

**SMOKE IN YOUR PANCREAS?**

Cigarette smoking — whether active or passive — may play a role in the development of glucose intolerance, suggest US researchers. They followed over 4500 young adults for 15 years as part of the Coronary Artery Risk Development In young Adults (CARDIA) study, looking at the relationship between smoking and glucose intolerance. A dose–response effect was found — increasing pack-years of smoking was linked with an increased risk of developing glucose intolerance. Further, those with passive tobacco smoke exposure were at greater risk than previous smokers. The researchers said passive smoke contains similar toxins to active smoke but is produced at different temperatures and different reducing conditions; thus, some toxic substances are even more concentrated in passive smoke. Smoking has previously been linked with chronic pancreatitis and pancreatic cancer, suggesting that tobacco smoke may be directly toxic to the pancreas.

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**STROKE BY MUTANT GENE**

People with a mutation in a specific gene may be predisposed, especially after environmental stress, to haemorrhagic stroke, says a group of international researchers.<sup>1</sup> The gene, *COL4A1*, affects the assembly of Type IV collagen, a component of the vascular basement membrane.<sup>2</sup> Gould and colleagues found that newborn and adult mice with a mutation in the equivalent mouse gene were at risk of trauma-associated intracerebral haemorrhage. They also identified a human family with a *COL4A1* mutation — members had experienced small-vessel brain disease, including retinal arteriolar tortuosity as well as intracerebral haemorrhage. The researchers suggested that the presence of the mutation compromises the vascular basement membrane and weakens the vessel.

1. *N Engl J Med* 2006; 354: 1489-1496

2. *N Engl J Med* 2006; 354: 1451-1453

**WAS PAULING RIGHT?**

Three decades ago, two-time Nobel Prize winner Linus Pauling co-authored papers which reported that high-dose vitamin C (ascorbic acid) therapy prolonged survival in patients with terminal cancer.<sup>1</sup> However, the treatment strategy was discarded when subsequent randomised clinical trials based at the Mayo Clinic did not confirm the benefit. Now, North American authors are calling for Vitamin C's role to be reassessed.<sup>2</sup>

Padayatty and colleagues reported three cases of usually progressive, advanced malignant disease (a renal cell carcinoma, a transitional cell bladder carcinoma and a diffuse large B cell lymphoma) that were effectively treated with high-dose intravenous vitamin C therapy. Although each case had a possible alternative explanation for good outcome, both the case report authors and commentators pointed out that there is a new known biological plausibility worthy of closer study — in vitro, high levels of vitamin C are selectively toxic to various cancer cell lines but not to normal cells, by a mechanism involving hydrogen peroxide.<sup>2,3</sup> Such high doses are achievable only with intravenous administration, as used by Pauling and in these reported cases; the Mayo Clinic studies used only oral administration.

1. *Proc Natl Acad Sci USA* 1976; 73: 3685-3689

2. *CMAJ* 2006; 174: 937-942

3. *CMAJ* 2006; 174: 956-957

**UPPING THE ANTI**

The HPV Vaccine Study Group has reported a follow-up study to their randomised controlled trial of a bivalent L1 virus-like particle vaccine against human papillomavirus types 16 and 18.<sup>1</sup> The original trial results were published in the *Lancet* in 2004.<sup>2</sup> At 4.5 years of follow-up, the story remains: “so far, so good”. The vaccine remains not only efficacious against HPV infection but also safe. Further, there is now evidence of cross-protection against infection with two other common HPV types associated with cervical cancers (HPV types 45 and 31).

1. *Lancet online*, 6 April 2006

2. *Lancet* 2004; 364: 1757-1765

**A BIT DEPRESSED?**

Which older patients with mild depression are most likely to benefit from close clinical monitoring? Analysis of data from the US PRevention Of Suicide in Primary care Elderly: Collaborative Trial (PROSPECT) has identified a trio of risk factors for a worse depressive outcome a year down the track — comorbidity, poor self-rated health and less social support.<sup>1,2</sup> An editorialist said that, like diabetes, hypertension and many other chronic medical disorders, depression also fluctuates in severity and requires regular monitoring and therapeutic adjustments.<sup>2</sup> The presence or absence of the three risk factors may help doctors target those most likely to benefit from a close eye.

1. *Ann Intern Med* 2006; 144: 496-504

2. *Ann Intern Med* 2006; 144: 528-530

**DIETING: THE ANTI-AGEING EFFECT**

Australia-based researcher Leonie Heilbronn is first author of an original *JAMA* article which reports that 6 months of calorie restriction in 48 overweight but otherwise healthy adults led not only to reduced weight but also favourable changes in biomarkers of longevity, such as fasting insulin level and core body temperature. Further, there was reduced damage to DNA.

*JAMA* 2006; 295: 1539-1548

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