SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

Alison Tonks, associate editor, *BMJ* atonks@bmj.com

"'Do you think it's strep, doctor?' is a question always posed in an American accent. In my experience, these patients are better at showing their throats too: none of that British gagging and tongue wagging through a barely open mouth"

Read Richard Lehman's journal blog at bmj.com/blogs

New egg-free vaccine gives good protection against matching influenza

Researchers in the US have developed a new influenza vaccine from viruses grown in cell culture rather than the more traditional egg substrate. In theory, vaccines derived from cell cultures should be faster to produce, safer for people allergic to egg, less susceptible to microbial contamination, and free from the vagaries of egg production. But do they work?

This trivalent vaccine induced a robust immune response in young adult volunteers participating in a placebo controlled trial (n=7250). It also prevented 78.5% of influenza caused by antigenically matching strains (95% CI 60.8% to 88.2%), including pandemic influenza A/H1N1. Protection against the other two strains—A/H3N2 and influenza B—was harder to gauge because so few participants had these infections during the 2008-9 season. The 3623 volunteers given the inactivated vaccine reported no serious side effects, although 1571 (43%) found the injection painful and 652 (18%) reported myalgia.

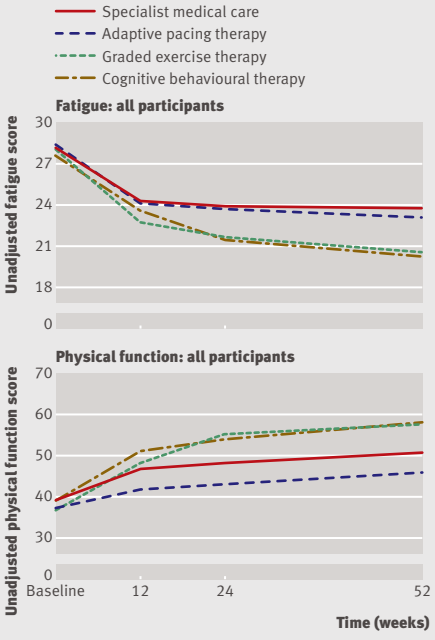
This vaccine looks effective, says a linked comment (doi:10.1016/S0140-6736(11)60174-8), and represents a step forward in vaccine development. Successful control of influenza depends on timing, particularly during pandemics. Cell cultures can accelerate vaccine production, shaving up to 10 weeks off the time it currently takes to produce a vaccine that matches circulating strains. Cell cultures are also better than egg substrates at preserving the structure of viral haemagglutinin, the surface antigen crucial to a successful immune response. This may prove to be their biggest advantage in the end.

Lancet 2001; doi:10.1016/S0140-6736(10)62228-3

CBT and graded exercise are safe and effective treatments for chronic fatigue syndrome

Cognitive behavioural therapy (CBT) and graded exercise are the best treatments for chronic fatigue syndrome, according to a rigorous trial of four different options. Both treatments looked safe when added to specialist medical care and worked better than adaptive pacing therapy or specialist care alone. The 641 participants were treated for six months and followed up for a further six months. All groups improved, but by the end of the trial

FATIGUE AND PHYSICAL FUNCTION BY TREATMENT GROUP



Adapted from *Lancet* 2011; doi:10.1016/S0140-6736(11)60096-2

patients treated with CBT or graded exercise had significantly less fatigue and significantly better function than any of the other groups. All secondary outcomes pointed in the same direction, including patients' own impressions—CBT and graded exercise therapy both doubled the odds of being much or very much improved, relative to specialist care alone (odds ratios 2.2, 95% CI 1.2 to 3.9; and 2.0, 1.2 to 3.5).

Adaptive pacing was the least successful active treatment in this trial, despite patients' high expectations. Some patient groups favour adaptive pacing because it teaches patients to live within their capabilities (adaptation) rather than risk exacerbating fatigue by increasing activity. Graded exercise therapy and CBT, both of which encourage patients to do more, did not worsen symptoms in this trial, and serious adverse events were rare in all groups. Only a handful of patients got much worse during or after any treatment.

Patients with chronic fatigue syndrome have nothing to fear from CBT or graded exercise, say the authors. Both work as a bolt on to specialist care, although their overall effects looked modest. Less than a third of patients were cured by either treatment (30% (44/148) after CBT and 28% (43/154) after graded exercise therapy).

Lancet 2011; doi:10.1016/S0140-6736(11)60096-2

Obesity and arthritis reduce quality and length of life

Roughly 40% of US adults aged 50-84 are obese or have osteoarthritis of the knee, or both. There are 86 million adults in this age group, so the public health impact of these chronic conditions is huge, say researchers. Their modelling study estimates that adults with both conditions lose 25% of their remaining quality adjusted life expectancy—an average of 3.5 quality adjusted life years per person. Men and women with arthritis alone lose 1.86 quality adjusted life years, those with obesity alone lose 2.46.

The relative contributions of obesity and arthritis varied with age and with ethnic background. Black and Hispanic women were disproportionately affected by both.

These figures are based on data from published studies and national surveys and can only ever be best guesses. But they do give a clear indication of just how much older US adults have to lose from obesity and arthritis, and how much they have to gain from measures to curb the obesity epidemic, say the authors. They further estimate that cutting the prevalence of obesity in this age group to where it was 10 years ago would head off 178 071 new cases of heart disease (0.7%), 889 872 new cases of diabetes (2.5%), and 111 206 (1.9%) knee replacements. It would also give older US adults an extra 6 318 030 years of life.

Ann Intern Med 2011;154:217-26

Bevacizumab looks better than laser treatment for retinopathy of prematurity

Bevacizumab is a monoclonal antibody directed against vascular endothelial growth factor. It helps prevent pathological neovascularisation and is an emerging treatment for the retinopathy that can blind severely premature babies. In its first head to head trial, bevacizumab worked significantly better than conventional laser treatment. Pathological new growth recurred in 26% (19/73) of babies treated with laser and 6% (4/70) of those treated with bevacizumab (odds ratio 0.17, 95% CI 0.05 to 0.53).

The 150 babies in this trial were born at a mean gestational age of 24 weeks. All had the kind of neovascular growth that was treatable (stage 3+) but associated with a high risk of recurrence. Intravitreal injections of bevacizumab seemed to work

best for babies with disease in zone 1 of the retina, the zone closest to the optic disc.

Bevacizumab is easier to administer than laser treatment, say the authors. The intravitreal injection can be given at the bedside by any trained ophthalmologist. Bevacizumab is kinder to the developing retina and unlike laser treatment allows normal vascularisation to continue. At least one observer (p 677) believes that bevacizumab should now overtake lasers as the treatment of choice for retinopathy of prematurity.

Safety data look reassuring so far but can't be established by a small trial or possibly even a large one. Careful, comprehensive, long term surveillance is probably the only way, he writes. Problems to look out for include systemic absorption and the (small) possibility of damage to a premature baby's developing organs.

N Engl J Med 2011;364:603-15

Topical nitrates for bone health?

A simple nitroglycerin ointment, applied with tape to the upper arm once a day, increased bone mineral density and measures of bone structure in postmenopausal women in a recent placebo controlled trial. Could this cheap and widely available drug help women maintain healthy bones or even prevent fractures?

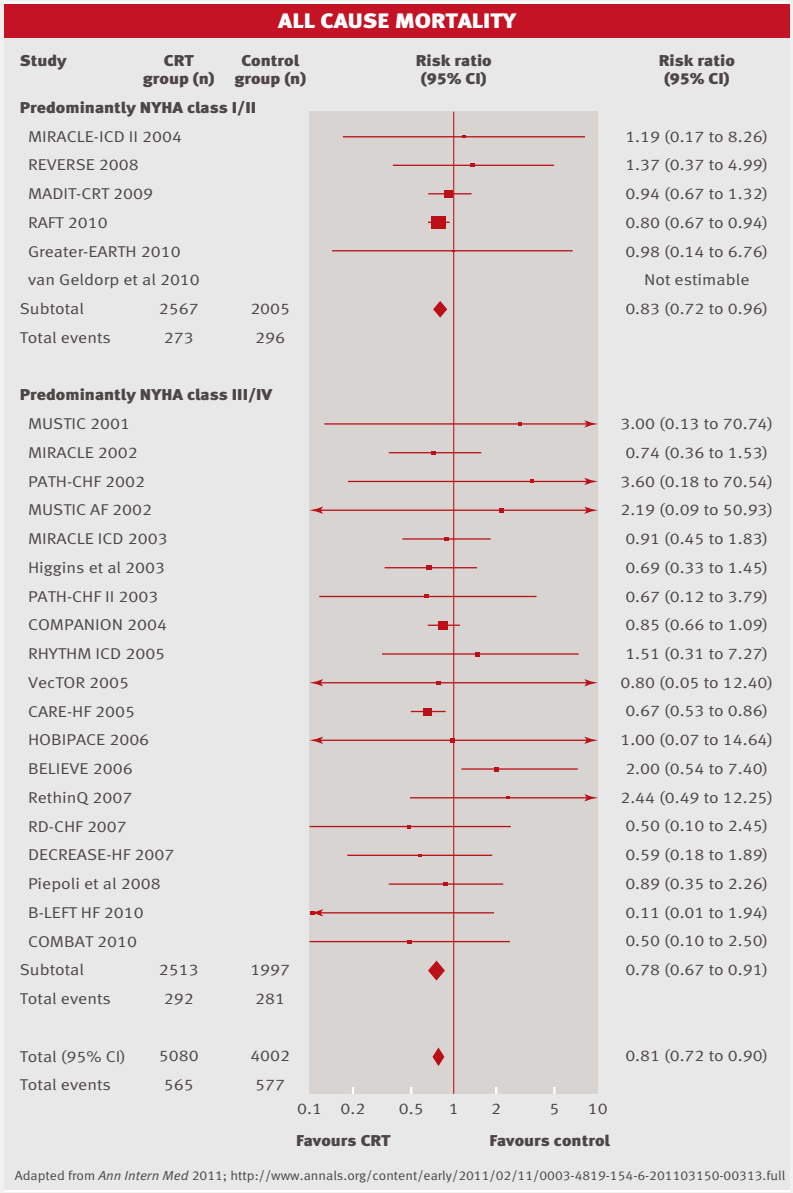
Quite possibly says an editorial (p 826). Nitrates, alone among skeletally active drugs, can increase bone formation and reduce resorption. In this trial, an ointment containing 15 mg nitroglycerin increased bone mineral density at the hip and lumbar spine by 6-7% more than placebo. The differences were significant and big enough to be clinically relevant. Nitroglycerin also increased the thickness and area of cortical bone in the radius and tibia, along with measures of bone strength. Women used the ointment or a placebo for two years. None had osteoporosis.

The problem with nitrates, however, is that they cause headaches. A quarter of the women recruited to a run-in phase dropped out citing headaches as the main reason. During the main trial, nitrate related headaches were common in the first month (35%), although few women still reported headaches after a year of treatment and only seven (of 126) stopped using the ointment because of headaches.

The results are promising enough to justify much bigger trials to find out if nitrates can actually prevent fractures, says the editorial.

JAMA 2011;305:800-7

Cite this as: *BMJ* 2011;342:d1168



Adapted from *Ann Intern Med* 2011; http://www.annals.org/content/early/2011/02/11/0003-4819-154-6-201103150-00313.full

Cardiac resynchronisation can help patients with milder symptoms too

Cardiac resynchronisation has traditionally been reserved for people disabled by their heart failure, but evidence is accumulating that people with more minor symptoms can also benefit. The latest, a meta-analysis and systematic review of 25 trials, shows that resynchronisation treatment saves lives (risk ratio for all cause mortality 0.80, 95% CI 0.67 to 0.96) and helps prevent hospital admission (0.69, 0.59 to 0.80), even when poor left ventricular function causes few, if any, limitations to daily life. Patients in these analyses had a left ventricular ejection fraction of no more than 40% (usually less), sinus rhythm, and wide QRS interval. Most of those with few symptoms were also fitted with an implantable cardioverter defibrillator, so these results represent benefits over and above those provided by the defibrillator and best medical treatment, say the authors. Cardiac resynchronisation did not improve quality of life for patients with mild symptoms.

International guidelines are gearing up to broaden their recommendations for cardiac resynchronisation, but an editorial (www.annals.org/content/early/2011/02/11/0003-4819-154-6-201103150-00314?aimhp) advises doctors to be careful not to over interpret findings from the highly selected patients lucky enough to be treated within randomised trials. Just because a technology can work does not mean we should use it indiscriminately in the rough and tumble of real practice, it says. Caution is needed while we fine tune the clinical and demographic profile of patients most likely to benefit and least likely to be harmed. Patients with atrial fibrillation—for example, remain "woefully underrepresented" in clinical trials of resynchronisation treatment.

Ann Intern Med 2011; www.annals.org/content/early/2011/02/11/0003-4819-154-6-201103150-00313.full