

## Some antidepressants linked to *Clostridium difficile* infection

Certain types of antidepressants have been linked to an increase in the risk of *Clostridium difficile* infection finds a study in *BMC Medicine* (Rogers et al, 2013). Awareness of this link should improve identification and early treatment of *C. difficile* infection.

*C. difficile* infection is one of the most common hospital-acquired infections, causing more than 7000 deaths each year in the USA. Several types of medications are thought to increase risk of *C. difficile* infection, including antidepressants, and a team from the University of Michigan investigated the exact nature of this risk.

They studied *C. difficile* infection in people with and without depression and found that people with major depression had a much higher chance of *C. difficile* infection (a 36% increase) than people without depression. This association held for a variety of depressive disorders and nervous or psychiatric problems.

Age and family support also affected the risk of *C. difficile* infection. Older, widowed Americans were 54% more likely to catch *C. difficile* than their married peers. Just living alone increased risk by 25%.

They then looked to see if there was an association

between antidepressant medication and hospital-acquired *C. difficile* infection. Use of most types of antidepressants did not affect *C. difficile* infection risk – of the twelve drugs tested only mirtazapine and fluoxetine increased risk of *C. difficile* infection, in each case the risk was doubled.

The researchers stress that it is not yet known whether the increase in *C. difficile* infection is caused by microbial changes in the gut during depression or to the medications associated with depression.

Dr Mary Rogers, who led this study, explained: 'Depression is common worldwide. We have

long known that depression is associated with changes in the gastrointestinal system. The interaction between the brain and the gut, called the "brain-gut axis" is fascinating and deserves more study.'

She continued: 'Our finding of a link between depression and *C. difficile* should help us better identify those at risk of infection and, perhaps, encourage exploration of the underlying brain-gut mechanisms involved.'

Rogers MA, Greene MT, Young VB, Saint S, Langa KM, Kao JY, Aronoff DM (2013) Depression, antidepressant medications, and risk of *Clostridium difficile* infection. *BMC Medicine* 11: 121

### Reducing risk of major disability in intracerebral haemorrhage

A new study, which involved more than 2800 patients from 140 hospitals around the world, found that intensive blood pressure lowering in patients with intracerebral haemorrhage, the most serious type of stroke, reduced the risk of major disability and improved chances of recovery by as much as 20% (Anderson et al, 2013).

Professor Thompson Robinson, Deputy Head, Department of Cardiovascular Sciences, University of Leicester, Leicester



Professor Thompson Robinson, Deputy Head of the Department of Cardiovascular Sciences, University of Leicester, was the UK coordinator for the study. He said: 'The results of the study show that intensively reducing high blood pressure within 6 hours of onset of a bleeding-related stroke is safe, and results in a significant shift from being dead and dependent to being alive and independent after stroke.'

He emphasized: 'Because it involves treatment with already available blood pressure-lowering treatments, the results should be easy to implement in all hospitals and be of benefit to patients.'

Anderson CS, Heeley E, Huang Y et al (2013) Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. *N Engl J Med* 29 May (Epub before print)

### Depression common in children with temporal lobe epilepsy

A new study determined that children and adolescents with seizures involving the temporal lobe are likely to have clinically significant behavioural problems and psychiatric illness, especially depression (Salpekar et al, 2013).

Research from the Children's National Medical Center in Washington, D.C highlights the importance of routine psychiatric evaluation for paediatric epilepsy patients – particularly those who do not respond to anti-seizure medications and require epilepsy surgery.

Researchers reviewed case records for 40 children between the ages of 6 and 17 years, who did not respond to anti-seizure medications. Patients were given pre-surgical psychiatric evaluations and their parents completed the Child Behavioral Checklist. The seizure location and suitability for surgi-

cal procedures were confirmed by epilepsy specialists.

The investigators found that these patients had psychiatric and behavioural problems well beyond what is typically reported in children with chronic epilepsy. Nearly 80% of participants had significant psychiatric symptoms – far greater than the 20–40% prevalence of mental illness generally found in chronic paediatric epilepsy.

Furthermore, children with seizures suspected to be localized in the temporal lobe were more likely to have depression symptoms and more significant behavioural issues reported by parents compared to children with seizures in other brain regions.

Salpekar JA, Berl MM, Havens K et al (2013) Psychiatric symptoms in children prior to epilepsy surgery differ according to suspected seizure focus. *Epilepsia* 10 May (Epub before print)

## Liver transplantation 'a valid option' for HIV-infected patients with hepatocellular carcinoma

Liver transplantation for hepatocellular carcinoma is feasible for HIV-infected patients, with no differences in post-transplant survival or hepatocellular carcinoma recurrence rates compared with liver transplantation for hepatocellular carcinoma in HIV-uninfected patients (Di Benedetto et al, 2013).

The study, led by Dr. Fabrizio Di Benedetto, Associate Professor of Surgery, University of Modena and Reggio Emilia, Modena, Italy, represents the largest multicentre study of liver transplant for hepatocellular carcinoma in HIV-infected patients to date.

Researchers evaluated post-transplant outcomes in 30 HIV-positive patients and 125 HIV-uninfected patients who underwent liver transplantation for hepatocellular carcinoma at three transplantation centres in northern Italy between 2004 and 2009.

Two patients in the HIV-positive cohort (6.7%) and 18 uninfected patients (14.4%) experienced a recurrence of hepatocellular carcinoma during the follow-up period of approximately 32 months ( $P=0.15$ ). Overall survival was similar for HIV-infected and -uninfected patients at 1 year (77% vs 86.4%) and 3 years

(65% vs 70%), respectively, after liver transplantation ( $P=0.32$ ).

'The key message of this study is that liver transplantation is a valid option for hepatocellular carcinoma treatment in HIV-infected patients,' said the authors. 'We suggest that HIV-infected patients must be offered the same liver transplant options for hepatocellular carcinoma treatment currently provided to HIV-uninfected subjects.'

Di Benedetto F, Tarantino G, Ercolani G et al (2013) Multicenter Italian experience in liver transplantation for hepatocellular carcinoma in HIV-infected patients. *The Oncologist* 18(5): 592-9

### Bigger birthweight babies at greater risk of autism

Babies whose growth is at either extreme in the womb are at greater risk of developing autism, according to new research published in the *American Journal of Psychiatry*. It is the first clear link between babies who grow to above average size at birth and risk of autism spectrum disorder.

### Targeted therapy for irritable bowel syndrome with constipation

Linaclotide (Constella) is available for the symptomatic treatment of moderate to severe irritable bowel syndrome with constipation in adults. Linaclotide is a first in class guanylate cyclase-C agonist that treats abdominal pain or discomfort, bloating and constipation. It has a dual mechanism of action and acts locally in the gastrointestinal tract.

### Voriconazole powder and solvent for solution for infusion

Voriconazole (Vfend) solution is now available as an all-in-one boxed kit for accurate reconstitution of the drug. A vial adapter and pre-filled solvent bag with a specific connector allows sterile, without the use of needles withdrawal of the reconstituted drug.

## Infants born to vaccinated mothers may lose initial measles immunity sooner than others

A Dutch study suggests that infants born to mothers who received the measles-mumps-rubella (MMR) vaccine lose their initial immunity to measles – acquired from their mothers – sooner than infants born to mothers who were naturally infected with measles (Waijnenborg et al, 2013).

The findings support earlier measles vaccination of infants where risk of exposure to measles is high, and infants who will be travelling to areas where measles is still endemic.

In the Netherlands, measles vaccination of young children was introduced in 1976 and the combined MMR vaccine was introduced in 1987. However, a portion of the Dutch population refuses vaccination based on religious beliefs, and endemic measles,

mumps, and rubella outbreaks still occur in the country.

Dr Sandra Waijnenborg and colleagues from the National Institute of Public Health and the Environment in the Netherlands studied the duration of protection against measles, mumps, and rubella by comparing antibody levels in infants in the general Dutch population with those of infants in orthodox protestant communities, where more mothers refuse vaccination, in 2006-7.

The investigators studied blood samples from randomly selected Dutch infants and women of childbearing age and measured the concentration of antibodies against viruses, comparing them against a level that is considered protective against infection. They then compared

antibody levels of the general population with those of the orthodox protestant community, where vaccination rates are low and outbreaks of measles, mumps, and rubella have been reported recently.

The duration of protection by passive immunity was shorter for infants born to mothers who received MMR vaccine than for infants born to mothers from a low vaccine coverage population. Duration of protection from measles was almost 2 months shorter for infants in the general public than for infants in the orthodox protestant communities.

Waijnenborg S, Hahné SJM, Mollema L et al (2013) Waning of maternal antibodies against measles, mumps, rubella, and varicella in communities with contrasting vaccination coverage. *J Infect Dis* 8 May (Epub before print)

**EUROPCR**  
PARIS, FRANCE, 21–24 MAY

## Optical coherence tomography gives insights into bioresorbable vascular scaffold position

Bioresorbable vascular scaffold implantation, guided by optical coherence tomography for accurate sizing, together with pre-dilatation and accurate post-deployment assessment are all vital to overcome problems arising from sub-optimal scaffold expansion and poor strut apposition rates.

Outlining the background to this research, Dr Nick West, Papworth Hospital NHS Foundation Trust, Cambridge,

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commented: ‘Suboptimal or incomplete metallic stent expansion is associated with increased rates of restenosis and target vessel revascularization.’

He continued: ‘While early clinical data suggest low complication rates, concerns remain regarding their mechanical strength and the incidence of recoil. Furthermore, there are limited real-world data on in-vivo bioresorbable vascular scaffold expansion rates.’

Dr West reported data on 25 bioresorbable vascular scaffolds implanted in 22 patients (mean age 57 years) under optical coherence tomography guidance. They showed that 99% of minimum scaffold diameters measured by optical coherence tomography (mean 2.84 mm) were smaller than those predicted from compliance charts (mean 3.43 mm).

Bioresorbable vascular scaffold expansion was significantly

reduced in central segments compared to peripheral segments (minimum scaffold diameter 79.9 vs 84.4%,  $P < 0.0001$ ; cross-sectional area 78.7% vs 84.6%,  $P < 0.0001$ ), an effect that persisted even in lesions that were aggressively predilated with 1:1 balloon:stent sizing.

Dr West commented: ‘... bioresorbable vascular scaffold expansion is significantly reduced in the region of treated target lesions. Since aggressive post-dilatation is not recommended, our data highlight the importance of optimal predilatation before bioresorbable vascular scaffold implantation.’

Dr West concluded: ‘Intracoronary imaging should be considered mandatory before implantation of bioresorbable vascular scaffolds to ensure unrecognized calcification does not lead to unnecessary malapposition.’

**Stephen Pinn**

## Cost effectiveness of renal sympathetic denervation in treating resistant hypertension

Use of renal sympathetic denervation results in substantial blood pressure reduction without serious procedure-related complications, but the economic consequences of this procedure had not previously been studied.

Dr Marc Dorenkamp from the Department of Cardiology, Charité Universitätsmedizin, Berlin, Germany and his colleagues used a Markov state-transition model to compare renal sympathetic denervation with best medical therapy in patients with resistant hypertension.

Renal sympathetic denervation gained 0.98 quality-adjusted life-years (QALYs) in men and 0.88 QALYs in women at 60 years of age at an additional cost of €2589 and €2044 respectively.

A willingness-to-pay threshold of €35 000/QALY gave a 95% probability that renal sympathetic denervation would be cost effective up to 78 years of age in men and 76 years in women.

They concluded that renal sympathetic denervation is cost effective for patients with resistant hypertension, and earlier treatment is more cost effective.

**Stephen Pinn**

## Renal sympathetic denervation improves nocturnal dipping in hypertensive patients

‘Nocturnal dipping’ is a phenomenon where a decrease in blood pressure of 10% or more occurs during sleep, and has been shown to be protective against cerebrovascular and cardiovascular disease.

Renal sympathetic denervation is an emerging treatment for patients with resistant hypertension, which reduces blood pressure in this group.

Dr Stephen Tuohy from University College Hospital,

Galway, Ireland outlined data from a study assessing the effect of renal sympathetic denervation on the 24-hour blood pressure profile of patients with resistant hypertension.

Twelve patients completed 9 months’ follow-up after bilateral renal artery ablations using the Symplicity system.

24-hour ambulatory blood pressure monitors showed an overall decrease of 5 mmHg systolic and 5.5 mmHg diasto-

lic despite a reduction of over 20% in antihypertensive medications. Both systolic and diastolic nocturnal dipping improved significantly.

Of the seven patients classified as diastolic non-dippers at baseline, four became diastolic nocturnal dippers.

Dr Tuohy concluded: ‘Renal sympathetic denervation is an effective method for management of resistant hypertension.’

**Stephen Pinn**

## 7TH GLOBAL ADDICTION CONFERENCE 2013 PISA, ITALY, 7–10 MAY

### Protocol reduces benzodiazepine deaths

Introducing a benzodiazepine prescribing guideline in a drug and alcohol service cut the volume of prescribing for these drugs by more than one-third over a year and was associated with a reduction in diazepam-related deaths, showed a study from NHS Lanarkshire.

‘In 2010 when we looked at the figures for drug-related deaths we saw a high prevalence of benzodiazepines reported as the cause – all diazepam,’ reported Dr Steve Conroy, Lead Medical Practitioner for Addiction.

The team developed a guideline to review all patients being treated by the drug and alcohol service who were prescribed an

opiate substitute and diazepam. The guideline increased the frequency of supply and supervision of benzodiazepines to daily. It also recommended prescribing only 2mg (white) diazepam tablets, which have the lowest value if sold illicitly and make dose reduction simpler.

The guidelines were implemented from 1 April 2011. ‘We saw a rapid reduction in the number of prescriptions for benzodiazepines and the volume supplied,’ said Dr Conroy. Within 3 months prescribing of diazepam 10 mg had nearly stopped and use of diazepam 5 mg was significantly reduced.

Within 12 months the service recorded a 16% reduction

in the number of prescriptions for benzodiazepines and a 35% reduction in the volume of benzodiazepine prescribed. There was a slight increase at 2 years but the volume of benzodiazepine prescribed was 26% lower than before the guideline was introduced.

Drug-related deaths involving diazepam in NHS Lanarkshire fell, in contrast to increases for Scotland as a whole. Diazepam accounted for only 6% of drug-related deaths in 2011 compared to 16% in 2010. The guideline is now used as part of routine practice and is also being used in GP surgeries.

**Susan Mayor**

### Outcomes system needed to evaluate opioid dependence management

A panel of European thought leaders agreed that universal outcome measures above the individual patient level are needed to more effectively assess the impact of services managing opioid dependence. These could define what recovery looks like at a clinical level.

‘Medical assisted therapy is an important strategy to address the health and social consequences associated with opioid dependence, which is a chronic relapsing medical condition that requires lifelong management,’ said Professor Icro Maremmani, Professor of Addiction Medicine, University of Pisa and University of Siena, Italy.

Many countries have an overall strategy for approaching opioid maintenance, but variations in treatment goals mean that it has not been possible to capture robust data on outcomes with opioid maintenance treatment.

When asked to vote on the issue, 92% of delegates agreed that developing a universal system for measuring outcomes would be a useful advance in opioid dependence management.

**Susan Mayor**

*Susan Mayor's attendance at the Global Addiction Conference and her time writing this report was supported financially by Reckitt-Benckiser Pharmaceuticals.*

### 1 in 3 patients diverts opioid maintenance therapy

The European Quality Audit of Opioid Treatment (EQUATOR) questioned 703 physicians working in addiction management, 2298 patients in treatment for drug dependence and 887 drug users not in treatment in 2010 to provide a snapshot of treatment experiences.

The main reasons the 248 UK patients began treatment was to improve their health (68%), reduce drug costs (63%) and end their dependence for good (60%). But Dr Farrukh Alam, Consultant Psychiatrist and Clinical Director of Central and Northwest London NHS Foundation Trust, felt that aspirations to end dependence were falling short in the UK, as shown by high diversion rates.

Nearly one-third (30%) of the UK patients taking part in

the survey said that they had ever sold, swapped or given away their opioid maintenance therapy – higher than the rate for Europe as a whole (24%).

Dr Alam suggested possible reasons: ‘Supervision of dosing may not always happen as it should, enabling patients to divert their opioid maintenance therapy, and limited use of some abuse-deterrent opioid maintenance therapy formulations may also provide clues to diversion rates.’

Only 1% of UK patients in the survey were treated with the abuse deterrent form of buprenorphine (buprenorphine-naloxone), the lowest rate of any country taking part in EQUATOR (average 14%).

During a session on health policy, Mark Gilman, Strategic Recovery Lead at Public Health England, said that

services will be making more assertive links to mutual support groups, including Narcotics Anonymous and SMART Recovery. UK clinicians in the audience challenged Mr Gilman to produce guidance on what clinical outcomes should be targeted and measured to establish that recovery is being achieved.

**Susan Mayor**

Mark Gilman, Strategic Recovery Lead, Public Health England

