SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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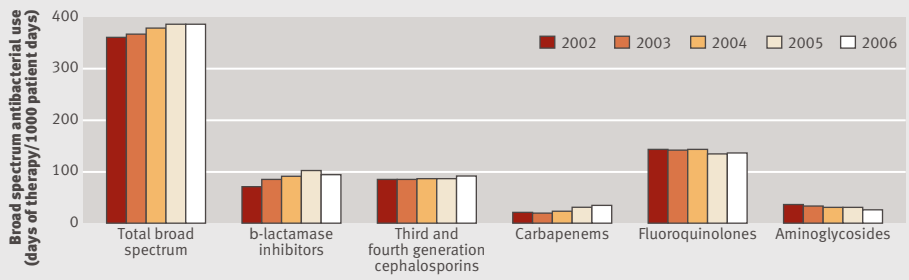
TRENDS IN USE OF BROAD SPECTRUM ANTIBIOTICS



Adapted from *Arch Intern Med* 2008;168:2254-60

Use of antibiotics increases at academic hospitals in the US

In 2006, nearly 800 000 adults were discharged from a sample of 35 academic hospitals in the US. Nearly two thirds (492 721/775 731, 63.5%) were treated with antibiotics—a significant increase in antibiotic use since 2002. Analysis of claims data from these hospitals shows a clear trend—doctors are prescribing more and more antibiotics, particularly agents with a broad spectrum.

In a smaller sample of 22 hospitals with continuous data, use of carbapenem antibiotics increased by 59% between 2002 and 2006, while use of pipericillin-tazobactam increased by a striking 84%. Use of vancomycin also rose sharply, and by 2004 it was prescribed more often than any other single agent. The authors blame upward trends in meticillin resistant *Staphylococcus aureus* infections and warn that creeping resistance to even vancomycin is likely to follow.

The implications of such widespread use of pipericillin-tazobactam are less clear. National authorities aren't yet tracking resistance to this antibiotic, which by 2005 was the third most commonly prescribed agent in these hospitals, behind vancomycin and cefazolin.

Few new antibiotics are under development, say the authors, and we must use the ones we have much more wisely. Smarter infection control and antibiotic stewardship programmes should help.

Arch Intern Med 2008;168:2254-60

Failed vaccine is another blow for HIV control

An adenovirus vaccine designed to boost cell mediated immunity against HIV has failed, disappointing HIV researchers and casting doubt on the animal models that suggested it might work. The vaccine, which expressed three HIV genes—gag, pol, and nef—did not prevent infections in participants in a placebo controlled trial and had no effect on viral replication in those infected. The data monitoring committee recognised the futility of the trial at its first meeting, when it became clear that men given the vaccine were, if anything, more likely than controls to get HIV (4.6% *v* 3.1% each year; hazard ratio 1.5, 95% CI 0.97 to 2.3). The trial included 3000 men and women at high risk, mostly men who have sex with men and women at high risk because of sex work or drug use. Exploratory analyses suggested the increased risk was confined to uncircumcised men (3.8, 1.5 to 9.3) and those with antibodies against the adenovirus vector (2.3, 1.2 to 4.3).

The researchers don't know yet why the vaccine failed, when a prototype worked well in standard primate models. They looked for differences in immune responses between men who became HIV positive and those who didn't (doi:10.1016/S0140-6736(08)61593-7). There weren't any—the vaccine looked immunogenic in both groups, inducing HIV specific T cells as expected. But the response clearly wasn't good enough, possibly because it was too weak, too narrow, or somehow qualitatively wrong, say the researchers. After decades of research, we still don't know what an effective immune response to HIV looks like.

Lancet 2008 doi:10.1016/S0140-6736(08)61591-3

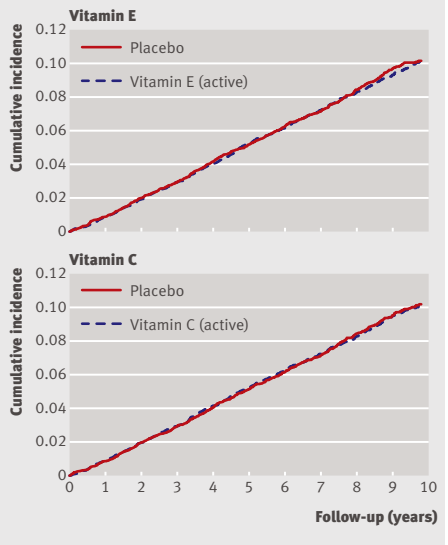
Antioxidant supplements fail to prevent cardiovascular disease, again

Antioxidant vitamins C and E do not prevent cardiovascular disease in healthy middle aged men, according to a placebo controlled trial of US doctors. The trial lasted 10 years and included 14 641 male doctors who were at least 50 when enrolled. Most (94.9%) had no cardiovascular disease when they signed up.

The cumulative incidence of serious cardiovascular events was almost the same in men taking vitamin C (500 mg/day), vitamin E (400 IU every other day), both, or neither. The supplements had no effect on the risk of heart attack, stroke (both types combined), death, heart failure, angina, or coronary revascularisation. Vitamin E was associated with an excess risk of haemorrhagic stroke (hazard ratio 1.74, 95% CI 1.04 to 2.91).

The negative results for vitamin E are consistent with previous work in higher risk populations, including men and women with pre-existing cardiovascular disease, say the authors. So are the results for vitamin C, although they say this is the first long term trial in men. Around one in eight US adults reported taking these antioxidant supplements at the last national survey between

CUMULATIVE INCIDENCE OF MAJOR CARDIOVASCULAR EVENTS



Adapted from *JAMA* 2008;300:2123-33

1999 and 2000. Long term cardiovascular benefits look increasingly unlikely.
JAMA 2008;300:2123-33

Aspirin still unproven for primary prevention in diabetes

Many people with type 2 diabetes take a low dose of aspirin each day in the hope that it will help protect them from cardiovascular events such as heart attack and stroke. Guidelines recommend aspirin for primary prevention in this population, and it makes sense biologically because of the high risk associated with diabetes. Researchers are struggling to produce conclusive evidence that it works, however. One of the few trials to test aspirin prophylaxis exclusively in people with diabetes recently reported no overall effect on a combination of cardiovascular events or death (hazard ratio 0.80, 95% CI 0.58 to 1.10), although a subgroup analysis suggested a possible benefit for those over 65. Controls had no aspirin. The trial was single blind. Aspirin had a significant effect on only one of 11 secondary end points—risk of cerebrovascular or coronary death (0.10, 0.01 to 0.79).

The trial was weaker than it should have been, because the 2539 Japanese participants did better than expected. Only a third of the anticipated number had an atherosclerotic event. They had no atherosclerotic disease at baseline and were slim, with a mean body mass index of 24. Diabetic populations in the West tend to be bigger and may have a higher risk, so it is unclear what this trial means for them. Fortunately, two more large trials are already in the pipeline, says an editorial (p 2180). Together, they will enrol more than 15 000 patients. Enough to help clarify this very grey area.
JAMA 2008;300:2134-41

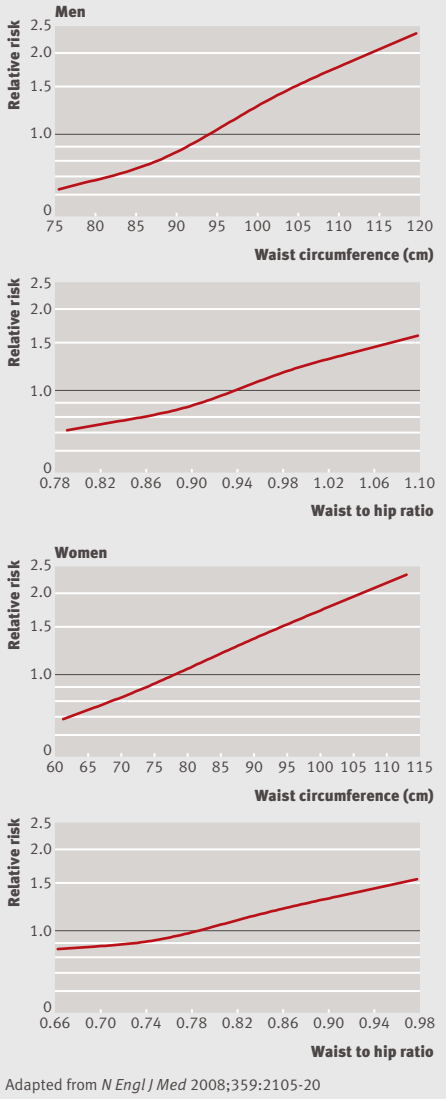
Measure abdominal fat as well as body mass index

Body fat is an important determinant of mortality. Too much and too little are both associated with reduced survival. Body mass index (BMI) is a measure of general adiposity and is the standard proxy for body fat in most studies. Waist circumference and waist to hip ratio are alternatives that give some indication of body fat distribution, unlike body mass index. Which of these measures should researchers use?

All three were significantly associated with mortality in a cohort study of 359 387 healthy men and women from nine European countries. The two measures of abdominal fat remained predictors of death, even after adjustment for body mass index. In other words, in men and women with the same body mass index, those with more abdominal fat (higher waist to hip ratio or higher waist circumference) had a higher risk of death. In this study, each additional 5 cm around the waist increased men's risk of death by 17% (95% CI 15% to 20%) and women's risk of death by 13% (11% to 15%). Risks also went up in both sexes in line with waist to hip ratio. The association between abdominal fat and death was strongest in adults with low body mass index.

The study's authors conclude that researchers should probably measure both general and abdominal adiposity in studies assessing mortality. Either waist circumference or waist to hip ratio will do.
N Engl J Med 2008;359:2105-20

MEASURES OF ABDOMINAL ADIPOSITY AND MORTALITY ADJUSTED FOR BMI



Adapted from *N Engl J Med* 2008;359:2105-20

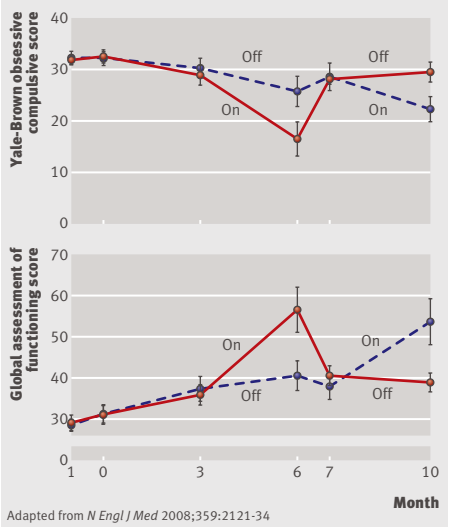
Deep brain stimulation for OCD is risky, but can work

A small crossover trial from France suggests that electrical stimulation of the subthalamic nucleus can help some patients with severe obsessive compulsive disorder by reducing symptoms and improving their day to day functioning. The treatment was associated with a high risk of serious side effects, however. Eleven out of 17 patients had one or more serious problems during the study, including one brain haemorrhage (that resulted in a permanent finger palsy) and two infections. Three patients became hypomanic during active stimulation, and three developed transient neurological side effects, such as facial asymmetry and walking difficulties.

The participants had already tried multiple treatments for obsessive compulsive disorder. They had been ill for many years, unable to work or socialise properly. Each one had surgery to implant the electrodes then three months of active stimulation and three months of sham stimulation in random order. Their symptoms and functioning improved significantly more after the active stimulation period. Active stimulation had no effect on symptoms of depression or anxiety, or on a self reported measure of disability.

Deep brain stimulation is also a treatment for Parkinson's disease. Serious side effects are common in these patients too, say the authors. They believe further investigation of this risky treatment is still worthwhile.
N Engl J Med 2008;359:2121-34

EFFECT OF STIMULATION ON SYMPTOMS AND FUNCTION



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