# SHORT CUTS

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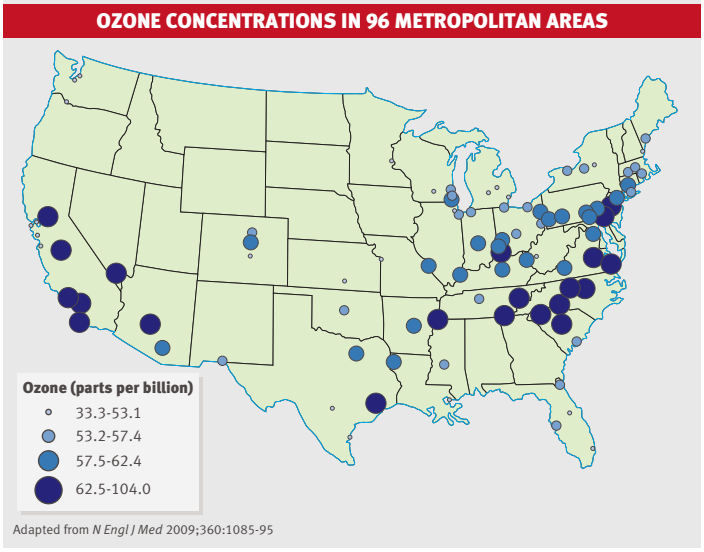
## Air pollution from ozone implicated in deaths from respiratory disease




Adapted from *N Engl J Med* 2009;360:1085-95

Scientists have long suspected that exposure to the air pollutant ozone might cause harm, but it has been hard to prove. A study from the US now reports the most convincing evidence to date—among nearly half a million US citizens, incremental increases in local ozone concentrations were associated with small but significant increases in the risk of death from respiratory causes (relative risk 1.040, 95% CI 1.010 to 1.067 for each increment of 10 parts per billion).

The link between ozone and respiratory deaths was independent of the harm caused by small particle pollution, and it survived adjustment for 20 potentially confounding factors such as poverty and smoking. It is also biologically plausible, say the authors. We already know ozone can inflame airways and cause asthma. Ozone was not associated with excess deaths overall, or deaths from cardiovascular disease.

The authors analysed data from an established cohort of adults living in 96 metropolitan areas across 50 states. The cohort was recruited in 1982 and followed for 18 years. There were 118 777 deaths. The Environmental Protection Agency's pollution monitors provided hourly readings for ozone concentration and enough data on small particle pollution to confirm a significant association between small particles and deaths from cardiovascular disease (1.206, 1.150 to 1.264).

***N Engl J Med*** 2009;360:1085-95

## New diagnostic test for a lethal genetic cardiomyopathy

Arrhythmogenic right ventricular cardiomyopathy causes potentially lethal arrhythmias and is one cause of sudden death in young people. About 40% of cases have a genetic component, and reliable diagnostic tests are urgently needed to help evaluate young people with warning arrhythmias and the relatives of people known to have the disease. Researchers from the US hope their recently developed technique will fit the bill. The test uses immunohistochemical analysis of an endomyocardial biopsy to look for a signal from one of the proteins seen at junctions between cells. In samples from known cases and controls, a low signal from the protein plakoglobulin had a diagnostic sensitivity of 91%, a specificity of 82%, a positive predictive value of 83%, and a negative predictive value of 90%. A low plakoglobulin signal was consistently visible in samples from known cases and consistently missing from samples from controls with no heart disease or end stage heart disease caused by something else. In cases, a low plakoglobulin signal was distributed throughout the heart, so it would be hard to miss with conventional biopsy techniques.

These authors performed a series of comparative experiments in just a few dozen samples. The test looks hopeful, they write, but we have some way to go before it is fit for routine practice.

***N Engl J Med*** 2009;360:1075-84

## Heart attack patients do better with a normal or near normal blood sugar

Hyperglycaemia is common in people admitted to hospital with heart attack but cardiologists disagree about how aggressively to treat it. In one cohort from 40 hospitals across the US, 39% (3049/7820) of patients who were hyperglycaemic after a myocardial infarction were given insulin. Further analyses of all 7820 patients found an independent association between higher serum concentrations of glucose after admission and a higher in-hospital mortality. Odds ratios relative to a normal concentration rose from 2.1 (95% CI 1.3 to 3.5) for concentrations 6.11-7.77 mmol/l to 13.0 (8.0 to 21.3) for concentrations of 11.1 mmol/l or more. The advantage of a lower post-admission glucose concentration persisted regardless of whether patients were given insulin. So it is the normalisation of blood sugar that counts, not how you achieve it, say the authors. The results were the same for people with and without diabetes.

In this retrospective observational study, people with glucose concentrations between 4.44 mmol/l and 7.22 mmol/l had the lowest adjusted mortality. Strategies to achieve this target should be tested in randomised trials, they write. Hyperglycaemia settles spontaneously in some patients, but they are hard to identify on admission. In reality, strategies to control blood glucose concentrations in patients with heart attack should probably start with insulin.

***Arch Intern Med*** 2009;169:438-46

## Delayed fatherhood linked to subtle impairments in children's intelligence

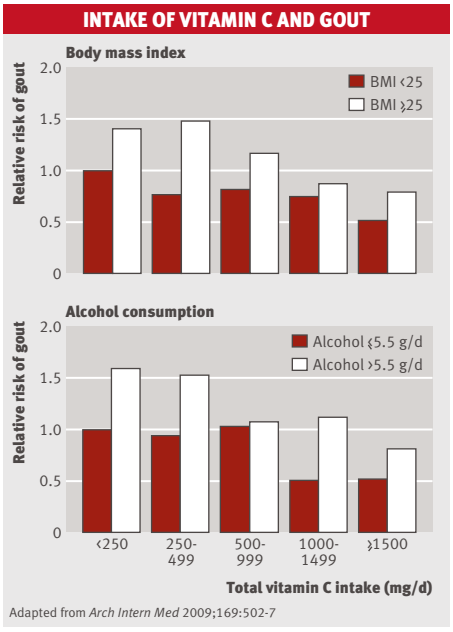
The children of older fathers had subtle but discernible neurocognitive deficits compared with the children of younger fathers in a cohort study of more than 33 000 children. They were born in the US between 1959 and 1965 and completed a range of tests up to the age of 7, designed to measure motor skills and cognitive abilities including concentration, memory, learning, speaking, and reading. All test scores, except those for motor skills, went down as paternal age went up, even in models adjusted for parental mental health, the child's sex, gestational age, mother's age, and measures of poverty. In

the fully adjusted model, children born to fathers aged 20 had estimated IQ scores of 105, compared with 103 for children born to fathers aged 50. Maternal age at birth had the opposite effect. The children of older mothers had higher test scores than the children of younger mothers.

The children in this study were born a long time ago. But the authors are fairly confident that their findings are still relevant to more recent birth cohorts. New fathers are getting older in many developed countries, they write. Even the subtle effects detected in this study could have public health consequences when played out across large populations.

***PLoS Med*** 2009;6:e1000040

## High vitamin C intake may help prevent gout




Adapted from *Arch Intern Med* 2009;169:502-7

Gout is common, painful, and hard to treat. A high daily intake of vitamin C may be one way to prevent it, according to a large cohort study. The 46 994 US health professionals were recruited in 1986 and filed detailed dietary reports every two years that researchers translated into average intakes of vitamin C. Higher intakes from dietary sources or supplements were associated with a lower risk of gout during 20 years of follow-up (relative risk per 500 g increase in total daily vitamin C 0.83, 95% CI 0.77 to 0.90).

The vitamin C effect was independent of the men's use of alcohol, body mass index, use of diuretics, age, hypertension, and renal function. It also survived adjustments for other dietary risk factors for gout, such as intake of dairy products and meat.

We already have good evidence that even modest doses of supplementary vitamin C can increase urinary excretion of uric acid and bring down serum concentrations, say the researchers. These new findings suggest this uricosuric effect may actually prevent gout, at least in middle aged white men who are relatively well educated. High intakes of at least 1500 g a day were associated with a 45% drop in incidence (0.55, 0.38 to 0.80) among the dentists, optometrists, osteopaths, pharmacists, podiatrists, and vets in this cohort.

***Arch Intern Med*** 2009;169:502-7

## Japanese armed forces test a live attenuated vaccine against smallpox

Fear of bioterrorism has prompted the Japanese armed forces to look for a safe and effective vaccine against smallpox. The most likely candidate so far is the live attenuated vaccine LC16m8, which was given to more than 100 000 Japanese infants in the early 1970s.

Recent tests in Japanese participants of the United Nations peacekeeping operations also look promising. A single intradermal dose produced a visible skin reaction in 94.4% (1443/1529) of those not vaccinated as children and 86.6% (1465/1692) of those that were. The skin reaction to smallpox vaccine is one measure of the immune response. These authors also measured antibody titres in a smaller subsample. The vaccine was immunogenic in 37 of 41 vaccinia naive adults and in 93 of 155 previously vaccinated adults. The only serious side effects within 30 days were one case of allergic dermatitis and another of erythema multiforme. Ninety six of the 1066 adults monitored for side effects reported swollen axillary lymph nodes.

A sample size of a few thousand isn't enough to establish the safety and effectiveness of any vaccine, say the authors. But this one seems to work in adults as well as children, and deserves further study. Rare side effects such as myopericarditis remain a possibility.

***JAMA*** 2009;301:1025-33

## PCI doesn't reduce mortality in chronic coronary artery disease

After 20 years of research and innovation, medical treatment may still be the best option for many adults with non-acute coronary artery heart disease. In a meta-analysis of 61 trials, percutaneous coronary interventions (PCI) with bare metal or drug eluting stents did not save lives or prevent heart attacks compared with best medical treatment.

The authors used state of the art network meta-analysis to overcome a paucity of head to head trials comparing medical treatment with stents. The comparisons are necessarily indirect, but they still support a strategy of best medical treatment first for patients with non-acute coronary artery disease, they write. They analysed data from more than 25 000 adults. A substantial minority had unstable angina, but all of them were in trials comparing different stent types or comparing bare metal stents with traditional balloon angioplasty. Patients with acute myocardial infarction were excluded.

PCI may not prolong survival, but we have some evidence that it can relieve symptoms and improve quality of life, particularly when combined with best medical treatment, says a linked comment (p 870). We still need trials of PCI as an adjunct not an alternative to drugs for people with stable disease, and they must include measures of quality of life.

***Lancet*** 2009;373:911-8

## Healthy lifestyles seem unattainable for many Europeans with heart disease

Efforts to control cardiovascular risk factors in people with heart disease are not working. Europeans with heart disease are getting fatter, few are reaching blood pressure targets, and more have diabetes than ever before, according to a series of cross sectional surveys. Between the first survey in 1995 and the last in 2007, obesity increased from 25% to 38%, diabetes increased from 17.4% to 28%, and hypertension remained essentially unchanged at around 60% despite a rise in prescriptions for antihypertensive drugs. Serum lipid concentrations improved (probably because of drugs treatments), but smoking rates remained unchanged overall and actually increased in women under 50. What is going wrong?

Poor access to cardiac rehabilitation programmes is one problem, say the authors. People who have acute coronary events need intensive support to take more exercise, eat better, and stop smoking. Even then, many find it hard to change. Secondary prevention by doctors and other health professionals just isn't enough without concerted political action to reverse disappointing lifestyle trends says a linked comment (p 873). Fighting the fast food and sugar industries, laying some safe cycle paths, and providing decent school meals would be a start.

***Lancet*** 2009;373:929-40

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