

cohort. The babies of women who tried for longer than one year to conceive their first child had a higher risk of neonatal death than those conceived sooner (adjusted odds ratio 2.82, 95% confidence interval 1.35 to 5.90). The finding needs to be corroborated elsewhere, the authors say.

Locked-in syndrome

In the locked-in syndrome, which is caused by damage to the ventral pons and leaves

the patient with quadriplegia, anarthria, and preserved consciousness, the 10 year survival rate is as high as 80%. This week's clinical review by Smith and Delargy (p 406) summarises what is known about the clinical features, classification, diagnosis, management, and prognosis of patients with locked-in syndrome. The authors emphasise the need for early rehabilitation management, which can significantly improve the quality of life of these patients and their carers.

POEM*

Combined vaginal treatment is more effective for bacterial vaginosis

Question Are metronidazole plus nystatin vaginal ovules a more effective treatment for bacterial vaginosis than metronidazole gel (Metrogel)?

Synopsis In Peru, the most commonly prescribed medication for treatment of vaginal discharge or malodour is intravaginal ovules with metronidazole 500 mg plus nystatin 100 000 U to be used nightly for five to seven nights. Researchers from Peru and the University of Washington compared the combined product with metronidazole 0.75% gel (Metrogel), 37.5 mg in one prefilled applicator nightly for five nights. Healthcare providers were blinded to treatment assignment, but patients knew which treatment they were using. The person who evaluated the diagnosis of bacterial vaginosis at follow up visits was also blinded to the treatment received. Women (n = 151) were enrolled if they complained of vaginal discharge or malodour and met criteria for diagnosis of bacterial vaginosis when at least three of four Amsel's criteria were present and a Gram stain had a Nugent score of 7-10. Follow up visits were at 14, 42, and 104 days after the baseline visit. A total of 138 (91%) of the women returned for evaluation at least once; 75 (50%) returned for all three follow up visits. At first follow up, five of 69 (7%) women treated with the ovules versus 18 of 69 (26%) treated with gel met both sets of criteria for diagnosis of bacterial vaginosis (number needed to treat = 5; 95% confidence interval 3 to 15). At subsequent visits the percentages were 17% v 38% and 33% v 52%, respectively.

Bottom line Metronidazole plus nystatin ovules resulted in higher cure rates than metronidazole gel in women with symptomatic bacterial vaginosis in this small study. It is not clear whether the better results were due to the higher metronidazole dose or the addition of nystatin. The combined product has not yet been marketed in the United States.

Level of evidence 1b (see www.infoPOEMs.com/levels.html). Individual randomised controlled trial (with narrow confidence interval).

Sanchez S, Garcia PJ, Thomas KK, Catlin M, Holmes KK. Intravaginal metronidazole gel versus metronidazole plus nystatin ovules for bacterial vaginosis: a randomized controlled trial. *Am J Obstet Gynecol* 2004; 191:1898-906.

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* Patient-Oriented Evidence that Matters. See editorial (*BMJ* 2002;325:983)

Editor's choice

Pills, thrills, and bellyaches

Drug safety, regulation, and happiness continue to dominate the health agenda. Last summer, New York's district attorney Elliot Spitzer forced GlaxoSmithKline to publish undisclosed trial results of paroxetine (*BMJ* 2004;328:1513). US and European drug regulators reassessed the use of selective serotonin reuptake inhibitors to treat depression in children—a condition that some psychiatrists argue should not be treated with drugs (p 418). In October the US Food and Drug Administration directed manufacturers to include a “black box” label warning about all antidepressants and risk of suicidal thoughts and suicide attempts in children.

It isn't just SSRIs that have taken a battering. Manufacturers of COX-2 inhibitors continue to reel from exposure of the link between rofecoxib and cardiovascular toxicity (p 381; *BMJ* 2004;329:867). The conduct of drug companies and regulatory authorities is under intense scrutiny from parliamentary committees, patient representative groups, and medical journals. Why have we become obsessed with drug safety? Is there some hidden—or not so hidden—campaign to destroy drugs and drug companies? The simple answer is no.

Hundreds of millions of people around the world depend on the innovation and product development skills of one of the richest industries to improve—or just prolong—their lives. Yet amidst this swirl of business creativity and pursuit of effective treatments there is an important failing—an information gap produced by incomplete data on drug harms. The purpose of filling the harms gap is not to ban drugs but to offer doctors reliable information to present to patients, who in turn can make an informed judgment before beginning drug treatment. Nor is the point to single out the pharmaceutical industry; regulators have an important responsibility here. And debates at the *BMJ* about what to publish increasingly focus on the importance of quantifying risk to help doctors help their patients (p 394).

In this spirit we present three papers, spontaneously submitted to us, on SSRIs and the risk of self harm and suicide. The messages are sometimes complex but simply put they are these. SSRIs may be associated with a doubling of risk of suicide attempts when compared with placebo (p 396). Increased risk of completed suicides cannot be ruled out, although the strength of evidence submitted to the UK's drug regulator might even be compatible with a beneficial effect (p 385). Patients should be warned of the potential hazard and monitored closely in the early stages of treatment. More research is urgently needed on the indications for treatment with SSRIs and identifying those at risk. SSRIs and tricyclic antidepressants have a similar risk profile for suicide and self harm but SSRIs increase risk of self harm in under 18s (p 389). The debate is not yet done, but these papers crystallise arguments that have been drifting in the ether these past months (p 373). How many people who turned to “happy pills” would not have done so if they had been fully aware of the potential harms?

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