Short cuts

What's new in the other general journals

Clopidogrel is a safe effective treatment for most people with acute myocardial infarction

The antiplatelet drug clopidogrel should be added to standard treatments for patients with acute myocardial infarction, say the authors of a large placebo controlled trial. It's relatively cheap, safe, and when combined with aspirin produces benefits equivalent to nine fewer serious events (death, further heart attack, or stroke) for every 1000 people treated for about two weeks.

The trial involved 45 852 patients from all over China. They got to hospital a mean of 10 hours after their symptoms started. All had aspirin, just over half were given fibrinolytic drugs, and three quarters were given anticoagulants, mostly heparin. Half the patients also had intravenous then oral metoprolol, as part of a sister trial. None had a percutaneous coronary intervention.

Addition of clopidogrel 75 mg daily to these other treatments reduced the risk of death, further heart attack, or stroke relative to placebo (2121 events (9.2%) *v* 2310 (10.1%), *P*=0.002). Clopidogrel also reduced overall mortality in hospital (1726 deaths (7.5%) *v* 1845 (8.1%), *P*=0.03), the first new drug treatment to do so for 10 years. Clopidogrel did not increase the risk of serious bleeding, including haemorrhagic stroke.

Lancet 2005;366:1607-21

Strategies to control antibiotic prescribing must go beyond the sore throat

Antimicrobial resistance is a global threat to health, and we are not doing nearly enough to combat it, writes a specialist from the US Centers for Disease Control and Prevention. Profligate and inappropriate prescribing of broad spectrum antibiotics is

one of the biggest problems, yet interventions to change doctors' behaviour and patients' expectations have focused on only a small number of upper respiratory tract infections such as sore throat.

The situation is becoming critical as drug manufacturers slowly withdraw from the antibiotic market. With fewer new compounds being licensed, the pressure is on to preserve the effectiveness of the antibiotics we already have. Fluoroquinolones are now the most commonly prescribed antibiotics for adults in the US, accounting for 24% of all antibiotic prescriptions. Resistant strains of *Streptococcus pneumoniae*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Clostridium difficile* have already appeared. Fluoroquinolones are increasingly ineffective against *Neisseria gonorrhoeae*, and there's a danger that *Mycobacterium tuberculosis* will follow.

More and better research on how to stop the rise and rise of antibiotic resistance is always required, the editorial concludes. But researchers must look beyond the sore throat and deeper into any territory where antimicrobial agents are prescribed—including agriculture. Poultry in the US are already infected with fluoroquinolone resistant *Campylobacter* species.

JAMA 2005;294:2354-6

Body mass index should be abandoned as a coronary risk factor

Body mass index is now obsolete as a measure of risk for heart attack, write two leading physicians (pp 1589-91). After years of debate, a case-control study of more than 27 000 people from diverse ethnic groups across the world has shown conclusively that, of the three measures of obesity, waist to hip ratio is best for assessing coronary risk and body mass index is the worst.

The study's findings were consistent across subgroups from Asia, Europe, the Middle East, Africa, Australia, North America, and South America. They held firm through four different analyses and adjustments for other risk factors such as smoking, hypertension, and diabetes. Waist to hip ratio was a better predictor of heart attack than body mass index in men and women, both young and old.

In most populations, obesity defined by waist to hip ratio was associated with substantially more heart attacks than obesity defined by body mass index (population attributable risk of heart attack

for increased waist to hip ratio 24% *v* 8% for increased body mass index). The study's authors conclude that obesity is a substantially bigger threat to public health than we thought.

Lancet 2005;366:1640-49

Coffee doesn't cause hypertension in women, but cola might

To find a link between caffeine and hypertension in women, researchers analysed data from two well known cohorts including 155 594 US female nurses. They found an association shaped a bit like an upturned U. Women drinking moderate amounts of caffeine a day had slightly higher risk of hypertension (about 12% higher) than those drinking less, and those drinking more.

Investigating further, the researchers found no association at all between coffee drinking and risk of hypertension in these young women. But they were moderately surprised to find a clear, linear association between hypertension and caffeinated cola drinks. Risk went up in parallel with consumption, so that nurses who drank

four or more cans a day were between 16% and 44% more likely to develop hypertension than nurses who drank less than one can a day. The trend was significant for diet colas and regular colas, and was adjusted to account for obesity, smoking, and other risk factors.

Given the size of these cohorts, it seems unlikely that coffee causes hypertension in women, say the authors. Researchers should focus their attention on other caffeinated drinks, especially colas.

JAMA 2005;294:2330-35

Vitamin D is the key to healthy calcium homeostasis

Vitamin D and calcium are both required for healthy bones, vitamin D probably more so than calcium, according to a study in 944 healthy Icelandic adults.

The authors found that in this select population, an adequate serum concentration of vitamin D was enough to keep calcium homeostasis healthy. Dietary calcium, on the other hand, became important only among people deficient in vitamin D. Serum parathyroid hormone was lowest, and healthiest, among adults with a serum concentration of vitamin D above 18 ng/ml. Only adults who took regular vitamin D supplements or cod liver oil (60% of the sample) maintained this level during the dark Icelandic winter.

These findings are only preliminary, but they do suggest that getting enough vitamin D from sunlight, diet, or supplements is more important than a high dietary intake of calcium. People living in northern latitudes are particularly vulnerable to vitamin D deficiency in the winter.

JAMA 2005;294:2336-41

Antenatal screening for Down's syndrome is best done early

Antenatal screening for Down's syndrome has become a bewildering experience for many women. The latest study to try to make sense of all the options compared first trimester screening, second trimester screening, and various combinations of both in a cohort of 38 167 women with singleton pregnancies.

They all had a combination of blood tests and ultrasonography in the first trimester (measurement of nuchal translucency, pregnancy associated plasma protein A, and the free β subunit of human chorionic gonadotropin at 10 to 13 weeks' gestation), and a quadruple blood test in the second (measurement of α fetoprotein, total human chorionic gonadotropin, unconjugated oestriol, and inhibin A at 15 to 18 weeks' gestation). Women with positive results from either first or second trimester screening were offered genetic counselling and amniocentesis.

Overall, first trimester screening at 11 weeks looked a better option than second trimester screening, detecting an estimated 87% of the 92 affected pregnancies with a false positive rate of 5%. Second trimester screening with the quadruple test detected 81%, and the popular triple test detected only 69%. Screening in both trimesters was the most accurate option of all with an estimated detection rate of 96%. But women would have to wait until late pregnancy for a definitive answer from amniocentesis. A linked editorial (pp 2068-70) concludes that combined screening in the first trimester is the most practical choice. It's accurate and gives women the option of an earlier, safer termination after chorionic villus sampling.

N Engl J Med 2005;353:2001-11

The diabetic foot ulcer that wasn't

When a 69 year old man with type 2 diabetes developed a nasty ulcer on the sole of his left foot, everyone assumed he had a diabetic ulcer. It refused to heal for nearly nine months, at which point doctors at his diabetic foot clinic did a biopsy. It was a malignant melanoma. Another nine months later, the patient died.

The team who treated his "ulcer" say they have seen at least three other malignant melanomas masquerading as diabetic foot ulcers in the past five years.

Melanomas on the foot or ankle have a poor prognosis. They don't look like typical melanomas and are often mistaken for other things, including warts, fungal infections, and benign ulcers. Ulcers that refuse to heal, or look at all suspicious, should probably be biopsied sooner rather than later, the team concludes.

Lancet 2005;366:1750

Babies with HIV can infect their mothers while breast feeding

In 1998, an outbreak of HIV infection in a children's hospital in Libya left 402 young children and 18 of their mothers infected. Investigators now think many of the infected mothers probably caught the virus while breast feeding their children. Everyone affected by the outbreak had an identical strain of HIV, making a source outside the hospital very unlikely. Infected mothers were

much more likely to have breast fed their children during the outbreak than uninfected mothers (15/16 (94%) v 23/77 (30%); odds ratio 35.2, 95% CI 4.7 to 1508.8), and they were more likely than uninfected mothers to report broken skin on their nipples at the time (9/18 (50%) v 1/84 (1.2%)). Fifteen of their husbands were tested for HIV infection and all were negative.

Although these retrospective data can never be conclusive, the investigators are fairly sure that child to mother transmission took place during this outbreak, and that breast feeding was probably responsible. Babies infecting their mothers has been reported only once before—during a similar hospital outbreak in Russia in 1990.

JAMA 2005;294:2301-2

Obstructive sleep apnoea is an important risk factor for stroke or death

Obese hypertensive patients with obstructive sleep apnoea have an increased risk of stroke. To find out if sleep apnoea is a risk factor on its own, researchers studied a cohort of 1022 adults referred to a specialist centre for sleep medicine for diagnostic tests. Of these, 697 were found to have obstructive sleep apnoea.

Three years later, the people with sleep apnoea were twice as likely to have had a stroke, a transient ischaemic attack, or to have died than those who were referred for tests but found not to have sleep apnoea (hazard ratio 1.97, 95% CI 1.12 to 3.48, $P = 0.01$). People with sleep apnoea had an increased risk of stroke, transient ischaemic attack, or death from any cause regardless of their other risk factors, including smoking, obesity, diabetes, hyperlipidaemia, atrial fibrillation, or high blood pressure.

If obstructive sleep apnoea is an independent risk factor for stroke or death, treating it should help. As yet there are no randomised trials big enough to find out if treatments, such as continuous positive airway pressure, prevent strokes or save lives. More than half (58%) of the people in this study had respiratory support most nights.

N Engl J Med 353:2034-41

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