Short cuts

What's new in the other general journals

Sentinel node biopsy improves outcome in people with medium thickness melanomas

Sentinel node biopsy should become the standard of care for people with medium thickness melanoma, according to an editorial. A large trial (pp 1307-17) has shown that sentinel node biopsy, coupled with immediate lymphadenectomy if positive, helps control regional recurrence for everyone, and improves survival among patients with nodal metastases.

Patients who had the biopsy had longer disease-free survival over five years than patients who were observed and offered lymphadenectomy only when their diseased nodes became obvious clinically (78% *v* 73%; hazard ratio for death 0.74; 95% CI 0.59 to 0.93). Sentinel node biopsy didn't prolong overall survival, but among the 16% of patients with nodal metastases, those who had the biopsy followed by immediate surgery survived significantly longer than those who had to wait for their surgery until their lymph nodes got big enough to palpate (72% five years survival *v* 52%; hazard ratio for death, 0.51, 0.32 to 0.81). During a median wait of 16 months, their tumours progressed and the mean number of malignant lymph nodes increased from 1.4 to 3.3 ($P < 0.001$).

N Engl J Med 2006;355:1370-1

US emergency medical services are in crisis

As the threat of terrorism becomes more real in the US, the emergency medical services required to deal with its aftermath are in serious decline, writes a professor of emergency medicine from Atlanta. His department and many others are overflowing, demoralised, and stretched beyond their capacity to cope with any kind of mass casualty event. Patients are being "boarded" in corridors and examination rooms waiting for beds, and overcrowded hospitals are increasingly turning away ambulances—at a rate of about one every minute.

He blames the "upside down world" of federal funding for these well documented and worsening problems. Between 2000 and 2006 the government increased spending on bioterrorism "preparedness" from \$237m (£126m, €187m) to \$9.6bn, funding 52 centres to help prepare for an attack. Yet there are no centres to help anyone cope with civilian casualties caused by bombs, the weapons of choice for most terrorists. Only 4% of the money earmarked for "first response" in 2002 and 2003 found its way to the emergency medical services, and important government programmes are being axed.

This author and others call on the government to reverse these trends and restore the country's much depleted

capability for emergency care as a matter of urgency. "When your life is on the line, you want your doctor—not your ambulance—to go the extra mile," he says.

N Engl J Med 2006;355:1300-3

Targeted treatment with azithromycin won't control trachoma in Vietnam

As part of the World Health Organization's campaign to eliminate blinding trachoma by 2020, researchers designed a trial to test a targeted strategy of oral azithromycin for school children and their contacts in Vietnam. The unexpected results indicate that the antibiotics, given at baseline and repeated a year later, may increase the prevalence of trachoma infection in the long term.

The trial included three communes. In two of them, school aged children with eye inflammation due to active trachoma and their families, had the two oral doses of azithromycin. All three communes had access to surgery for sight threatening disease. Over three years, infection rates fell in all three communes. But in the two communes given targeted antibiotics, infection rates went up again significantly between 24 and 36 months after randomisation. The risk of reinfection after cure also went up significantly in the two actively treated communes. By the end of the study, living in either commune was associated with quadruple the odds of repeat infection (odds ratios compared with the control commune 4.1, 95% CI 1.5 to 9.8 and 4.2, 1.1 to 17.3).

The authors think that this rebound is probably caused by antibiotics preventing treated children from developing a full immune response to infection.

JAMA 2006;296:1488-97

Islet cell transplants can work, but not for long

Islet cell transplants may help a few selected patients with unstable type 1 diabetes, but the improved control, or even cure, doesn't last long. Out of the 36 patients given transplants in an uncontrolled trial, 16 had stopped using insulin by the end of the first year, but only five were still independent of insulin a year later. Only one was cured for the full three years of the trial.

Overall, 26 of the 36 patients got some benefit from their graft. But the technique is unlikely to be widely adopted in the near future, says an editorial (pp 1372-4). The researchers had to screen 2000 patients before they found 36 who were suitable, most of them had unpleasant side effects from the intensive immunosuppression, and nearly one in ten transplants caused intraperitoneal bleeding. More than half the attempts at isolating islets from donors failed. These problems, coupled with the soaring prevalence of diabetes and a shortage of cadaver donors, mean that most patients with diabetes will never have an islet cell transplant unless islets can be found from some other source. Researchers are already looking at the potential of stem cells from adults and embryos.

N Engl J Med 2006;355:1318-30

Gaining weight between pregnancies is bad for women and their babies

Women who gain weight between pregnancies increase their risk of gestational diabetes, pre-eclampsia, gestational hypertension, a baby that is large for dates, caesarean delivery, and even stillbirth, reports a large study from Sweden. The link between weight gain and adverse pregnancy outcomes was linear, and started after an increase of only one or two units of body mass index, even in women who were neither overweight nor obese. Women whose body mass index was three or more units higher at the start of their second pregnancy than it had been at the start of their first had a 60% increase in their odds of a stillbirth (odds ratio 1.63, 95% CI 1.2 to 2.21), and a 78% increase in their odds of pre-eclampsia (1.78, 1.52 to 2.08).

These findings from a cohort of 15 1025 Swedish women support the notion of a causal link between increased body weight and adverse pregnancy outcomes, write the authors, and should prompt prospective trials of weight control before conception. Gaining even modest amounts of weight seems to be bad for women and their babies in a way that is unexplained by poor social circumstances, limited education, or smoking. In a woman of average height and weight (1.65 m and 63 kg), 3 extra kilograms between pregnancies increases the risk of gestational diabetes by more than 30%.

Lancet 2006;368:1164-70

Viral load at first presentation is a poor prognostic indicator in HIV

The immunopathology of HIV remains poorly understood, but the received wisdom is that a patient's viral load is closely linked to the rate at which their CD4 T cell count falls, and their disease progresses. The implication is that replicating viruses destroy the T cells directly. It may not be that simple, according to this study. Using data from two cohorts of untreated patients, the researchers found, as expected, that patients with higher viral loads at presentation tended to lose their CD4 T cells faster than patients with a lower viral loads. But the association was weak. Overall, viral load explained less than 10% of the variability in CD4 T cell loss, which makes it an unreliable prognostic indicator for people presenting for the first time, and indicates that viral load should be divorced from decisions about when to start treatment.

So what drives the loss of CD4 T cells in patients with HIV? It could be something to do with the global activation of the immune system that accompanies infection. Unmeasured events during the acute infection stage, or genetic make up may also contribute. Further research is already under way, but in the meantime doctors should probably stop using the combination of CD4 T cell count and viral load to predict prognosis.

JAMA 2006;296:1498-1506

Statins help prevent coronary heart disease among Japanese men

Treatment with statins is an effective prophylactic against cardiovascular events in countries with high rates of hypercholesterolaemia and heart disease. But do they protect people from cardiovascular disease in Japan, where coronary arteries and serum lipid profiles

are generally healthier than they are in Europe and the US? A large randomised trial shows that a low dose of pravastatin can prevent coronary heart disease among Japanese adults with moderate hypercholesterolaemia, but the absolute reduction in risk was only small—0.8%—so the number needed to treat (119) was much higher than previously reported in other populations.

The trial compared a low cholesterol diet with or without pravastatin (5 mg-20 mg, mean dose 8 mg) over five years in nearly 8000 adults, 70% of whom were women. The generally positive results were driven by the men, however (hazard ratio for coronary heart disease 0.63, 95% CI 0.42 to 0.95). A question mark remains over the effects of statins in women. A low dose of pravastatin did not protect them from coronary heart disease in this trial (0.71, 0.44 to 1.14). The effects on total mortality were equivocal for both sexes combined (0.72, 0.51 to 1.01, $P = 0.055$).

Lancet 2006;368:1155-63

People with Lynch syndrome need better evidence to guide their management

Lynch syndrome is an inherited susceptibility to colorectal and other cancers, caused by mutations in genes that help repair DNA. Men and women with these mutations have an estimated risk of colorectal cancer approaching 70% by the age of 70 years, while women have a lifetime risk of endometrial cancer between 40% and 60%.

Finding out who has the syndrome is one problem, and researchers continue to work on algorithms to help decide who should be tested for the mutations and when (pp 1469-78, 1479-87), but the main issue for families with Lynch syndrome is how to reduce their inherited risk. A systematic review finds little to help them. Although the weight of evidence supports colonoscopic surveillance, the screening interval and target age are still unclear. Expert consensus recommends colonoscopy every one or two years starting between the ages of 20 and 25 years.

Prophylactic hysterectomy and oophorectomy is the other intervention supported by data. In the only study, which was purely observational, none of the women who had prophylactic surgery developed endometrial cancer over 10 years, compared with one third of the women who didn't have surgery. For women who want to have children, ultrasound surveillance for endometrial cancer doesn't seem to work, so the review's authors recommend regular endometrial biopsies instead, pending proper clinical trials.

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