported from a hospital introducing this innovative approach.

A research group at Poole Hospital NHS Trust analysed data for length of hospital stay, discharge within 48 hours, readmission rates and total number of elderly medicine bed days before and after establishing a RACE unit. The unit included: a dedicated elderly medicine e-admissions ward; consultant-led 'triage' ward rounds each morning for patients appropriate for discharge within 48 hours; referrals being taken by a consult-

ant or specialist registrar, involving early senior assessment and facilitation of early supported discharge; daily multidisciplinary meetings; integration with community services and intermediate care; specialist nursing staff; and a rapid access clinic.

Results reported at the congress showed that the mean length of hospital stay decreased by 14%, from 13.5 to 11.6 days after the RACE unit was established. Three years after setting up the unit the length of stay has fallen even further, to 8.1 days. The proportion of patients discharged within 48 hours increased from 20.8% to 36.5%. The average monthly

occupied bed days in the Department of Elderly Medicine fell by 22%, from 6078 to 4726. However, the readmission rate increased from 12% to 16%.

The researchers said: 'The RACE unit has led to significant, sustained improvements in length of stay, discharge within 48 hours and number of occupied bed days.'

They felt that three main factors were responsible for these improvements: increased consultant involvement in the admission and discharge processes; the daily, focused multidisciplinary meeting; and strong nursing leadership and expertise in geriatric care.

**Susan Mayor**