SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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"Here's a landmark paper that will save the sight of thousands of patients with neovascular age-related macular degeneration and will avert a drug bill of billions of pounds in advanced health systems"
Read Richard Lehman's journal blog at bmj.com/blogs

Selenium improves quality of life for people with mild Graves' orbitopathy

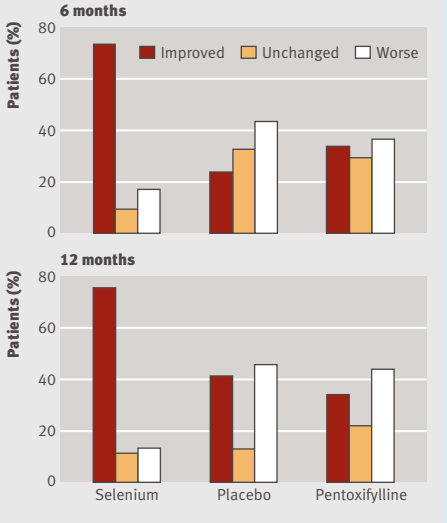
Even mild Graves' orbitopathy can be hard to live with, so researchers are currently looking for well tolerated active treatments that work better than the current strategy, which is to "wait and see." The trace mineral selenium improved patients' quality of life in a recent European trial, and it also seemed to slow progression of eye disease compared with placebo. Pentoxyphilline, another candidate treatment tested in the same trial, did neither.

Selenium is an antioxidant that may also be immunologically active. A real benefit for patients with mild Graves' orbitopathy is biologically plausible, and the researchers say it should be investigated further. None of the 55 people given selenium in this trial reported any side effects. They were treated for six months, and they reported an 8.7 point improvement in quality of life associated with visual function and a 10.6 point improvement associated with appearance. Placebo controls reported no overall improvement in either of the scores, which run from 0 to 100, with higher scores indicating better quality of life. Baseline scores were between 74 and 84 in all groups.

Improvements continued for a further six months in patients given selenium, and they seemed to result mainly from a reduction in the aperture between the eyelids and a reduction in soft tissue involvement. Selenium had no effect on proptosis, which remained unchanged in more than four fifths of the patients in all three groups. The trial was independently funded by government and university grants.

N Engl J Med 2011;364:1920-31

QUALITY OF LIFE AT 6 AND 12 MONTHS (GO-QOL)



Adapted from *N Engl J Med* 2011;364:1920-31

Don't destroy the last remaining smallpox samples, plead experts

Two public health experts have urged the World Health Assembly not to destroy the final remaining stocks of smallpox virus, ahead of a forthcoming meeting. On the agenda are the only two known stocks of the virus, currently stored securely at sites in the US and Russia.

Researchers need live variola to develop vaccines and antivirals—the only defences against a global pandemic should variola re-emerge. Half the world's population was born after vaccination programmes ended in the 1980s. They have no immunity whatsoever. When global eradication of smallpox was declared in 1980, remaining stocks were transferred to protected sites, but there is no international verification that the process was complete, write the experts.

Work on vaccines and antivirals is only half finished and must be allowed to continue. Not least because this work has important implications for other threats, including a related virus called monkey pox. Monkey pox is already a serious public health problem in central Africa, where reported infections have increased 20-fold in the 30 years since it was first discovered. Destroying the only remaining samples of variola would be particularly bad news for the populations of central and sub-Saharan Africa, where a pandemic would hit hardest. Simply hoping for the best is not enough for them, or for anyone else, the experts write. Researchers working on smallpox must be allowed to finish what they started.

Lancet 2011; doi:10.1016/S0140-6736(11)606946

Weight gain and hypoglycaemia separate third line agents for type 2 diabetes

Researchers use network meta-analysis to simulate head to head comparisons from placebo controlled trials. Direct comparisons between drugs are always better, but not always available, particularly in areas such as the treatment of type 2 diabetes, where many options exist. One team of researchers from Brazil had to use network meta-analysis to compare third line drugs for adults whose type 2 diabetes was poorly controlled, despite treatment with metformin and a sulphonylurea. They found 19 trials that tested five classes of antihyperglycaemic agent. Nine were placebo controlled, and the rest compared a non-insulin agent with insulin.

All drug classes, including insulin, looked equally effective. The addition of any third treatment reduced glycated haemoglobin concentrations between 0.7% and 1% from a mean baseline of 8.8%. Patients given a thiazolidinedione or insulin put on weight (4.25 kg, 95% CI 2.76 to 5.66; 2.84 kg, 1.76 to 3.9). Those given acarbose or a glucagon-like peptide-1 agonist tended to lose it. Insulin and the glucagon-like peptide-1 agonists caused more hypoglycaemia than other agents when added to metformin and a sulphonylurea.

The researchers were surprised that insulin looked no more effective than oral agents but warn that these analyses were based on a small number of trials that tested relatively low doses of insulin. It is also possible that weight gain limits the diabetic control achievable with insulin in these patients.

Ann Intern Med 2011;154:672-9

Atrial fibrillation signals reduced survival for middle aged women

A large observational study has confirmed that middle aged women who develop atrial fibrillation can expect a shorter life than their healthy peers. Researchers followed up 34 722 apparently healthy women for a mean of 15 years. The 1011 women who developed new onset atrial fibrillation were twice as likely to die during follow-up than women without atrial fibrillation (hazard ratio 2.14, 95% CI 1.64 to 2.77). They were four times more likely to die of cardiovascular disease (4.18, 2.69 to 6.51). Risk of a non-cardiovascular death was also increased.

Women who developed atrial fibrillation started the study older, fatter, and less healthy than others, but this didn't explain their reduced survival. The main results remained significant through full adjustments for body mass index, hypertension, smoking, diabetes, hypercholesterolaemia, and education.

Atrial fibrillation was also associated with new strokes, heart attacks, and heart failure. Non-fatal cardiovascular events probably shortened the life expectancy of at least some of the women with atrial fibrillation, say the authors. Adjustments for these events reduced but didn't abolish the excess risk.

Structural abnormalities of the left atrium and ventricle are also a "common denominator" linking atrial fibrillation, cardiovascular events, and death, says an editorial (p 2116). More than 40% of the women with atrial fibrillation in this study had an enlarged left atrium at diagnosis, and a third had left ventricular hypertrophy.

JAMA 2011;305:2080-7

Intensive lifestyle counselling fails to prevent gestational diabetes

Advising women at risk of gestational diabetes to eat better and exercise more helped control their baby's birth weight but failed to have any effect on the incidence of gestational diabetes in a cluster randomised trial from Finland. Women in the seven municipalities assigned to the intervention were counselled repeatedly during pregnancy and given targets for exercise levels, healthy eating, and weight gain. Only a quarter of them managed to meet their targets (55/229; 24%), and this may have contributed to the negative result.

Babies born to women in intervention municipalities were 104 g lighter (95% CI 7.6 to 201; P=0.035) at birth than babies born to control women given usual care, after statistical adjustments to control baseline differences between the two groups.

All 399 participants had a normal glucose tolerance test 10-12 weeks into pregnancy, but were considered high risk because of their body mass index (at least 25), history (macrosomia or gestational diabetes in a previous pregnancy), or family history. By the start of the third trimester, 15.8% (34/216) of women given counselling and 12.4% (22/179) of controls had gestational diabetes.

PLoS Med 2011;8:e1001036

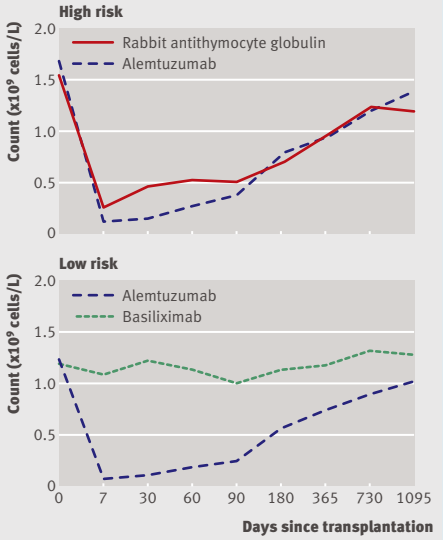
Which induction therapy for renal transplant patients?

Alemtuzumab is a monoclonal antibody that depletes both T cells and B cells. It is one of three agents commonly used to induce intense immunosuppression around the time of a renal transplant so patients can be weaned quickly off corticosteroids. Is it any better, or safer, than the others?

That depends on the baseline risk of rejection, according to a head to head trial by the manufacturer. In low risk adults, alemtuzumab prevented more acute rejections in the first year than the alternative antibody basiliximab (3% *v* 20%; P<0.001), a benefit that persisted for three years. In high risk patients, the drug worked no better than conventional rabbit antithymocyte globulin. Alemtuzumab had no significant effect on the survival of patients or grafts in either risk group.

A closer look at the timing of rejections suggested an excess of late rejections associated alemtuzumab, but only in analyses combining both cohorts (8% *v* 3%; P=0.03). A linked editorial (p 1968) warns that patients given this agent may need closer monitoring for longer than is currently standard practice.

EFFECT OF INDUCTION THERAPY ON LYMPHOCYTE COUNT



Adapted from *N Engl J Med* 2011;364:1909-19

Other safety differences emerged only among low risk patients—alemtuzumab caused more persistent leucopenia than the comparator, and more serious infections (35% *v* 22%; P=0.02). Both were expected, says the editorial.

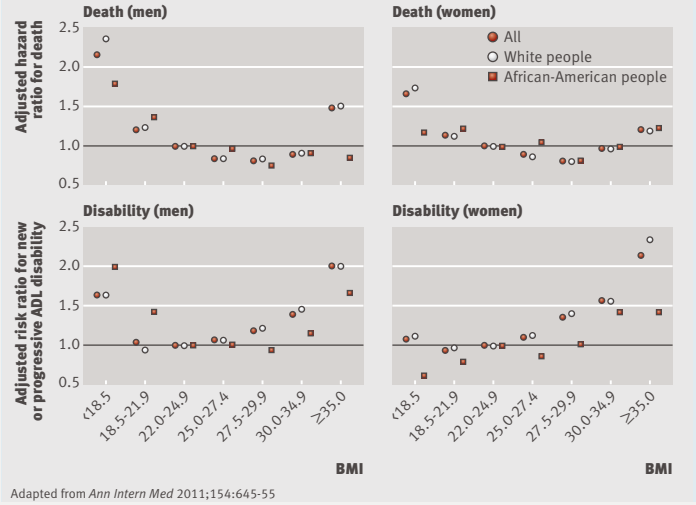
The trial looked at 501 patients having a renal transplant operation. More than half had living donors, and all were taken off corticosteroids within five days of surgery. They were given recommended maintenance immunosuppression for the duration of the trial.

N Engl J Med 2011;364:1909-19

Cite this as: *BMJ* 2011;342:d3219

Overweight is linked to disability, not death, in older adults

ASSOCIATION BETWEEN BMI AND DEATH OR DISABILITY



Adapted from *Ann Intern Med* 2011;154:645-55

Being overweight, or even obese, doesn't necessarily reduce survival for older adults, say researchers. It does, however, mean a higher risk of disability. In a cohort of adults aged at least 65, body mass index (BMI) wasn't associated with mortality until it rose to at least 35. But the risk of a new or progressive disability during two years of follow-up rose in line with BMI for both men and women. The significant trend was most noticeable for disabilities that limited activities of daily living such as bathing, dressing, and walking. Higher than normal BMI was also associated with struggling to answer the phone, shop, cook, and manage money. The researchers analysed longitudinal survey data from 20 975 adults who were eligible for Medicare, national health insurance for older people in the US. The link between BMI and disability was independent of age, smoking, education, and chronic illness not related to obesity, and it emerged from analyses that excluded adults with disabilities at baseline.

Overweight and obesity are clearly associated with a loss of functional independence in older adults, say the researchers. Now we need to know if weight control can reverse these problems without causing others. Falling bone mineral density and malnutrition can both follow weight loss in this age group. Perhaps we should focus instead on improving balance, flexibility, and muscle strength.

Ann Intern Med 2011;154:645-55