

Medibytes

Medibytes offer readers short, informative synopses of important or interesting papers published in specialty and other general medical journals. They are edited by Dr J Ferguson.

LIST OF ABBREVIATIONS Estimated glomerular filtration rate (eGFR), Food and Drug Administration (FDA), Framingham Heart Study (FHS), randomised controlled trial (RCT)

PSYCHIATRY

Antidepressant treatment following myocardial infarction

The presence of depression following myocardial infarction is associated not only with poorer psychosocial adjustment, but, worse, with cardiovascular outcome including death. The second RCT of antidepressant treatment in this clinical presentation found no benefits over usual care, either with regard to mood state, or subsequent cardiac events over the following 18 months. However, the study was seriously underpowered. An appraisal of this study and the previous trial, which had also produced a negative result, concluded that a much larger study, with tighter aims and a more sophisticated design, was required before a definitive answer would be obtained.

G Masterton

From Van Melle JP, de Jonge P, Honig A *et al.* Effects of antidepressant treatment following myocardial infarction. *Br J Psychiatry* 2007; **190**:460–6.
Carney RM, Freedland KE. Does treating depression improve survival after acute coronary syndrome? Invited commentary. *Br J Psychiatry* 2007; **190**:467–8.

Suicide and hot weather

Seasonal fluctuation in suicide has been recognised for over 100 years, but its explanation remains unknown despite exploring many meteorological variables. This study linked daily suicide numbers in England and Wales over ten years to daily temperature parameters for central England. No seasonal trends were identified, but suicide numbers correlated linearly with average daily temperature above 18°C, each additional degree being associated with a 3.8% increase in suicides. There was a 47% increase in suicides during one heatwave (1995) but –2% in another (2003). These data suggest hot weather may play a role in some suicides, but replication is required.

G Masterton

From Page LA, Hajat S, Kovats RS. Relationship between daily suicide counts and temperature in England and Wales. *Br J Psychiatry* 2007; **191**:106–12

Cannabis use, psychosis and affective disorders

This comprehensive meta-analysis studied the relation of cannabis use to psychosis and affective disorders in later life. It included 11 studies on psychosis based on 7 cohorts, and 24 studies on affective disorders based on 15 cohorts from 4,804 references. Analysis, including consideration of confounding factors, showed an increased risk of later psychosis following any cannabis use (OR 1.41, 95% CI 1.2–1.65) with greater risk from frequent use (OR 2.09, 95% CI 1.54–2.84). This association does not prove causation, but as most studies excluded those psychotic at baseline, a causative link is possible. Forty percent of young people use cannabis, and in the UK, an estimated 14% of psychotic episodes would not have occurred had cannabis not been used. The relation of cannabis to affective disorders was less clear.

N Finlayson

From Moore THM, Zammit S, Lingford-Hughes A *et al.* Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet* 2007; **370**:319–28.

PHARMACOLOGY

Elimination of Helicobacter pylori by glutamate racemase inhibitors

The bactericidal action of penicillin can be explained by an interference with bacterial cell wall synthesis in which the inhibition of the transpeptidation enzyme prevents peptide chains cross linking with the peptidoglycan backbone. Presumably with this in mind, Fisher and his colleagues at AstraZenica targeted the peptidoglycan biosynthetic pathway in their search for novel broad spectrum antibacterial compounds. However, their characterisation of glutamate racemase, a key enzyme in the synthetic pathway which converts L-glutamate to D-glutamate, proved rather more interesting when they identified a group of inhibitors specific for *Helicobacter pylori*. Studies of the glutamate racemase purified from several pathogenic bacteria revealed three different and species specific regulatory mechanism and that for *H. pylori* proved unique. Specific inhibition of the *H. pylori* enzyme by pyrazolopyrimidine analogues was not only non-

competitive, but the allosteric binding site was only present when the substrate glutamate was bound. Furthermore, mutagenesis of single amino acids in the allosteric binding site suggest that drug resistance is unlikely to prove a problem. Although the current therapy for *H. pylori* infection, involving two antibacterials and an antacid, has proved to be highly successful, this work may have identified a single compound which is unlikely to interfere with the normal gut flora or to generate antibacterial resistance, which is ideal for long term prophylaxis of gastric ulceration and possibly malignant change.

JS Kelly

From Lundqvist T, Fisher SL, Kern G et al. Exploitation of structural and regulatory diversity in glutamate racemases. *Nature* 2007; **447**:817–22.

NEONATOLOGY

Optical imaging of the neonatal brain

The human brain may be damaged *in utero*, during delivery or postnatally. New non-invasive methods of assessing neonatal cerebral function would be of great benefit prognostically, and perhaps therapeutically. Near infrared spectroscopy has been available as a research tool for 30 years, but has not been adopted widely as a clinical tool.

The new technique of optical tomography depends on interrogating light transmitted through the brain. Optical fibres fixed to the baby's scalp are the sensors. 'Photon flight times' provide information on the light-absorbing and scattering characteristics of the tissues being interrogated. It is now possible to obtain three-dimensional images of the entire neonatal head during motor evoked responses. By measuring oxyhaemoglobin and deoxyhaemoglobin independently, it is possible to study local brain activation from changes in regional blood volume due to local vasodilation. Passively moving a baby's arm shows an increase in total haemoglobin concentration in the contralateral motor and sensory cortex. The challenge now is to develop this promising technique into a valuable clinical tool.

I Laing

From Austin T, Optical imaging of the neonatal brain. *Arch Dis Child Fetal Neonatal Ed* 2007; **92**(4):F238–41.

GENERAL MEDICINE

Social factors in obesity

There seems no end to the value of the FHS. This study investigates obesity in the 5,124 members of the offspring cohort of the original FHS subjects, and any person to whom they were linked over 32 years. Obesity seems to spread in social networks in relation to social ties. Friends, siblings and spouses were more likely to become obese if their opposite members became obese, and this was most notable in same-sex relationships. Opposite-sex friendships and female friendships did not increase the risk of obesity when their opposite members became obese. Geographic proximity (e.g. neighbours), smoking cessation and associations of the obese were not important. Social factors in obesity may be important in prevention.

N Finlayson

From Christakis NA, Fowler JH. The spread of obesity in a large social network over 32 years. *N Engl J Med* 2007; **357**:370–9.

Cardiotoxicity and Rosiglitazone

Type 2 diabetes mellitus is common, glycaemic control prevents long-term complications, and treatment extends over years. Rosiglitazone is used for glycaemic control in such patients and millions of patients worldwide use it, but questions have arisen about its cardiovascular safety. A recent meta-analysis reported rosiglitazone associated with a 40% increase in risk of myocardial infarction, leading to an interim analysis of the RECORD trial of Rosiglitazone treatment which has reported less concern about its cardiovascular safety. These editorials review Rosiglitazone cardiotoxicity, and a diabetologist, a cardiovascular epidemiologist and a drug safety specialist conclude there is significant evidence for Rosiglitazone cardiotoxicity. The FDA in the US has been advised to recommend it be avoided in those with cardiovascular disease; patients should consult their doctors rather than stop the drug themselves, and drug regulators should ponder the difficulty of identifying adverse drug effects.

N Finlayson

From Drazen JM, Morrissey S, Curfman GD. Rosiglitazone – continued uncertainty about safety. *N Engl J Med* 2007; **357**: 63–4.

Nathan DM. Rosiglitazone and cardiotoxicity – weighing the evidence. *N Engl J Med* 2007; **357**:64–6.

Psaty BM, Furberg CD. The record of rosiglitazone and the risk of myocardial infarction. *N Engl J Med* 2007; **357**:67–9.

Passenger discomfort on long-duration commercial flights

Five hundred and two volunteers who had not ascended above 4,000 feet (1,219m) or travelled in commercial aircraft for >3 hours in the previous month were investigated. Tests were conducted in a hypobaric chamber at altitudes of 650 feet (sea level, n=103), 4,000 feet (n=102), 6,000 feet (n=93), 7,000 feet (n=108) and 8,000 feet (commercial aircraft pressure, n=96). Mean oxygen saturation decreased by a maximum of 4.4% at 8,000 feet. This hypoxaemia was not related to symptoms of mountain sickness and did not impair sensory or psychomotor performance but was associated with increased discomfort after 3–9 hours. A cabin altitude of 6,000 feet would reduce passenger discomfort on long-duration commercial flights.

N Finlayson

From Muhm JM, Rock PB, McMullin DL *et al.* Effect of aircraft-cabin altitude on passenger discomfort. *N Engl J Med* 2007; **357**:18–27.

NEPHROLOGY**heading two**

Randomised trials have not so far found that anti-inflammatory drugs are useful in preventing dementia. This study investigated 6,377 healthy women in the US aged 65 years and over (average age 72) who were given aspirin 100mg/day (an antiplatelet but not anti-inflammatory dose) or placebo. Tests of general cognition, verbal memory and category fluency were done at 5.6 years and biannually until about 10 years. Low-dose aspirin did not preserve these functions, though aspirin users performed better on category fluency. The study does not support the use of low-dose aspirin in the prevention of dementia, but does not exclude the possibility that aspirin started at an earlier age, or at anti-inflammatory doses might be effective.

N Finlayson

From Kang JH, Cook N, Manson J, Buring JE, Grodstein F. Low dose aspirin and cognitive function in the women's health study cognitive cohort. *BMJ* 2007; **334**:987–90.

eGFR and mortality

Even mild renal dysfunction increases the risk of death and of cardiovascular disease. This study of 441 generally healthy Jerusalem residents, living in the community and aged 70 years and over, related eGFR, based on the plasma creatinine and calculated from three different formulae, to mortality. Coincident illnesses included hypertension (72%), ischaemic heart disease (26%) and diabetes mellitus (16%). The different methods identified eGFRs <60 ml/min/1.73m² in 51%, 34% and 16% of subjects; each showed a significantly increased 12-year mortality for those in the lowest quartile (eGFR <30) compared to the highest quartile (>90). Reduced eGFR in the elderly is associated with increased mortality. The efficacy of preventive measures remains to be proved.

N Finlayson

From Maaravi Y, Bursztyn M, Hammerman-Rosenberg R, Stressman J. Glomerular filtration rate estimation and mortality in an elderly population. *QJM* 2007; **100**:441–9.