SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS
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"Pneumococcal vaccination does not reduce the risk of myocardial infarction or stroke in men. I didn't find this very interesting, because it never entered my head that it might."
Richard Lehman's journal blog, doc2doc.bmj.com

Performance enhancing drugs on trial

Growth hormone is a popular performance enhancing drug, banned by the World Anti-Doping Agency. But does it actually work?

It didn't work terribly well for 96 volunteer athletes from Sydney, who were persuaded to take part in a randomised trial to help inform anti-doping policy. Daily injections of growth hormone helped improve the athletes' sprint capacity on a cycle ergonometer, compared with placebo injections. But growth hormone had no discernible effect on any other measure of performance including endurance, strength, and power (as measured by jump height from a standing start). The drug's effect on sprint capacity was a modest 3.9% relative improvement for men and women combined (95% CI 0.0% to 7.7%), although that figure doubled in the small group of men given both testosterone and growth hormone (8.3%, 3.0% to 13.6%). Again, the combination had no effect on other performance measures, compared with a double placebo.

Participants were recreational athletes given a modest dose of growth hormone for an eight week period, say the authors. Elite athletes probably take more, for longer. We don't yet know what that does for their performance, but side effects are not trivial. In this trial, athletes given growth hormone reported significantly more swelling, joint pain, and parasthesias (men only) than controls.
Ann Intern Med 2010;152:568-77

More evidence against erythropoiesis stimulating agents

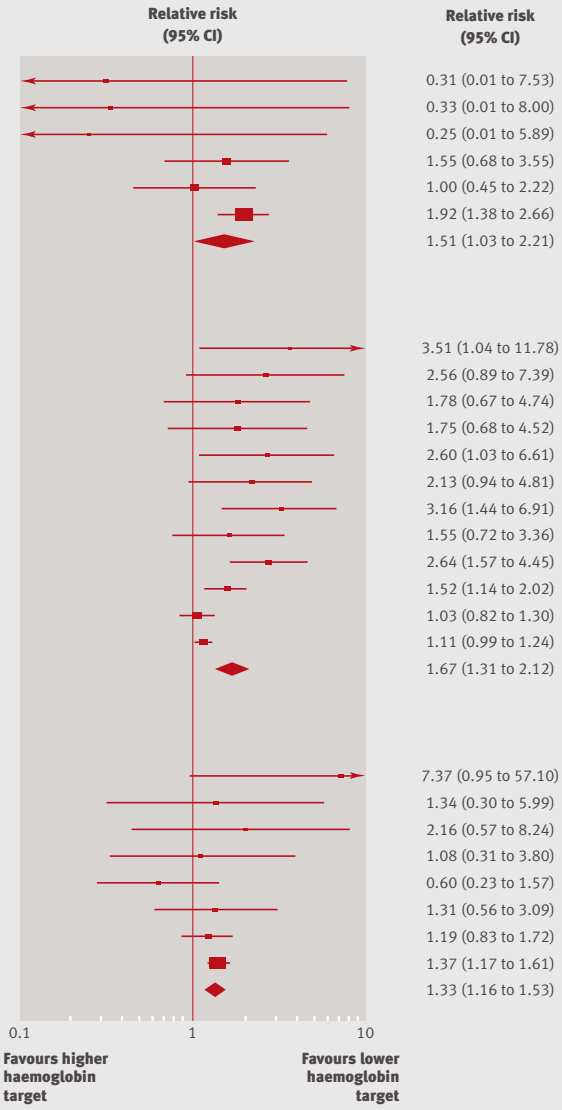
The latest meta-analysis of erythropoiesis stimulating agents confirms that people with chronic kidney disease risk thromboses and hypertension if their target haemoglobin is set too high. In an analysis of 27 trials, higher targets were associated with more strokes (relative risk 1.51, 95% CI 1.03 to 2.21), more thromboses of vascular access for dialysis (1.33, 1.16 to 1.53), and more hypertension (1.67, 1.31 to 2.12) than lower targets.

There were also more deaths and more cardiovascular events in patients treated aggressively, although the excess wasn't statistically significant. The authors say their findings probably rule out any net benefit.

Precise targets varied and have crept up over time. For the past decade or so, trials have compared higher targets between 120 g/l and 150 g/l with lower targets between 90 g/l and 120 g/l. The authors had inadequate data on the doses of erythropoietins or darbepoetin needed to meet haemoglobin targets. So it is still unclear whether the problem lies with the drugs or the way we use them. Data on quality of life, arguably the most important outcome for patients, were too poor to be useful.

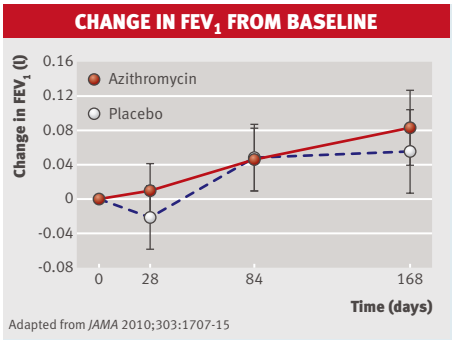
We now know that these agents are not the panacea they were originally thought to be, says an editorial (www.annals.org/content/early/2010/04/29/0003-4819-153-1-201007060-00250.full%20?aimhp). But it is too early to abandon them and return to a time when chronic kidney disease meant intractable severe anaemia and multiple transfusions. There is a middle way, and further trials are needed to find it.
Ann Intern Med 2010; www.annals.org/content/early/2010/04/29/0003-4819-153-1-201007060-00252.full

TARGET HAEMOGLOBIN LEVEL AND CLINICAL OUTCOMES



Adapted from *Ann Intern Med* 2010; published online 6 April

Mixed results for azithromycin in children with cystic fibrosis



Adapted from *JAMA* 2010;303:1707-15

Azithromycin is an established treatment for cystic fibrosis, recommended only for patients with cystic fibrosis who are chronically infected with *Pseudomonas aeruginosa*. Because the drug has anti-inflammatory as well as antimicrobial properties, researchers recently tested it in affected children and adolescents without pseudomonas infection. Trial results were mixed.

Azithromycin had no effect on any measure of lung function over six months compared with placebo. It didn't prevent hospital admission or accelerate growth. Pulmonary exacerbations dropped by half, however (21% (28/131) *v* 39% (50/129); hazard ratio 0.5, 95% CI 0.31 to 0.79). Children given azithromycin put on more weight than controls (0.58 kg difference, 0.14 to 1.02), reported less cough and less productive cough than controls, and needed fewer courses of oral—but not intravenous—antibiotics.

The researchers stop short of any recommendations based on these findings. Their participants were relatively young and fit, with a mean age close to 11 years. They had mild lung disease and good lung function at the start of the trial, making it harder to detect improvements. Recruitment was difficult despite the cooperation of 40 different treatment centres in the US and Canada. In the end the trial was smaller and weaker than planned. Further trials are justified, say the researchers.

JAMA 2010;303:1707-15

Medication errors fall after patients are given bar codes to match their drugs

Medication errors fell significantly when a large tertiary care hospital in the US rolled out technology to match each patient with their drugs using a unique bar code. When nurses at the bedside scanned bar codes on the patient's wristband and on the drug before giving drugs, the rate of administration errors fell from 11.5% (776/6723 doses) to 6.8% (495/7318 doses) in a few weeks. Potentially harmful mistakes such as giving the wrong drug or the wrong dose fell by more than half (3.1% (213/6723) *v* 1.6% (114/7318); 50.8% decrease, 95% CI 39.1% to 61.7%). The study looked at 35 surgical, medical, and intensive care units. Full implementation took four months in 2005.

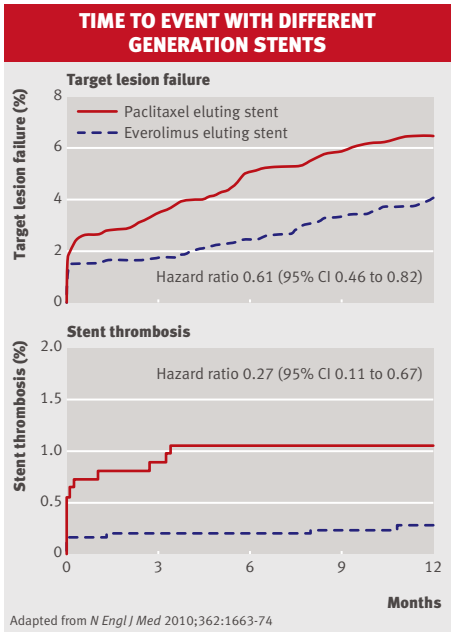
The new system imported doctors' orders from a computerised order entry system and imported pharmacists' orders directly from the pharmacy. Researchers found no transcription errors in 1283 orders reviewed after roll out.

The authors are confident that bar code technology had a real effect on drug errors, although before and after observations are generally weak evidence of cause and effect. Implementation was hard work and expensive. These researchers feel it was worth the effort, but they warn others to expect challenges, including a substantial change in working patterns on the wards. This hospital already had technologically sophisticated physician order entry and bar code scanning at the pharmacy. Results may be different in hospitals without them.

N Engl J Med 2010;362:1698-707

Second generation drug eluting stent looks safer

A second generation drug eluting stent made by Abbot Vascular has a more flexible frame than first generation models. It is coated with a thinner layer of a new polymer and releases everolimus, rather than paclitaxel. A large head to head trial, funded by the manufacturer, suggests that these changes have made the new coronary stent safer. Adults given the everolimus eluting stent had a lower risk of treatment failure in the target artery than controls given an established paclitaxel eluting stent (4.2% (101/2416) *v* 6.8% (81/1195); relative risk 0.62, 95% CI 0.46 to 0.82). Treatment failures (called "target lesion failures" in the trial) included cardiac death, myocardial infarction, and revascularisation. Late stent thromboses were rare but significantly less likely after treatment with the everolimus eluting stent (1/2389 *v* 4/1181, P=0.04). Main outcomes were reported one year after treatment.



Adapted from *N Engl J Med* 2010;362:1663-74

It is unclear whether the new drug, the new polymer, the new flexible frame, or all three were responsible for improved outcomes, says an editorial (p 1728). Doctors probably shouldn't assume that these results apply to other second generation stents with different specifications. Nor should they assume that Abbot Vascular's stent is cost effective—it costs $300 (£200; €236) more than the paclitaxel eluting control. The everolimus eluting stent did not reduce target lesion failures in patients with diabetes, who account for 20-30% of patients treated.

N Engl J Med 2010;362:1663-74

Which blood test for coeliac disease?

Coeliac disease is difficult to diagnose in primary care, where patients present with non-specific symptoms such as diarrhoea, abdominal pain, or weight loss. Serological tests can help, but which ones? Blood tests for IgA antitissue transglutaminase antibodies (IgA-tTG) and IgA antiendomysial antibodies (EmA) looked most useful in a systematic review. The authors reviewed 16 studies of unselected adults with abdominal symptoms, three of which were done in well defined primary care settings.

They pooled results where they could and reported a sensitivity of 0.89 (95% CI 0.82 to 0.94), a specificity of 0.98 (0.95 to 0.99), a positive likelihood ratio of 37.7, and negative likelihood ratio of 0.11 for IgA antitissue transglutaminase antibody tests. Corresponding figures for IgA antiendomysial antibodies were 0.90 (0.80 to 0.95), 0.99 (0.98 to 1.00), 171, and 0.11. A combination of the two tests performed even better, although the evidence was limited. In practice, the simpler IgA-tTG test should probably be done first, say the researchers, while we wait for trials testing different sequential strategies for adults presenting specifically to primary care.

All studies used small bowel biopsy as a reference standard. Symptoms, alone or in combination, were too insensitive to be diagnostically useful. Tests for IgA and IgG antigliadin antibodies performed erratically in this review.

JAMA 2010;303:1738-46

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