Short cuts

What's new in the other general journals

Half of all age related macular degeneration could be genetic

Age related macular degeneration is an important cause of blindness among older people, particularly in developed countries. The aetiology is still unclear, but a new study suggests that about half of all cases are caused by polymorphism at the gene coding for complement factor H, an important inflammatory mediator that inhibits the complement cascade.

In a cohort of people aged over 55 from Rotterdam in the Netherlands, carriers of the *Y402H* allele were significantly more likely than non-carriers to develop age related macular degeneration over a median follow-up of 10 years. They were also more likely to get worse. People homozygous for the allele had an 11-fold increase in risk of sight threatening degeneration (odds ratio 11.02; 95% CI 6.82 to 11.81), relative to non-carriers. Overall, 36.2% (4116/11 362) of the cohort carried at least one allele. Genetic predisposition became more important after the age of 75, and the authors estimate that nearly half the homozygotes in their cohort would develop a sight threatening form of the disease by the age of 95.

Smoking is a well known risk factor for age related macular degeneration, but in this study it was particularly risky for people with an existing genetic predisposition. Homozygotes for the *Y402H* allele were over 30 times more likely to develop serious age related macular degeneration than non-carriers who did not smoke (odds ratio 34.0; 13.0 to 88.6).

JAMA 2006;296:301-9

Obese adolescents are more likely to die young

Being overweight or obese at age 18 increases your chances of a premature

death, according to a cohort study of over 100 000 American nurses. Even nurses who remembered being only moderately overweight at 18 had an increased risk of dying before late middle age (hazard ratio 1.66; 95% CI 1.31 to 2.10 for a body mass index of 25.0 to 29.9 relative to an index of <22). The hazard ratio for obesity (≥ 30) was 2.79.

The link between body mass index at 18 and an early death persisted through various analyses designed to adjust for the effects of smoking and lifestyle. It also survived adjustment for body mass index during adulthood. This means, say the authors, that being an overweight adolescent is a danger to health, whether or not the weight problem persists in later life.

The figures in this analysis, which is confined to women, translate into a substantial increase in the absolute risk of death for overweight and obese adolescents—an extra 36.4 deaths per 100 000 persons a year for a body mass index of 25-29.9 and an extra 92.5 deaths per 100 000 persons a year for an index of ≥ 30 . A closer look at causes of death showed significant associations between being overweight at 18, cardiovascular disease, and “external causes of death,” a category dominated by suicide.

Ann Intern Med 2006;145:91-7

HAART contributes to declining infection rates in children with HIV

Children with HIV are living increasingly longer, thanks to highly active antiretroviral therapy (HAART). Many are surviving long enough to have children themselves. Potent modern drugs help restore their immune systems, enabling the lucky few to fight the common infections that still kill so many children with no access to treatment.

A new study has found that, since HAART arrived in the United States in 1996, the incidence of bacteraemia in American children with HIV has fallen 10-fold (from 3.3 per 100 person years to 0.35). The incidence of bacterial pneumonia has also fallen—fivefold (11.1 to 2.15)—and the incidences of more specific opportunistic infections such as *Pneumocystis jirovecii* pneumonia and disseminated *Mycobacterium avium* complex have fallen even more dramatically.

Despite the usual problems associated with a before and after design, the new drugs are likely to be at least partly responsible for these trends, says a linked editorial

(pp 330-1). The use of specific prophylactic agents declined during the same period.

The big challenge now is to ensure that children with HIV can get access to this “extraordinary therapy” wherever they live, says the editorial. There are 2.3 million children with HIV worldwide. Fewer than 14 000 live in the US.

JAMA 2006;296:292-300

Migraine with aura is linked to ischaemic heart disease

For years, experts have been debating the possibility of a link between migraine and ischaemic heart disease. Migraine with aura is already an established risk factor for stroke. Now, an analysis of 10 years’ prospective data from the large women’s health study shows a clear association between migraine with aura and a range of cardiovascular outcomes including heart attack.

The women in the study who said they had active migraine with aura were roughly twice as likely as women without a history of migraine to have a heart attack (adjusted hazard ratio 2.08; 95% CI 1.30 to 3.31), angina (1.71; 1.16 to 2.53), or coronary revascularisation (1.74; 1.23 to 2.46) during the 10 years of follow-up. They were also twice as likely to die from ischaemic cardiovascular disease (2.33; 1.21 to 4.51). As expected, they had an increased risk of ischaemic stroke (1.91; 1.17 to 3.10). The researchers found no association between any cardiovascular outcome and migraine without aura.

In all, over 27 000 apparently healthy American healthcare professionals contributed to this analysis; 3610 had active migraine, but only a minority (1434 (40%)) had migraine with aura. While researchers continue to unravel the complex relations between migraine and the human cardiovascular system, the remaining majority can be reassured.

JAMA 2006;296:283-91

Diastolic and systolic heart failure have a similarly poor prognosis

The prognosis for people with heart failure is traditionally related to their ejection fraction, the received wisdom being that patients with a preserved ejection fraction (so called diastolic heart failure) do better than those whose ejection fraction has fallen below 50% or so (systolic heart failure). Two new studies have recently challenged this established belief. In both, patients admitted to hospital for diastolic heart failure had a similar prognosis to patients admitted for systolic heart failure; one year mortality was between 22% and 29% for diastolic heart failure and between 26% and 32% for systolic heart failure. At five years, mortality was 65% and 68% respectively.

A linked editorial describes both studies as provocative (pp 308-10). Both are at odds with previous research, including the only large randomised trial of treatment for diastolic heart failure. It's not entirely clear why these latest studies yielded a different result, but one possibility is that patients with diastolic heart failure did worse than expected because they were older in both studies. Whatever the reason, it seems clear that diastolic heart failure is a dangerous diagnosis with a substantial mortality that hasn't improved much since the late 1980s. The outlook for patients with systolic heart failure, on the other hand, has improved significantly (pp 251-9).

N Engl J Med 2006;355:251-9, 260-9

Active children have a lower risk of cardiovascular disease

The recommended half to one hour a day of moderate exercise may be enough for adults, but children probably need more, says an editorial (pp 261-2). The author was commenting on a cross sectional study looking at the link between physical activity and markers of the metabolic syndrome in 1732 children aged 9 and 15 years. The study found a clear negative association—the least active children were the most likely to have a high risk factor score calculated from their blood pressure, plasma lipid profiles, insulin resistance, aerobic fitness, and skinfold thickness (odds ratio 3.29, 95% CI 1.96 to 5.52 for least v most active). When the researchers divided children up into fifths of physical activity, only those in the top two fifths had “normal” risk factor profiles, and they were exercising at least 88 minutes a day. The younger children in these fifths were exercising at least 116 minutes a day. The link between activity and risk was the same for fat and for thin children. In this study, exercising meant physical activity equivalent to walking faster than 4 km/hour in bursts of at least five minutes.

Even young children should probably be encouraged to do at least 90 minutes a day of physical activity, say the authors. Walking to and from school would be a start.

Lancet 2006;368:299-304

Sibutramine helps some obese adolescents lose weight

Obesity is an increasing problem for adolescents in many developed countries. Lifestyle changes such as eating less and exercising more should help, but behavioural treatments alone have failed to halt the epidemic that is threatening the health and even the lives of the next generation. Drug treatments such as sibutramine are a last resort, but a large trial suggests they can work, at least for some.

The trial, which was sponsored by the manufacturer of sibutramine, included 498 children aged 12-16 years who had a body mass index more than two units above the

95th centile for their age and sex. They had a tailored behaviour programme to help them eat less and move around more, as well as taking sibutramine or a placebo for one year. The drug's effects were modest, but significantly better than the behaviour therapy alone—teenagers taking sibutramine lost 8.4 (95% CI 9.7 to 7.2) kg more weight than controls and reduced their body mass index by an extra 2.9 (95% CI 3.5 to 2.2) over the year. They also had significant improvements in their serum lipid profiles and some measures of glucose metabolism. Tachycardia was the main side effect (in 12.5% of the sibutramine group v 6.2% of controls).

Ann Intern Med 2006;145:81-90

The right to essential medicines can be enforced through the courts

Many countries have signed up to international human rights treaties guaranteeing the right to health for all. Many also have constitutions that specify a right to health. Access to essential medicines is part of that right. But can it be enforced?

A careful search for legal cases that tested an individual or a group's right to essential medicines found 71. In 59 of them, the right was upheld by the courts, the defendant (usually the government) was over-ruled, and the plaintiff or plaintiffs got the drugs they needed. The researchers confined their search to low and middle income countries, but even so their findings indicate that skilful litigation can force governments to fulfil their obligations. In over a third of the successful cases, the courts upheld that someone's right to health “is stronger than limitations in the national essential medicines list.” In nearly a third of successful cases, the courts concluded that this right “is stronger than limitations in social security benefits.” In a quarter of successful cases, the ruling was extended to everyone in similar circumstances.

Most of the legal activity in this area seems concentrated in Central and South America. The researchers found only seven cases outside these regions—two from India (both successful), one from Nigeria (unsuccessful), and four from South Africa (two successful).

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