Short cuts

What's new in the other general journals

Azithromycin works for severe cholera in adults

The choice of antibiotics for treating cholera is primarily determined by the patterns of bacterial resistance and antibiotic toxicity. Tetracycline and its derivatives have for decades been the antibiotics of choice for treating cholera in adults, but they should be avoided in children and pregnant women. Erythromycin has often been used as an alternative, but, unlike tetracycline, it is not effective in a single dose. Azithromycin, a derivative of erythromycin, has less gastrointestinal toxicity than erythromycin and has been shown effective for treating cholera in children with a single dose.

A recent equivalence trial of a single dose of azithromycin versus a single dose of ciprofloxacin, which had previously been shown to be effective for treating severe cholera in adults, showed that azithromycin was effective, but ciprofloxacin was not. The trial included almost 200 adult men with severe cholera who were treated in one hospital in Bangladesh in a period of a year and a half. Watery stools stopped within two days of giving azithromycin in more than 70% of patients. Ciprofloxacin was clinically effective in less than a third of people randomised to receive this drug. Similarly, azithromycin eliminated *Vibrio cholerae* from stool within two days from the start of treatment in almost 80% of people, compared with ciprofloxacin's 10%. The authors say that a single dose of ciprofloxacin may be too low a threshold for *V. cholerae*, 01 strain.

N Engl J Med 2006;354:2452-62

Maori people get poorer hospital care

Maori people, New Zealand's large indigenous minority, have previously been reported to have disadvantaged health

status compared with the rest of the population. It is notoriously hard to distinguish, however, whether differences in the quality of care between ethnic groups result from discrimination by the system and staff or from other variations, such as access, appropriateness of treatment, or patients' choice.

A recent retrospective study looked at preventable adverse events as the indicator of the quality of care in a nationally representative sample of people admitted in 1998 to New Zealand's public hospitals, which are funded by tax. The sample of more than 6500 patients was 15% Maori. Researchers excluded descendants of migrants from the nearby South Pacific area from their analysis. Admitted Maori patients were younger, had a different case mix (with more pregnancies and less chronic diseases), and were more likely to come from poor areas than non-Maori, non-South Pacific people.

After adjustment for age, sociodemographic characteristics, and case mix, Maori patients had a slightly increased risk of in-hospital preventable adverse events than non-Maori, non-South Pacific people ($P=0.05$). Deprivation score was not linked with occurrence of preventable adverse events and no evidence showed consistent differences between the groups in regard to possible causal factors for the disparities seen.

Lancet 2006;367:1920-5

Naps and coffee help on long shifts

Even after many countries officially restricted the length of shifts that healthcare workers can work, shifts of 30 hours are not unusual. Research in real life settings into the effects of such long working hours on alertness and the quality of care is scarce. Research into interventions to reduce possible harm to patients and healthcare workers is also patchy. Two recent studies help fill the gap.

In one study, 38 interns of internal medicine alternated for one year between two weeks of being able to find cover and take a nap on long shifts and two weeks of not having this option. With cover, the interns slept an average of 41 minutes longer per shift, reported less fatigue, and slept more efficiently compared with when cover was not provided. The study was underpowered, however, to assess the impact of napping on the quality of care.

A small randomised crossover trial (pp 785-91) of night time driving showed that drinking coffee and taking naps did improve objectively measured driving performance as well as self reported fatigue and sleepiness. The study also found large variations between people in functioning when deprived of sleep and responding to coffee and naps.

Ann Intern Med 2006;144:792-8

Early revascularisation improves survival

Early revascularisation, with either percutaneous coronary intervention or coronary artery bypass grafting, improves long term survival in patients with myocardial infarction complicated by cardiogenic shock due to ventricular failure. Previous studies showed that more people had survived a year after treatment.

A multicentre randomised trial of 300 patients with follow-up lasting between one and 11 years, with a median of six years, compared overall survival in patients who had early revascularisation with patients who were initially stabilised by drugs. More than 30% of people randomised to early revascularisation survived until the end of follow-up, compared with less than 20% in the group stabilised by drugs ($P=0.02$).

In people who survived until they were discharged from hospital, almost two thirds of those who received early revascularisation were alive at the end of follow-up, compared with less than half in the group stabilised by drugs. The authors argue that the data call for direct admission or early transfer of patients with myocardial infarction to centres with facilities for early revascularisation and advanced intensive care.

JAMA 2006;295:2511-5

Type A personality traits are not linked to atherosclerosis

CALCIFICATION AND DEPRESSION SCORES

Much anecdotal experience and evidence from epidemiological studies has linked the risk of coronary heart disease to type A patterns of behaviour, characterised by time urgency and hostility. Prospective epidemiological studies had shown depression, anxiety, hostility, and anger to be associated with the increased risk of coronary heart disease. A recent study, however, failed to find a link between such personality traits and subclinical coronary atherosclerosis, assessed by coronary calcium that has been shown to predict cardiovascular events in previously asymptomatic people, independently of risk factors.

A multiethnic population based cross sectional study included more than 6500 adults aged 45 to 84 with no history of cardiovascular disease. Coronary calcium, assessed by electron beam computed tomography of the chest, was not associated with anger, anxiety, depression, or chronic burden, which researchers measured using validated questionnaires.

The accompanying editorial (pp 858-60) says that these findings rule out the possibility that atherosclerosis or cardiovascular events cause type A traits. It also seems evident that the traits do not cause atherosclerosis, but several biologically plausible explanations exist to support the notion that they still might cause cardiovascular events. The observed association between the traits and cardiovascular events are possibly confounded by still unknown characteristics, although the association has been shown to be independent of age, diabetes, smoking, lipids, obesity, physical activity, and baseline cardiovascular disease.

Ann Intern Med 2006;144:822-31

ACE inhibitors are not safe throughout pregnancy

Despite the lack of appropriate safety studies, angiotensin converting enzyme (ACE) inhibitors have been considered safe in the first trimester of pregnancy, although

they are contraindicated in the second and third trimester because of the increased risk of fetopathy (which includes oligohydramnios, intrauterine growth retardation, hypocalvaria, renal dysplasia, anuria, renal failure, and death).

A large retrospective cohort study has found a fourfold increased risk for congenital malformations of the cardiovascular and central nervous systems in babies whose mothers took ACE inhibitors in the first trimester of pregnancy, compared with mothers who did not receive treatment with antihypertensives.

The researchers used the Medicaid data from Tennessee, which included nearly 30 000 infants born between 1985 and 2000 to mothers without diabetes. The cohort included 209 infants whose mothers were taking ACE inhibitors in only the first trimester of pregnancy and 203 infants whose mothers were taking other antihypertensive drugs, also in only the first trimester.

The risk ratio of serious congenital malformations associated with ACE inhibitors, compared with mothers who did not take antihypertensive drugs, was 2.71 (95% CI 1.72 to 4.27). No increased risk was found for infants whose mothers were taking other antihypertensives.

N Engl J Med 2006;354:2443-51

Whole brain radiation before stereotactic radiosurgery for metastases does not improve survival

Preceding stereotactic radiosurgery with whole brain radiation does not seem to improve survival or neurological functioning, compared with stereotactic surgery alone, in people with brain metastases. A recently published randomised controlled trial included 132 patients with one to four brain metastases of up to 3 cm in diameter and treated in 11 hospitals in Japan from 1999 to 2003.

Median survival was 8 months in people who received whole brain radiation and 7.5 months in people who did not ($P = 0.42$). But the relapse rate after one year in people who did not receive whole brain radiation was more than 75%, compared with less than 50% of patients who did. The study did not find any significant differences between the groups in preservation of systemic and neurological functioning, toxic effects of radiation, and causes of death.

An accompanying editorial (pp 2535-6) discusses how both treatment regimens are a reasonable first choice for most people with four or fewer brain metastases, and the choice should take into account the patient's age, extracranial disease, and performance status.

JAMA 2006;295:2483-91

Clopidogrel plus aspirin is inferior to oral anticoagulation

People with atrial fibrillation, at high risk of stroke, are candidates for oral coagulation treatment, but only about half of them receive it, mostly because of the high risk of bleeding and the need for regular monitoring. Clopidogrel and aspirin are both antiplatelet drugs with different mechanisms of action, and, because aspirin alone reduces the risk of stroke in people with atrial fibrillation by 22% compared with placebo, the combination was thought to be a possible safer alternative to oral coagulation.

A recent non-inferiority trial was stopped early, however, after a median follow-up of just over a year. Compared with people given oral anticoagulants, people randomised to clopidogrel plus aspirin had a 1.4-fold increased risk of first occurrence of stroke, non-central nervous system systemic embolus, myocardial infarction, or vascular death. Surprisingly, bleeding was less in the oral anticoagulants group than in the clopidogrel-aspirin group (2.2% v 9.4% a year). Differences were seen, however, between subgroups of people who were or were not receiving oral anticoagulants at the start of the study.

The accompanying commentary (pp 1877-8) proposes that effects of the clopidogrel-aspirin combination in people naive to oral anticoagulants could be assessed in a new trial, but new developments in preventing stroke in people with atrial fibrillation are possibly going to come from oral direct thrombin blockers or oral factor Xa inhibitors, rather than antiplatelet drugs.

Lancet 2006;367:1903-12

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