
From the journals

Efficacy of statins in diabetes – evidence from a meta-analysis

The efficacy of statins in reducing the vascular and non-vascular mortality was studied in a meta-analysis of 14 trials involving about 18 000 patients with both type 1 and type 2 diabetes mellitus. During a follow up of 4.3 years there was 9 % reduction in all cause mortality per millimol/l reduction in LDL cholesterol. There was a significant reduction in vascular mortality with no effect on non-vascular mortality. Major vascular events were reduced by 21% per mmol/l reduction in LDL. Myocardial infarction, coronary death, coronary revascularisation and stroke were all significantly reduced irrespective of whether there was a history of vascular disease or not. *Lancet* 2008; **371**: 117-25.

All patients with diabetes should be considered for statins to reduce the vascular mortality.

Risk of coronary heart disease falls quickly after quitting smoking

Smokers have a higher risk of death from all causes than non-smokers. Quitting reduces their risk but it takes 20 years to get back to the same level of all cause mortality in people who have never smoked, according to a cohort study of USA nurses. The risk of death from vascular diseases fell slightly faster, with the excess risk of coronary heart disease gone by the end of 5 years, but the excess risk of death from lung cancer persisted for nearly 30 years in ex-smokers.

The authors also reported a clear link between smoking (past and present) and colorectal cancer. Current smokers were 63% more likely to develop colorectal cancer. *Journal of the American Medical Association*; 2008; **299**: 2037-47.

The early benefits of quitting smoking should be conveyed to the patients who smoke, particularly those having increased cardiovascular risk.

Metformin as an alternative to insulin for women with gestational diabetes

Women with gestational diabetes are often treated with insulin. Metformin was tested for the treatment of gestational diabetes in a randomised trial, where women were first given metformin and then insulin only if they needed it. The women given metformin did just as well as women who were given insulin alone, and so did their babies. About a third of each group had one of the following problems included in the combined outcome; neonatal hypoglycaemia, respiratory distress, phototherapy, birth trauma, 5 minute Apgar score less than 7 and prematurity. Babies in the metformin group were born a day earlier than the control group and they were also more likely to be born before 37 weeks. A two-year follow up is planned to assess longer term outcome. The women in the study preferred metformin, presumably because they could take it orally. About half of those in the metformin group needed insulin to control their blood glucose. They were heavier at the start of the trial and had worse glucose intolerance. *New England Journal of Medicine* 2008; **358**: 2003-15.

Based on results of this trial many pregnant women may not require treatment with insulin for gestational diabetes. They may be treated with metformin initially and insulin added only if glycaemic control is not satisfactory.

Carotid bruit could be a quick and easy marker for heart disease

Carotid bruit is not recognised as a valuable physical sign as it is not a reliable predictor of stroke. However, a recent meta-analysis of 22 mainly cohort studies has shown that people with a carotid bruit were twice as likely to die from cardiovascular disease and twice as likely to have a myocardial infarction than people without a bruit. Although there were shortcomings in the studies, the authors suggest that listening to a carotid bruit may not be as obsolete as suggested by recent American guidelines. In this analysis the risk of myocardial infarction associated with a carotid bruit was an estimated 37% over the next 10 years and similar to the risk associated with being a 65-year old male smoker with hypertension or high LDL cholesterol. *Lancet* 2008; **371**: 1587- 94.

Clinicians should listen for a carotid bruit as it may indicate increased cardiovascular risk for the patient, requiring appropriate risk reduction measures.

Current treatments for intestinal worms are inadequate

Intestinal nematodes infect millions of children and adults worldwide and experts estimate that they cause a global burden of disease similar to malaria. The WHO is attempting for three quarters of people at risk to be treated regularly by 2010. The evidence for efficacy of four drugs currently available for treatment of intestinal nematodes *Ascaris lumbricoides*, *Trichuris trichiura*, and the hookworms *Ancylostoma duodenale* and *Necator americanus* was carefully evaluated. Many of the 20 trials were old, small, badly done and hard to interpret. No trials tested modern doses of levamisole, and publication bias hampered evaluation of albendazole, mebendazole and pyrantel pamoate. Despite these limitations, the researchers were convinced that a single doses of albendazole, mebendazole or pyrantel pamoate are effective treatment for *A lumbricoides*, albendazole is probably the best treatment for hookworm, and nothing works particularly well for *T trichiura*.

The researchers conclude that the world's poor need new drugs to protect them from serious morbidity caused by these parasites and that they also need proper trials to guide better use of the drugs we already have. *Journal of the American Medical Association* 2008; **299**: 1937-48.

Heparin contaminant linked to clusters of anaphylaxis worldwide

Earlier this year clusters of serious hypersensitivity to heparin alerted regulatory authorities in the USA and Germany to a possible contamination of supply. An unusual over-sulphated chondroitin sulphate has since been found in over a dozen countries and recent experiments have confirmed that the contaminant can cause the kind of symptoms reported by patients worldwide. The contaminant activated the kinin-kallikrein pathway in human plasma and induced potent anaphylatoxins derived from complement. There were 81 related deaths in the USA; one manufacturer recalled all heparin products at the end of February, and deaths in the USA related to heparin returned to expected numbers in March. *New England Journal of Medicine* 2008; **358**: 1056-72.

Contaminants causing anaphylaxis should always be suspected when a drug which is normally not associated with allergic reactions is reported to have serious allergic reactions.

Emergency treatment of anaphylaxis

The resuscitation council of the UK recently updated its guidelines on the emergency treatment of anaphylactic reactions. They introduce the ABCDE approach [airway, breathing, circulation, disability (level of consciousness), and exposure (of the skin)]. They emphasise that prompt intramuscular injection of adrenaline is the initial treatment of choice, along with other measures as indicated. These may include placing the patient on a comfortable position, providing airway management, giving high flow oxygen and rapidly administering large amounts of IV fluids. They also advise subsequent referral to an allergy clinic, for risk assessment and long term management. No new drugs are available to treat anaphylaxis. Currently used treatment such as adrenaline, steroids, H1 antihistamines and H2 antihistamines were introduced before the era of evidence-based medicine. Systematic reviews of these are being conducted to document the existing evidence base. *British Medical Journal* 2008; **336**: 336-7.

The updated UK guideline on management of anaphylaxis also emphasises the prompt intramuscular injection of adrenaline.

Calcium supplements in older women may increase vascular events

A randomised controlled clinical trial was done to determine the effect of calcium supplementation on myocardial infarction, stroke and death in healthy post-menopausal women. There were 1471 participants. Myocardial infarction was reported more commonly in the calcium group than in the placebo group (45 events in 31 women compared to 19 events in 14 women). The composite end-point of myocardial infarction, stroke or death was also more common in the calcium group than the placebo (101 events in 69 women vs 54 events in 42 women; $p = 0.008$). The authors conclude that calcium supplementation in healthy post menopausal women should be balanced against the likely benefits of calcium on bone. *British Medical Journal* 2008; **336**: 262-6.

Mechanical bowel preparation before colorectal surgery may not be needed for all patients

Cleaning the bowel before elective surgery makes sense in theory but whether it helps to prevent anastomotic leaks in practice was studied in a randomised trial. In this trial, the absolute difference in the risk of leak was only 0.6% between the patients who had and did not have mechanical bowel preparation before surgery (4.8% with preparation vs 5.4% without; $p=0.69$). The researchers concluded that the practice was unnecessary, but the authors of an accompanying comment are more cautious. They say that patients who did not have bowel preparation were significantly more likely to get an abdominal abscess (4.7% vs 2.2%; $p=0.02$), and it is unclear how many had septic complications that were too minor to need intervention but could still cause strictures or poor bowel function in the long run. They conclude that surgeons should assess the need for mechanically prepared bowel on a case-by-case basis. *Lancet* 2007; **370**: 2112-7.

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