

SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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Hints of a link between paracetamol and asthma deserve a closer look

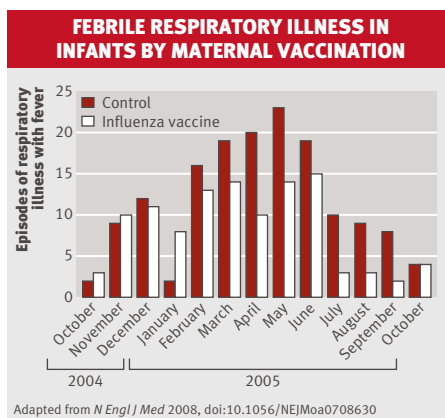
The prevalence of asthma in childhood has gone up dramatically since the 1950s. So has the use of paracetamol for febrile infants. Looking for a possible link, researchers analysed cross sectional data from more than 200 000 children living in 31 different countries. Those given paracetamol during the first year of life were significantly more likely to have wheeze (odds ratio 1.46, 95% CI 1.36 to 1.56), severe asthma symptoms (1.43, 1.30 to 1.58), rhinoconjunctivitis (1.48, 1.38 to 1.60), or eczema (1.35, 1.26 to 1.45) at the age of 6 or 7 than those who weren't. Current use of paracetamol was also associated with symptoms in 6 and 7 year olds.

One explanation is that paracetamol causes childhood asthma. The other is that these associations are artefacts of the study's methods and analysis, says an editorial (pp 1011-2). All the data came from parental questionnaires. Parents with wheezy children may be more likely than others to remember giving paracetamol in infancy (recall bias); babies given paracetamol may have had viral infections that increase the risk of wheeze later in childhood; they may also have been given other treatments not captured by the questionnaires such as ibuprofen (confounding). The researchers agree that observational data, however extensive, can never establish causality. It's much too early to start warning parents not to give paracetamol to their children.

Lancet 2008;372:1039-48, 1011-2

Vaccinating pregnant women protects infants against influenza

Influenza is a serious infection for small babies. Since vaccines aren't licensed for this age group, could they be protected by vaccinating mothers during pregnancy instead? Maternal vaccination worked reasonably well for both mothers and babies in a randomised trial in Bangladesh. A trivalent inactivated vaccine reduced the incidence of confirmed influenza by 63% (95% CI 5% to 85%) among babies up to 6 months old, compared with a control pneumococcal vaccine. Babies of mothers given the influenza vaccine had 29% (7% to 46%) fewer febrile respiratory illnesses



than control babies. Their mothers had 36% (4% to 57%) fewer febrile respiratory illnesses than control mothers.

Overall, 340 women took part in the trial. All were vaccinated in the third trimester of pregnancy. Their babies were further randomised to test the immunogenicity and safety of the pneumococcal vaccine. The influenza results were analysed independently and seemed unaffected by this parallel trial.

The World Health Organization has recommended vaccinating pregnant women against influenza since 2005, but so far few have received it. This new evidence should help, say the researchers. They estimate that fewer than 16 women would need to be vaccinated to prevent one case of influenza in an infant.

N Engl J Med 2008, doi:10.1056/NEJMoa0708630

Cirrhosis caused by hepatitis C can be reversible

New evidence suggests that cirrhosis of the liver caused by hepatitis C could be reversible, at least in some patients. In a case series from France, 18 out of 96 patients had regression of cirrhosis after antiviral treatment. In one patient, cirrhosis improved despite enduring viraemia.

Researchers followed patients for nearly 10 years after a course of interferon with or without ribavirin. Regression of cirrhosis confirmed by biopsy was associated with a significantly better clinical outcome. None of the 18 patients with regression died of liver disease or needed a transplant during

follow-up, compared with 22 of the 78 (28%) without regression ($P=0.01$). Patients with a good virological response to treatment also did significantly better than the rest. These authors defined a good response as clearance of viral RNA from the blood and normal concentrations of alanine aminotransferase during follow-up.

This series isn't the first to suggest that cirrhosis can get better, says an accompanying editorial (pp 427-9), and it's probably time we stopped thinking of cirrhotic scarring as permanent. It may become permanent eventually, but treatment with antiviral agents is probably justified for those who can tolerate it.

Ann Intern Med 2008;149:399-403, 427-9

CT colonography is a sensitive screening tool for larger colorectal lesions

Computed tomography (CT) of the colon is a non invasive tool for screening asymptomatic individuals for colorectal cancers and adenomas. Compared with colonoscopy, CT had a sensitivity of 0.9 (95% CI 0.84 to 0.96) in the most recent and largest prospective study to compare the two. In other words, the less invasive option correctly identified 90% of the larger adenomas and cancers (≥ 10 mm in diameter) detected by colonoscopy. Sensitivity for smaller adenomas (≥ 6 mm) was 0.78 (0.71 to 0.85).

So CT is good at finding the bigger and most clinically important lesions, but there is a downside, says an editorial (pp 1285-7). About 17% of the participants had what looked like a large polyp on their CT scan: three quarters of them turned out to be false alarms. CT also tends to pick up extracolonic lesions that may not be clinically relevant, triggering further investigations and incurring costs. Patients choosing between the two must bear in mind the radiation dose associated with repeated screening scans, and the fact that a positive scan must be confirmed with a diagnostic colonoscopy.

In this study, 2531 asymptomatic adults had both screening tests. Most were white and middle aged. Fewer than one in 10 had a family history of colorectal polyps or cancer.

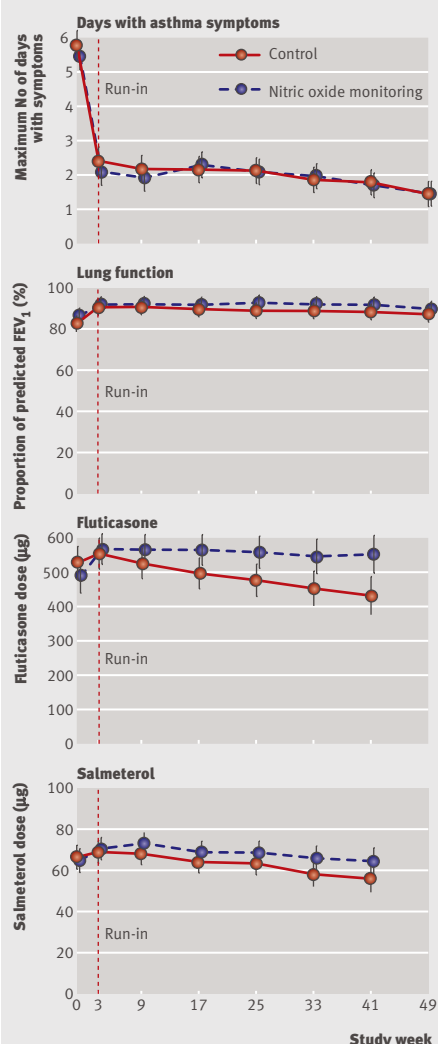
N Engl J Med 2008;359:1207-17, 1285-7

Nitric oxide monitoring of little use to most adolescents with asthma

Exhaled nitric oxide is an indirect marker for airway inflammation. In theory it should be a useful test of asthma control that helps guide treatment decisions. Results of the biggest trial so far have been disappointing, however. The addition of exhaled nitric oxide to standard monitoring and management based on authoritative guidelines made no difference to asthma symptoms, exacerbations, or pulmonary function in 546 US adolescents. The study was cleverly blinded by measuring exhaled nitric oxide in all participants but allowing a computer program to generate a management plan with or without the nitric oxide measurement.

Participants who had the extra monitoring had higher doses of inhaled corticosteroid than controls during the 46 week study (118.9 µg more fluticasone per day by the final visit; 95%

ASTHMA OUTCOMES AND DRUGS USE



Adapted from *Lancet* 2008;372:1065-72

CI 48.5 to 189.3). The extra treatment had no clinical benefits, except possibly among participants with a body mass index of at least 30 and those with multiple allergies. In both subgroups, monitoring of exhaled nitric oxide was associated with fewer days with asthma symptoms. But the numbers were small and these positive results are still preliminary, say the authors.

Lancet 2008;372:1065-72

Pelvic floor symptoms are common and increase with age, weight, parity, and poverty

Almost a quarter of US women have a symptomatic pelvic floor disorder (23.7%, 95% CI 21.2% to 26.2%), according to a nationally representative survey. One in six respondents reported urinary incontinence (15.7%, 13.2% to 18.2%), one in 11 reported faecal incontinence (9.0%, 7.3% to 10.7%), and just under 3% reported symptomatic prolapse (2.9%, 2.1% to 3.7%).

The prevalence of urinary incontinence increased with age, parity, family poverty, and body mass index. The prevalence of faecal incontinence increased in line with age and body mass index. Obese women were twice as likely to have a pelvic floor disorder than women of normal weight (30.4% (25.8% to 35.0%) v 15.1% (11.6% to 18.7%)).

Questions about pelvic floor symptoms were added to the US National Health and Nutrition Examination Survey in 2005. The survey had a response rate of 75%, and included data from 1961 women over 20 years old from across the US. Women living in institutions were excluded. Participants were not examined, so their responses are likely to underestimate the true prevalence of anatomical abnormality of the pelvic floor, say the authors.

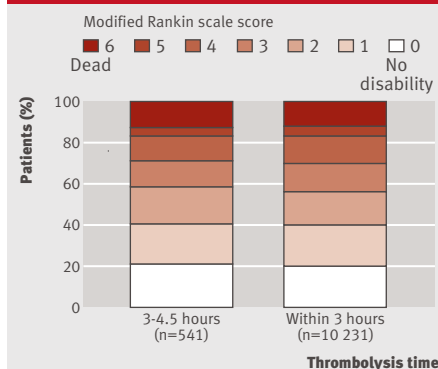
JAMA 2008;300:1311-6

Late thrombolysis probably safe for patients with stroke

Only a minority of patients with ischaemic stroke get to hospital fast enough for thrombolysis, which must be given within three hours of symptom onset. Circumstantial evidence suggests that this brief window of opportunity could be extended, and randomised trials are on the way. In the meantime, researchers have been analysing observational data on safety from an international register of patients treated with alteplase.

The results look promising. The 664 patients treated during 3-4.5 hours after the start of

TIME OF THROMBOLYSIS FOR STROKE PATIENTS AND MODIFIED RANKIN SCALE SCORE AT 3 MONTHS



Adapted from *Lancet* 2008, doi:10.1016/S0140-6736(08)61339-2

symptoms were no more likely to die than patients treated more quickly (odds ratio 1.02, 95% CI 0.90 to 1.17) and were no less likely to recover their independence (1.04, 0.95 to 1.13) and no more likely to have a symptomatic intracranial bleed (1.18, 0.89 to 1.55). The differences remained non-significant, though more borderline, once the researchers adjusted for the fact that patients treated late were slightly younger and fitter than the rest.

An editorial (doi:10.1016/S0140-6736(08)61340-9) says the results remain reassuring, particularly for patients treated soon after the deadline: 60% of the patients treated late missed the three hour window by 20 minutes or less.

Lancet 2008, doi:10.1016/S0140-6736(08)61339-2

Young adults with bicuspid aortic valve have normal medium term survival

Young adults with a bicuspid aortic valve have about the same 10 year survival rate as the general population, according to a cohort study from Canada. The 642 men and women had a mean age of 35 when referred to specialist centres for a cardiac assessment. Twenty eight of them died during an average of nine years' follow-up, giving an estimated 10 year survival of 96%. Adults of the same age and sex in the general population have an estimated 10 year survival of 97%, say the authors.

A quarter of the cohort had some kind of cardiac event, most commonly surgery involving the aortic valve or ascending aorta (142/642, 22%). Seventeen (3%) died a cardiac death, most commonly heart failure. Only 11 (2%) had an aortic complication such as dissection or aneurysm, but almost half had a dilated aortic sinus or ascending aorta at their last assessment (280/619, 45%).

JAMA 2008;300:1317-25

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