

## Medibytes

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

**LIST OF ABBREVIATIONS** Body mass index (BMI), *Clostridium difficile* (*C. difficile*), chronic hepatitis C virus (HCV), ethyl-eicosapentaenoic acid (EPA), faecal occult blood (FOB), irritable bowel syndrome (IBS), magnetic resonance imaging (MRI), positron emission tomography (PET)

### SCIENCE

#### Placebo – response not purely imagination?

Functional MRI and PET with <sup>11</sup>C carfentanil showed that intravenous saline given as a placebo can activate appropriate cortical and sub-cortical regions of the brain and release endogenous opioids in human volunteers, using a blind, randomised and counterbalanced design. The painful stimulus was maintained for 40–60 minutes by injecting hypertonic saline into a relaxed masseter muscle. Placebo activation of the opioid system in the nucleus accumbens may be related to dopamine's role in reward. Other work has shown neuronal firing in the striatum and the symptoms of Parkinson's disease to be attenuated during the administration of placebos to patients with an expectation of symptom relief. The authors caution that rates of placebo responding are much lower in severe and persistent forms of disease.

JS Kelly

*From* Zubieta J, Bueller JA, Jackson LR et al. Placebo effects mediated by endogenous opioid activity on  $\mu$ -opioid receptors. *J Neurosci*. 2005; **25**:7754–62.

#### A drug answer to antibiotic resistance

Most contemporary antimicrobials target a small number of essential cell functions, and the development of new compounds has failed to outstrip the development of antibiotic resistance. The paper draws attention to the development of a new class of compounds which block the expression of genes that are essential for enhancing bacterial virulence; in this instance the transcription factor ToxT which regulates cholera toxin production and a factor, toxin coregulated pilus, which promotes intestinal colonisation. Other research targets include *staphylococcus aureus*, *pseudomonas aeruginosa* and anthrax. It is thought that virulence inhibitors will act synergistically with conventional antibiotics, and the use of multiple diverse targets may slow the development of antibiotic resistance.

JS Kelly

*From* Hung DT, Shakhnovich EA, Pierson E et al. Small-molecule inhibitor of *Vibrio cholerae* virulence and intestinal colonization. *Science* 2005; **310**:670–4.

### PSYCHIATRY

#### Fish oils and depression

Interest in the potential role of fish oils in the treatment of depression stimulated a randomised controlled trial evaluating EPA as an adjunct in the treatment of outpatients with bipolar depression. A highly significant antidepressant effect emerged. This was in spite of participants being unable to guess their therapy, intention to treat analyses that took account of altered main therapy during the trial, and the large placebo effect that complicates this type of trial. Crucially, benefit was gained without triggering mania or recognisable side effects. Ethyl-eicosapentaenoic acid appears to be a promising, 'natural' new line of therapy.

G Masterton

*From* Frangou S, Lewis M, McCrone P. Efficacy of ethyl-eicosapentaenoic acid in bipolar depression: randomised double-blind placebo-controlled study. *Br J Psychiatry* 2006; **188**:46–50.

#### Predicting dieters who will develop an eating disorder

Can we identify high-risk dieters? A general population cohort of 3,000 dieting young women was followed up for two years. Eating disorders were screened by repeated questionnaire, with potential cases then interviewed to confirm the diagnosis. One hundred and four women (3.5%) developed an eating disorder. These women, who also had a lower initial BMI, could be distinguished from normal dieters by five questionnaire responses – frequency of binge eating; frequency of vomiting/laxative use; secret eating; fear of loss of control over eating; desire for an empty stomach. A screening instrument based on these variables would have identified 70% of cases.

G Masterton

*From* Fairburn CG, Cooper Z, Doll HA, Davies BA. Identifying dieters who will develop an eating disorder: a prospective, population-based study. *Am J Psychiatry* 2005; **162**:2249–55.

### Risk of recurrence following puerperal psychosis

Puerperal psychosis is a serious complication of childbirth, occurring after 1–2 per thousand deliveries. A cohort (n=103) who had experienced the most common illness, a bipolar affective disorder, was followed up for a median nine years after their index episode. Around 60% experienced another mood illness, but this was irrespective of whether they had another baby or not. For affected couples, hazarding another pregnancy is often a difficult decision. Medical advice has traditionally concentrated on the high risk of recurrent puerperal psychosis following another pregnancy, without acknowledging adequately the equally high risk of non-puerperal episodes.

G Masterton

*From* Robertson E, Jones I, Haque S, Holder R, Craddock N. Risk of puerperal and non-puerperal recurrence of illness following bipolar affective puerperal (post-partum) psychosis. *Br J Psychiatry* 2005; **186**:258–9.

### Schizophrenia and cancer

Among intriguing physical correlates of schizophrenia, a negative association with cancer has spawned hypotheses about the aetiology of both disorders. Now a cohort comparison of linked hospital and death records reports an adjusted odds ratio of 0.99 (95% CI 0.90–1.08) for the rate of all cancers in schizophrenic patients refuting this overall negative association. Only skin cancers were much less likely in schizophrenia, which may reflect life style differences, or may be a chance finding. However, vitamin D deficiency could link the reduced risk of skin cancer to the established excess of winter births in people who develop schizophrenia – and so a new hypothesis emerges.

G Masterton

*From* Goldacre MJ, Lianne M *et al.* Schizophrenia and cancer: an epidemiological study. *Br J Psychiatry* 2005; **187**:334–8.

## INFECTIOUS DISEASE

### The emergence of a more severe strain of *C. difficile*

Two large studies have described a new more severe strain of *C. difficile* that seems to be associated with fluoroquinolone use. Loo *et al* describe the clinical, epidemiological and microbiological experience of *C. difficile* enteric disease in 1,703 patients from Canada. They found a high incidence in the elderly and a 30-day mortality rate of 6.9%. The predominant strain was found to be resistant to fluoroquinolones. McDonald *et al.* studied microbial analysis of isolates taken from patients with *C.*

*difficile* disease in the United States. They demonstrated that a previously rare strain of *C. difficile* associated with higher toxin production and fluoroquinolone resistance, was becoming more common.

J Ferguson

*From* McDonald LC, Killgore GE, Thompson A *et al.* An Epidemic, Toxin Gene-Variant Strain of *Clostridium difficile*. *N Engl J Med* 2005; **353**(23):2433–41; Loo VG, Poirier L, Miller MA *et al.* A predominantly clonal multi-institutional outbreak of *clostridium difficile*-associated diarrhea with high morbidity and mortality. *N Engl J Med* 2005; **353**(23):2442–9.

## CARDIOVASCULAR DISEASE

### Premature cardiovascular disease after maternal placental syndrome

A large population-based cohort study has shown that women with maternal placental syndromes have a higher risk of early cardiovascular disease. Maternal placental syndromes include hypertension in pregnancy, abruption and infarction, and are probably due to diseased placental vessels. The authors demonstrated that the 7% of women affected by this syndrome had an incidence of cardiovascular disease of 200 per million person-years in comparison to 500 per million person-years in the unaffected cohort. This suggests that early implementation of primary prevention measures is important in this at risk cohort.

J Ferguson

*From* Ray JG, Vermeulen MJ, Schull MJ. *et al.* Cardiovascular health after maternal placental syndromes (CHAMPS): population-based retrospective cohort study. *Lancet* 2005; **366**:1797–1803.

## GASTROENTEROLOGY/HEPATOLOGY

### Treatment duration for hepatitis C virus genotype 4

This prospective randomised double-blind study treated 287 patients with HCV genotype 4 infection with combined peginterferon and ribovirin for 2 weeks (95), 36 weeks (96), and 48 weeks (96). Sustained viral responses at 48 weeks was checked by serum HCV-RNA measurement. Sustained viral responses of 29% at 24 weeks, 66% at 36 weeks, and 69% at 48 weeks were obtained. Only 8 patients (2.8%) discontinued treatment, mainly for haematological, psychiatric or hypothyroid complications. HCV genotype 4, like HCV genotype 1, with which it has a close phylogenetic relation, requires 36 to 48 weeks treatment to obtained optimal results.

N Finlayson

*From* Kamal SM, el Tawil AA, Nakano T *et al.* Peginterferon alpha-2b and ribavirin therapy in chronic hepatitis C genotype 4: impact of treatment durations and viral kinetics on sustained virological response. *Gut* 2005; **54**:858–66.

### **Amitriptyline acts in the brain to relieve pain in irritable bowel syndrome**

Pain in IBS is probably attributable to abnormal intestinal motility and intestinal hypersensitivity made worse by psychosocial stress. It is often treated with amitriptyline. Amitriptyline 50 mg daily reduced pain due to balloon distention of the rectum, particularly during auditory stress, in 19 female IBS patients. Simultaneous functional MRI during amitriptyline treatment showed reduced brain activation in the anterior cingulate cortex while patients were on treatment. Amitriptyline in painful IBS seems to work centrally in the brain.

N Finlayson

*From* Morgan V, Pickens D, Gautam S *et al.* Amitriptyline reduces rectal pain related to activation of the anterior cingulate cortex in patients with irritable bowel syndrome. *Gut* 2005; **54**:601–7.

### **Beware of single negative faecal occult blood tests!**

Single digital FOB tests are widely used, but how valuable are they? Two thousand six hundred and sixty-five men aged 50 to 75 years had a single digital FOB test and six-sample FOB tests followed by colonoscopy. Advanced neoplasia, defined as an adenoma > 10 mm diameter, a villous adenoma, an adenoma with high-grade dysplasia, or invasive cancer, was found at colonoscopy in 284 patients. A single FOB test was positive in 4.9% of these 284 patients, and six-sample FOB tests gave a positive result in 23.9%. Positive FOB tests lead to further investigation, but negative tests do not exclude important colonic disease.

N Finlayson

*From* Collins JF, Lieberman DA, Durbin TE, Weiss DG *et al.* Accuracy of screening for fecal occult blood on a single stool sample obtained by digital rectal examination: a comparison with recommended sampling practices. *Ann Intern Med* 2005; **142**:81–5.

## **PUBLIC HEALTH**

### **Copycats cause accidents?**

All TV commercials for cars and trucks  $\geq 30$  seconds broadcast in the US or Canada in January and July from 1998 to 2002 were studied. One hundred and thirteen of 250 commercials (45%) contained an unsafe driving sequence. Multiple unsafe sequences occurred in 14%. Most were of aggressive driving (85%), mainly high speed (60%).

High speed was shown in 58% of commercials; power was mentioned in 23%. Inattentive driving (11%) comprised mobile phone use and driver distractions. Eighty-two per cent of drivers and 84% of narrators were male. Bad driving is common in television adverts, but whether this contributes to accidents is unknown. Television adverts should show safe product use.

N Finlayson

*From* Shin PC, Hallett D, Chipman ML *et al.* Unsafe driving in North American automobile commercials. *J Public Health* 2006; **27**:318–25.

## **PROFESSIONALISM**

### **Leopards don't often change their spots**

Two hundred and thirty-five US doctors disciplined by state medical boards were compared with 469 control doctors in a case-control study. Disciplined physicians were three times more likely to have displayed unprofessional behaviour in medical school. Irresponsibility (unreliable clinic attendance, patient care failures) and poor capacity for self-improvement (poor attitude, argumentative, criticism resistance) independently predicted disciplinary action. Highest irresponsibility levels increased later disciplinary action eight times. Poorer academic results also predicted later disciplinary action but less strongly. Unprofessional students probably improve with training and experience as disciplinary action by boards is much less frequent than a medical school record of unprofessional behaviour.

N Finlayson

*From* Papadakis MA, Teherani A, Banach MA *et al.* Disciplinary action by medical boards and prior behavior in medical school. *New Engl J Med* 2005; **353**:2673–82.