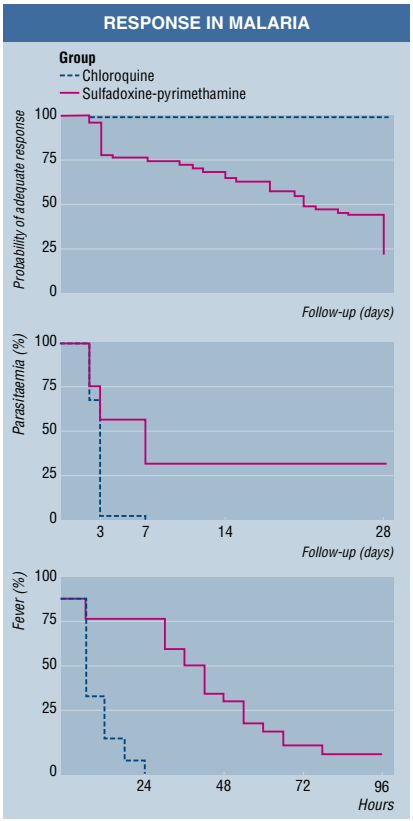
Short cuts

What's new in the other general journals

Chloroquine sensitive malaria returns to Malawi



Back in 1993, Malawi was the first country in Africa to abandon chloroquine as a treatment for malaria. It had stopped working because of widespread chloroquine resistance and was replaced by sulfadoxine-pyrimethamine. But after an absence of 12 years, the parasite sensitive to chloroquine seems to be back. Encouraged by a decline in the genetic marker for resistance among falciparum malarial parasites, researchers recruited 210 infected children for a clinical trial. The old drug cured 99% (95% CI 93% to 100%) of those who took it, compared with a success rate of only 21% (13% to 30%) among those who took sulfadoxine-pyrimethamine. Chloroquine cleared the parasite in a mean of 2.6 (SD 2.5 to 2.8) days.

The return of chloroquine would be good news for children throughout sub-Saharan Africa, where falciparum malaria continues to be a leading killer. Chloroquine is safe, cheap, fast acting, and long lasting. But the authors and a linked commentary (pp 1956-7) agree that bringing it back now would be a mistake. "Malawi is surrounded by a sea of chloroquine resistance" which would soon break through its borders if choloroquine became widely available again, says the commentary. Resistance must be eliminated throughout the region first, a strategy that depends entirely on rich countries bringing down the cost of effective artemisinin-based combination treatments to less than 10 US cents a day.

N Engl J Med 2006;355:1959-66

Disabled women get suboptimal treatment for early breast cancer

Disabled women are less likely than other women to get the recommended treatments for early stage breast cancer, according to an analysis of routine data from the US. Women receiving disability benefits and medicare insurance were less likely to have breast conserving surgery (adjusted relative risk 0.80, 95% CI 0.76 to 0.84), and if they did they were less likely to have radiotherapy (0.83, 0.77 to 0.90) or lymph node dissection (0.81, 0.74 to 0.90) than other women. All cause mortality and mortality associated with breast cancer were higher among women with disabilities, although the women's disabilities and associated illnesses could have been partly responsible. The authors had no reliable data on chemotherapy.

It seems likely that some disabled women are missing out on the best treatments for early breast cancer, but it's far from clear why. Perhaps women already burdened with disability choose not to embark on intensive and lengthy treatments such as radiotherapy. Perhaps they can't because a daily trip to the radiotherapy centre is simply impossible or because they can't lie flat or lie still for treatment. Or perhaps their doctors give them the wrong advice, informed by acknowledged or unacknowledged prejudices about disabled people's quality of life. It's time to find out, say the authors.

Ann Intern Med 2006;145:637-45

Low systolic blood pressure signals a high risk of death in people with acute heart failure

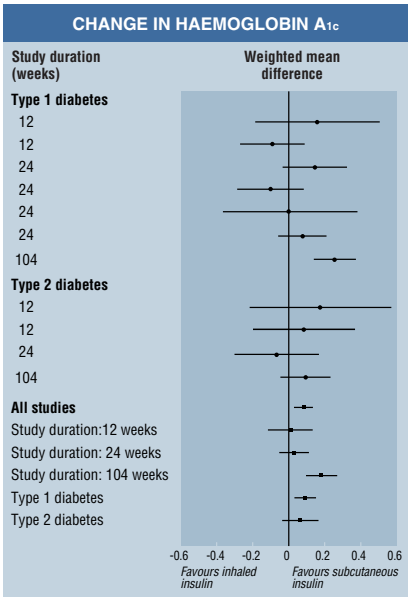
A simple systolic blood pressure reading on admission can provide important prognostic information for people presenting to hospital with acute heart failure, say researchers from the US who found a clear link between higher systolic blood pressure and lower mortality among more than 48 000 adults. In-hospital mortality was 7.2% for patients with the lowest blood pressures (<120 mm Hg), falling to 1.7% among those with the highest (>161 mm Hg). The trend was significant, with no apparent ceiling to the effect.

Overall, the odds of dying in hospital increased by 21% (95% CI 17% to 25%) for every 10 mm decrease in systolic blood pressure below 160 mm Hg.

It's likely that systolic blood pressure on admission divides patients with acute heart failure into two distinct groups, write the researchers. Women, African Americans, and people with a well preserved ejection fraction seem over-represented at the top end of the blood pressure range, while men, and people with ischaemic heart disease and poor ejection fraction, are over-represented at the bottom. Clinical trials of treatments should probably consider these groups separately.

JAMA 2006;296:2217-26.

Inhaled insulin is a promising alternative for patients who won't inject



Until recently, people with diabetes had to inject their insulin. Now they can inhale it instead. A meta-analysis of 16 trials

concluded recently that inhaled insulin works almost as well as subcutaneous insulin for patients with either type 1 or type 2 diabetes. More specifically, subcutaneous insulin reduced concentrations of haemoglobin A_{1c} slightly more than inhaled insulin (weighted mean difference 0.08%, 95% CI 0.03% to 0.14%), but similar proportions in both groups reached the treatment target of less than 7%. Inhaled insulin worked significantly better than oral hypoglycaemic agents, but it was more likely to cause severe episodes of hypoglycaemia (9.4% *v* 3.5% of patients reported at least one episode; risk ratio 3.06, 1.03 to 9.07). Patients with both types of diabetes preferred inhaled insulin to subcutaneous insulin despite an increase in the incidence of cough and a slight but significant reduction in lung function.

These results are promising, but they don't support a wholesale switch to insulin inhalers, say the authors. The trials were mostly short, open label, and funded by the manufacturers of inhaled insulin. They couldn't rule out bias, and long term side effects are unknown. For now, inhaled insulin should be offered only to patients who face damaging delays in their treatment because they won't or can't inject.

Ann Intern Med 2006;145:665-75

Heart disease and a diet low in carbohydrate aren't linked

Low carbohydrate diets can help people lose weight, but many observers worry that encouraging women to replace carbohydrate with protein and fat might increase their risk of heart disease. A large randomised trial would take decades, so researchers looked for evidence among the 82 802 nurses who have been filling in food frequency questionnaires every two years since 1980 for the nurses' health study.

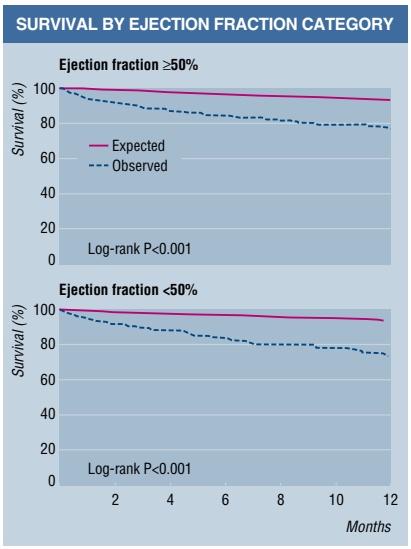
Their findings were reassuring. Women with diets low in carbohydrate but relatively rich in proteins and fats were no more likely to get coronary heart disease than women who reported the opposite kind of diet (relative risk 0.94, 95% CI 0.76 to 1.18). In fact, a diet with a high glycaemic load was associated with an increased risk of heart disease, while a diet rich in vegetable fats and vegetable proteins was associated with a slightly lower risk (relative risk comparing top and bottom groups 0.70, 0.56 to 0.88). The study spanned 20 years.

The researchers weren't able to look for other potentially damaging effects of Atkins-type diets such as reduced renal function and osteoporosis.

N Engl J Med 2006;355:1991-2002

Most patients with heart failure have diastolic dysfunction

Heart failure is caused by systolic dysfunction (poor contraction of the left ventricle with reduced ejection fraction),



diastolic dysfunction (impaired relaxation with preserved ejection fraction), or a mixture of both. The latest researchers to study the relative importance of these features found that in a cohort of 556 American adults with clinical heart failure, 80% (446) had Doppler evidence of diastolic dysfunction, 37% (204) had combined systolic and diastolic dysfunction, and 44% (242) had isolated diastolic dysfunction and a preserved ejection fraction.

So diastolic heart failure is an important cause of symptoms. It's also an important cause of death. In this study 16% (95% CI 11% to 20%) of patients with preserved ejection fraction were dead within six months, a rate almost identical to that among patients with a low ejection fraction (16%, 11% to 21%).

Despite their abundance, patients with symptoms of heart failure and a preserved ejection fraction—over half this cohort—have received little attention from researchers. Patients with documented diastolic dysfunction have received even less. Doctors thus have no good evidence to guide their treatment decisions. Until they do, a linked editorial (pp 2259-60) argues that angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers would be a reasonable treatment to start with, since most of these patients also have hypertension.

JAMA 2006;296:2209-16

High blood glucose concentrations cause millions of cardiovascular deaths worldwide

There's a fairly straightforward, direct, and continuous association between plasma concentrations of glucose and risk of heart disease and stroke, and it starts well below the conventional thresholds used to define diabetes. So it's important to look beyond frank diabetes for a clearer picture of the global impact of impaired glucose tolerance on public health. The latest estimates, derived from population surveys and meta-analyses of published data, show that worldwide at least three million people a year die from cardiovascular disease because their blood glucose concentrations are less than ideal. About one million of them have diabetes. "Higher than optimum" blood glucose concentrations are responsible for the remaining one and a half million deaths from heart disease and about 700 000 deaths from stroke. The bulk of these deaths occur in low and middle income countries, which are least able to tackle the problem. In 2001, an estimated 548 000 people in South Asia alone died of heart disease caused by high blood glucose concentrations—37% of the global total.

If these estimates are accurate, high blood glucose concentrations, not including diabetes, are responsible for a greater proportion of cardiovascular deaths than smoking.

Lancet 2006;368:1651-9

Patients with achalasia often need repeat procedures, usually balloon dilatation

Achalasia is a rare disorder of oesophageal motility that causes obstruction at the lower end of the oesophagus, resulting in dysphagia, regurgitation, and chest pain. The main treatment options are pneumatic dilatation, which is done as a day case, and surgical myotomy, which requires a general anaesthetic and a short period in hospital. There's little decent evidence to help patients choose between them, so researchers took a look at what happened in the long term to unselected patients who had one or other procedure. A substantial proportion of both groups needed at least one repeat intervention during a follow-up of five years: 56% of those who had a pneumatic dilatation and 30% of those treated initially with myotomy (adjusted hazard ratio for pneumatic dilatation 2.37; 95% CI 1.86 to 3.02). Pneumatic dilatation was the commonest repeat intervention for both groups. The difference between initial myotomy and initial pneumatic dilatation persisted after adjustments for age, sex, other illnesses, and income, which suggests (but doesn't prove) it was due to the treatment, not the characteristics of the patients selected for each procedure.

The authors used Ontario's administrative health databases, which don't include information on symptoms or quality of life, so they can't say much about the effectiveness of either treatment. But it does seem clear that when patients have a procedure for achalasia, particularly dilatation, they have a good chance of eventually needing another one.

JAMA 2006;296:2227-33

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