Short cuts

What's new in the other general journals

Smoking seems to be on the rise among young Indian urban teenagers

A study from India reports that the prevalence of smoking among primary school students (aged 10-16) in two cities, Delhi and Chennai, is two to four times as high in sixth grade students than in eighth grade students. The cross sectional survey, with a response rate of over 90%, included more than 11 000 students from governmental and private schools. Overall, nearly 15% of students had ever used tobacco and almost 5% were current users. The prevalence was significantly higher among boys than girls (17% *v* 11%), governmental schools than private schools (17% *v* 11%), and sixth graders than eighth graders (25% *v* 9%).

Young adolescents are particularly likely to internalise messages from society, say the authors. India is a leader in global tobacco control and prohibits all direct and indirect advertising of tobacco products, smoking in public places, sales of tobacco products to people under 18, and sales of tobacco products near educational institutions. The findings in this survey suggest, however, that young urban teenagers are starting to use tobacco at increased rates. Since early use of tobacco predicts greater likelihood of addiction, longer lifetime use, and higher rates of lung cancer, these findings are important to public health.

Lancet 2006;367:589-94

Rimonabant can help treat obesity

Rimonabant, a selective cannabinoid-1 receptor blocker, could be a novel aid in treating obesity. In the RIO-North America double blind controlled trial, researchers randomised 3045 overweight or obese people to placebo, 5 mg per day of rimonabant, or 20 mg per day of rimonabant for one year, all in addition to diet and exercise. After one year, people receiving rimonabant were randomised to placebo or continued with the same dose of rimonabant during year two.

People who were taking 20 mg of rimonabant lost more weight than those in the control group (6.3 (SE 0.2) kg *v* 1.6 (0.2) kg; *P* < 0.001), had a greater reduction in waist circumference and triglyceride concentrations, and had a higher increase in high density lipoprotein concentrations. People who continued with rimonabant

during year two maintained the favourable effects, but those who switched to placebo did not.

The main limitation of the trial was a high dropout rate: almost half of the participants discontinued the programme by the end of year one, and only about a third of those who were randomised again finished the trial. However, the beneficial effects of rimonabant remained after researchers used different imputation methods to adjust for drop-out.

JAMA 2006;295:761-75

TNF- α axis is upregulated in refractory asthma and etanercept shows promise in treating it

A new piece has been fitted into the puzzle of the role of TNF- α in the pathogenesis of asthma and TNF (tumour necrosis factor) inhibitors in treating it. A study of 10 people with refractory asthma, 10 with mild to moderate asthma, and 10 healthy controls showed that TNF- α axis is upregulated in patients with refractory asthma. Compared with the other two groups, people with refractory asthma had higher expression of membrane bound TNF- α , TNF receptor 1, and TNF- α

converting enzyme by monocytes in peripheral blood.

A 10 week, placebo controlled randomised double blind crossover pilot study of people with refractory asthma showed that etanercept—soluble TNF receptor fused to human IgG—significantly reduced the baseline expression of membrane bound TNF- α by peripheral blood monocytes and improved PC₂₀, the asthma related quality of life, FEV₁, and symptom scores, compared with placebo.

TNF- α inhibitors can cause serious adverse effects, which include reactions at the site of injection, demyelinating disorders, lymphoproliferative diseases, and the reactivation of tuberculosis with dissemination to the miliary form. One patient withdrew from the pilot study due to developing productive cough and repeated isolation of *Haemophilus influenzae* despite a course of oral antibiotics. It would be prudent to wait for the results of large ongoing multicentre trials before TNF- α inhibitors are used in individual patients, warns the accompanying editorial (pp 754-8).

N Engl J Med 2006;354:697-708

Autoimmunity is a prognostic marker of advanced melanoma

People with advanced stages of melanoma (American Joint Committee on Cancer stage IIB, IIC, or III) have poor prognosis and are candidates for adjuvant postoperative treatment with interferon alfa-2b—but its serious side effects (most people have fatigue, fever, arthralgias, anorexia, and toxic hepatic effects, and some have severe depression), the

high cost of treatment, and evidence that only a subgroup of patients benefits from the treatment all limit uptake of treatment.

This study explored the association between serological and clinical signs of autoimmune response and prognosis in 200 people with advanced melanoma who were participating in a larger ongoing randomised controlled trial. During a median follow-up of 45 months, 115 patients had a relapse and 82 died. However, of 52 patients with manifestations of autoimmunity, only seven had a relapse and two died. The occurrence of autoimmunity was associated with a 50-fold reduction in the risk of a relapse and a significant increase of relapse-free and overall survival.

The accompanying editorial warns that, since autoimmunity was observed a median of three months after the start of the treatment, it cannot yet be used for prospective identification of patients who will benefit from interferon, sparing the rest from ineffective toxic treatment.

N Engl J Med 2006;354:709-18

Functional capacity and heart rate recovery are independently associated with socioeconomic status

We know that lower socioeconomic status confers greater risk of cardiovascular morbidity and mortality, but mechanisms for this are unclear. A group of researchers has pinpointed functional capacity and heart rate recovery after exercise, both modifiable physiological characteristics, as potential partial explanations.

More than 30 000 consecutive patients who were referred to symptom-limited treadmill stress testing for evaluation of known or suspected coronary artery disease were included in a prospective cohort study that had a median follow-up of 6.5 years. Lower socioeconomic status was significantly associated with impaired functional capacity, and this remained robust after adjustment for demographic and clinical confounders. Similarly, the likelihood of an abnormal heart rate recovery increased as socioeconomic status score decreased. Further, functional

capacity and heart rate recovery explained almost half of the association between socioeconomic status and all cause mortality.

Although the study population may not be representative of the general population and the observed associations may not be causal, these factors could help identify disadvantaged people at greatest risk in a clinical setting. Also, the two physiological characteristics could be used to monitor the effectiveness of population based interventions to reduce disparities in mortality. The authors say that their results support policy approaches that, for example, invest in recreational facilities.

JAMA 2006;295:784-92

Calcium and vitamin D supplements don't seem to protect against bone fractures . . .

A report of a women's health initiative trial that included more than 35 000 healthy postmenopausal women adds to the evidence against the protective role of food supplementation with calcium and vitamin D against bone fractures. Women aged between 50 and 79 at baseline were randomised to receive 500 mg of elemental calcium as calcium carbonate with 200 IU of vitamin D-3 twice daily or placebo. After an average follow-up of seven years, women who were taking calcium and vitamin D supplementation had significantly greater hip bone density than women randomised to placebo, but there was no difference in the rate of hip and total fractures. Women who were taking supplements had a higher risk of kidney stones (hazard ratio 1.17, 95% CI 1.02 to 1.34).

N Engl J Med 2006;354:669-83

. . . nor do they seem to protect against colorectal cancer

The report of the designated secondary outcome in the women's health initiative trial of food supplementation with calcium and vitamin D failed to support previous findings from observational studies that such supplementation might protect against colorectal cancer. After seven years of follow-up, the incidence of invasive colorectal cancer was similar in the placebo and the intervention group (hazard ratio 1.08, 95% CI 0.86 to 1.34), as were tumour characteristics. The accompanying editorial (pp 750-2) discusses the reasons that might have led to masking of the effect in the trial and a false negative finding: women's age, duration of follow-up, and too low a dose.

N Engl J Med 2006;354:684-96

Myocardial infarction should not be treated with facilitated angioplasty

The ASSENT-4 percutaneous coronary intervention trial, the largest to date comparing facilitated and standard primary angioplasty for myocardial infarction—and an updated systematic review that includes this trial—clearly show that facilitated angioplasty (use of pharmacological treatment before a planned immediate percutaneous coronary intervention) should be avoided. The trial was planned to include 4000 people but was stopped after recruiting less than a third because significantly more patients randomised to receive tenecteplase before angioplasty died in hospital (6% *v* 3%). People who received tenecteplase also had a 40% greater risk of the primary end point (death or congestive heart failure or shock within 90 days) and significantly more strokes and ischaemic cardiac complications than people randomised to the standard intervention.

The systematic review, which included 17 trials and 4500 patients, found that facilitated regimens more than doubled the number of patients with pre-interventional TMI grade 3 flow, but they were also associated with significantly higher rates for mortality, non-fatal reinfarction, urgent target vessel revascularisation, major bleeding, and stroke. Regimens that included thrombolytic therapy had the highest rates of adverse events.

The accompanying commentary summarises the evidence for treatment of myocardial infarction and asks the question that is still open to researchers: how much delay to primary angioplasty is acceptable before thrombolytic treatment should be given instead.

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