Short cuts

What's new in the other general journals

Finnish people with diabetes have a low incidence of renal failure

Between 1965 and 1999, 20 005 Finnish children and adults were diagnosed as having type 1 diabetes. During a follow-up period lasting up to 35 years, 632 of them developed end stage renal failure—an overall incidence of only 2.2% at 20 years and 7.8% at 30 years after diagnosis. A study linking three national Finnish registers (one for diabetes, one for renal failure, and one for death) found that risk of end stage renal failure was virtually zero for the first 15 years after diagnosis, rose rapidly between 15 and 20 years, then reached a plateau for the 15 years after that. Children who were diagnosed as having type 1 diabetes before the age of 5 had the best prognosis; only 3% of them developed end stage renal failure during the ensuing 30 years.

These estimates indicate that the outlook for patients with type 1 diabetes is better than previously thought, especially for the under 5s. Prognosis improved steadily throughout the study (which ran up to 2001), indicating that diabetes is now less of a threat to renal function than it has ever been. Survival also improved; people who developed diabetes in the late 1970s were half as likely to die during the study as people diagnosed in the late 1960s (relative risk 0.52, 95% CI 0.44 to 0.61).

JAMA 2005;294:1782-7

Older Americans have healthier serum lipids despite the obesity epidemic

Serum concentrations of total cholesterol have been declining in US adults since the 1960s, and the trend continues, according to the latest look at data from serial national surveys. Between 1988 and 2002, total cholesterol levels among adults over

20 fell from 5.34 mmol/l to 5.26 mmol/l ($P = 0.009$), with the biggest decreases in women over 50 and men over 60. During the same period, the percentage of adults with total cholesterol of at least 6.22 mmol/l fell from 20% to 17% (the current US government target). Mean concentrations of low density lipoprotein (LDL) cholesterol also fell, predominantly among older adults, although concentrations of triglycerides did not.

Increased prescribing of lipid lowering drugs may be at least partly responsible for these trends. In the last US survey, done between 1999 and 2002, 9% of people over 20 were taking lipid lowering drugs, including over a fifth of those aged 60 or older. Improvements in the American diet are unlikely to have done it. American adults are consuming almost as much saturated fat and cholesterol as they were in 1988, and in the last survey nearly two thirds of respondents were classified as overweight or obese.

JAMA 2005;294:1773-81

A second vaccination doesn't protect Brazilian school children from tuberculosis

The World Health Organization recommends against revaccinating school children who were vaccinated against tuberculosis at birth, although there's little evidence either way, and some countries still revaccinate. A randomised trial now shows that, in Brazil at least, revaccinating children is probably a waste of time. The trial included 767 schools and over 200 000 children in two distinct areas of Brazil. Of the schools, 386 were randomised to revaccinate children with BCG if they already had an existing vaccination scar. The researchers then tracked cases of tuberculosis in vaccinated and unvaccinated children aged 7 to 14 through the government's tuberculosis control programme. All patients with tuberculosis must access the programme for treatment, which is free.

During the study 279 cases of tuberculosis were recorded. Revaccination made no difference to the crude incidence, which was 29.3 per 100 000 person years in the revaccinated group, and 30.2 per 100 000 person years in the control group. The authors admit their analysis was unorthodox, but say the trial was big enough and robust enough to exclude any benefits to public health from revaccinating

school children aged 7 to 14. The trial was powered to find a protective effect of at least 30%.

Lancet 2005;366:1290-5

Candesartan reduces the combined risk of heart attack or death in people with symptomatic heart failure

The cardiovascular effects of the renin-angiotensin-aldosterone system can be blocked in two ways—angiotensin converting enzyme (ACE) inhibitors stop the production of angiotensin II, and angiotensin receptor blockers stop angiotensin II binding to its receptors. We know that ACE inhibitors can help prevent heart attacks in people with heart failure. To find out if angiotensin receptor blockers can do the same, researchers analysed data from a trio of placebo controlled trials in patients with heart failure, collectively known as the CHARM programme (candesartan in heart failure: assessment of reduction in mortality and morbidity).

Overall, 20% of the 3803 patients given candesartan and 23% of the 3796 patients given placebo died from a cardiovascular cause or had a non-fatal heart attack during three years of follow-up. That's a small but significant difference translating to one event prevented for every 40 patients treated with candesartan. The difference between the groups for non-fatal heart attack alone was also significant (3.9% v 3.1%, hazard ratio 0.77, 95% CI 0.6 to 0.98),

although the number needed to treat was a much larger 118.

The authors, two of whom worked for the sponsors, AstraZeneca, say candesartan offers about the same magnitude of benefits to patients with heart failure as ACE inhibitors. Candesartan seemed to work even for patients already taking ACE inhibitors, which could mean that two ways of blocking the renin-angiotensin-aldosterone system work better than one.

JAMA 2005;294:1794-8

Pathogen in raw oysters causes septicæmia and cellulitis

Doctors from Louisiana report a case of severe haemorrhagic cellulitis in a 52 year old man living in the southern part of the state. The infecting pathogen, a Gram negative rod called *Vibrio vulnificus*, lives in the warm waters of the Gulf coast and is especially prevalent in summer, when water temperatures peak. The man, who had septicæmia and severe cellulitis in both legs, could have caught the infection wading through the filthy flood waters left behind by hurricane Katrina. But actually he became ill after eating raw oysters. Oysters and other filter feeding shellfish concentrate free living pathogens such as *V vulnificus* and, eaten raw, are particularly dangerous for people who are vulnerable to infections. This man had a history of steatohepatitis. He survived his severe illness, but only after a spell in intensive care. The mortality rate for septicæmia caused by *V vulnificus* is about 40%.

N Engl J Med 2005;353:1604

Acellular vaccine prevents whooping cough in teenagers and adults

Childhood immunisations for whooping cough do not protect people for life, and waning immunity has been blamed for recent increases in the incidence of whooping cough among adolescents and adults in the United States. Some countries, including Canada, France, and Germany, already revaccinate adolescents, and authorities in the United States are considering it after recently licensing two combined vaccines for whooping cough, diphtheria, and tetanus.

Acellular pertussis vaccines designed for adolescents and adults, which contain only a third of the concentration of pertussis toxin in children's vaccines, produce a good immunological response. But do they prevent whooping cough? In the only randomised trial to date, one dose of a single acellular pertussis vaccine prevented about 90% of infections during a follow-up lasting two and a half years. More than 2700 Americans aged between 15 and 65 took part. They were given the pertussis vaccine or a control vaccine against hepatitis A. Careful monitoring detected 10 confirmed pertussis infections during

follow-up, nine of them in the control group. That's an incidence in an unvaccinated population of 370 per 100 000 person years—or over a million preventable infections across the United States each year. The number of reported cases of whooping cough among adults or adolescents doubled during the 1990s in the United States and in Canada.

N Engl J Med 2005;353:1555-63

New biomarker for mesothelioma shows promise

Up to 10% of people with occupational exposure to asbestos will eventually develop a mesothelioma. Most will present late and die within a few months or years of diagnosis. Screening people in risky occupations might help pick up tumours earlier and offer patients a better chance of survival, but only if researchers can find a sensitive biomarker with which to screen them. The glycoprotein osteopontin is the latest candidate and it did reasonably well in one study, distinguishing between exposed people with and without mesothelioma, with a sensitivity of 77.6%.

Researchers compared serum concentration of the marker in 76 people with mesothelioma, 69 people with benign lung disease caused by asbestos, and 45 people with no history of asbestos exposure. People with mesothelioma had significantly higher serum concentrations of the biomarker than people in either of the other groups, a difference that was evident even among the small minority with stage I tumours. Among those without mesothelioma, high concentrations were linked to long duration of exposure to asbestos and more severe benign lung disease. A threshold of 48.3 ng/ml osteopontin seemed the most accurate for detecting any mesothelioma in exposed populations (sensitivity 77.6%, specificity 85.5%).

N Engl J Med 2005;353:1564-73

NSAIDs help prevent oral cancer in heavy smokers

Heavy smokers who take non-steroidal anti-inflammatory drugs (NSAIDs) long term are less likely than other heavy smokers to develop oral cancer, according to a case-control study from Norway. The protection against oral cancer in this population (hazard ratio 0.47, 95% CI 0.37 to 0.60, $P < 0.0001$) seems about the same as the protection they might expect from quitting. Overall though, the reduced risk of oral cancer was completely offset by an equal and opposite increase in the risk of a cardiovascular death associated with all NSAIDs except aspirin (hazard ratio 2.06, 1.34 to 3.18, $P = 0.001$). The drugs had no overall effect on survival.

The study included 454 Norwegian men and women with oral cancer who were or had been heavy smokers. Researchers matched them with 454 other heavy smokers without cancer. Data on drug use and other health and lifestyle data came from established national health surveys conducted every five years, and from a central prescriptions registry.

The authors hope that NSAIDs might one day be useful as a prophylactic against oral cancer for people at high risk, such as heavy smokers or former heavy smokers with aneuploid oral leucoplakia.

Prospective clinical trials are planned. Researchers will have to look carefully for extra cardiovascular events, however. The protection against oral cancer may not be worth the added risk.

Lancet 2005;366:1359-66

Physician assisted suicide in Oregon is under threat

Doctors in Oregon can legally prescribe lethal doses of medicine to any resident in the state with a life expectancy of less than six months, so long as the patient asks for the prescription twice and in writing. An editorial describes how the US government tried again last week to halt physician assisted suicides in Oregon—by threatening to revoke the licence of any doctor caught writing a prescription for lethal doses of controlled substances such as barbiturates.

The legality of the move, which invokes an old law designed to combat drug trafficking, is now being considered by the US Supreme Court after two lower courts ruled against it. The editorial describes the US government's actions as unfortunate, and urges the Supreme Court to stand in their way once again "not because physician-assisted suicide is right but because it is an issue of such importance that it can only be resolved through open democratic debate."

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