

## Hepatitis A vaccine for post-exposure prophylaxis

A randomised controlled clinical trial compared the efficacy of hepatitis A vaccine directly with immunoglobulin, which is known to be highly effective in preventing hepatitis A if given within 2 weeks to persons after exposure to the virus.

One standard age appropriate dose of hepatitis A vaccine or immunoglobulin was given to 2-40 year age group contacts within 14 days of exposure.

Twenty-five contacts out of 568 (4.4%) who received the vaccine and 17 out of 522 contacts (3.3%) who received the immunoglobulin developed hepatitis A. The authors conclude that low rates of hepatitis A in both groups indicate that both interventions provided good protection after exposure. The slightly higher rates of hepatitis A among vaccine recipients may indicate a true difference in efficacy, which might be clinically important in some settings. Vaccine has other advantages including long term protection, and may be a reasonable alternative to immunoglobulin for post-exposure prophylaxis in many circumstances. *New England Journal of Medicine* 2007; **357**: 1685-94.

In Sri Lanka, for prevention of hepatitis A after exposure, hepatitis A vaccine has a significant place, particularly during epidemics.

## Management of Dupuytren contracture

Dupuytren disease is a disabling condition common in elderly men. Treatment is often unnecessary, but regular follow up is needed to detect early joint contracture. An appropriately timed referral to a surgical specialist before irreversible contracture develops can prevent a permanent loss of function.

Injection with collagenase has shown early clinical promise for mild disease limited to the metacarpophalangeal joint. Surgery corrects contracture but recurrence remains an unsolved problem. *British Medical Journal* 2007; **332**: 397-400.

## Ototoxicity caused by aminoglycosides: it is severe and permanent in genetically susceptible people

Aminoglycosides are well known to cause dose-related renal and ototoxicity, in people who receive a toxic dose. It is less well known that some individuals have an inherited predisposition that renders them highly sensitive to the ototoxic effects. Aminoglycosides taken at levels that are well within the normal range can result in rapid, profound and irreversible hearing loss. In countries that use aminoglycosides widely, a quarter of people with hearing loss induced by aminoglycosides have maternal relatives who also have deafness related to drug induced ototoxicity. The most common predisposing mutation is a mitochondrial DNA mutation (m.1555A>G) inherited by every child of a mother who has the mutation, as mitochondrial DNA is exclusively maternally inherited.

Even in the absence of exposure to aminoglycosides, some families carrying this mutation may also develop deafness. Variable penetrance known to occur with this mutation, accounts for different degrees of deafness in those with the mutation. In some populations the mutation seems to be common. In Spain 27% of families with at least two deaf people were positive for this mutation. Everyone who was exposed to aminoglycosides became deaf. The probability of becoming deaf by the age of 30 in individuals who had received aminoglycosides was 96.5% compared to 39% if they were never exposed. Thus aminoglycosides are a major environmental modifier of m.1555A>G mutation. The mutation can now be commercially available for detection at a cost of 35 GBP in UK and screening for this mutation before aminoglycoside therapy is shown to be cost effective. *British Medical Journal* 2007; **335**: 784-5.

As aminoglycosides are widely used in Sri Lanka, often without blood level monitoring, avoiding aminoglycosides in those with a family history of deafness may be reasonable advice until the prevalence of this mutation in our population is known, in the absence of screening for the mutation.

## Stress at work is bad for the heart

Stress at work has two components for the purpose of research; high workload and low autonomy. Jobs with both characteristics are unhealthy, especially for people with coronary heart disease. In a Canadian study, chronic job strain doubled the risk of recurrent heart disease in 972 adults (mostly men) returning to work after a myocardial infarction. The

researchers measured the participant's job strain soon after return to work and 2 years later. Those who scored high on both occasions were significantly more likely to die of coronary heart disease, have another non-fatal myocardial infarction, or develop unstable angina than those with less stressful jobs, over a follow up of 6 years. There were only 106 women in this study (11%) so that researchers were unable to analyse the effects on sexes separately. *Journal of the American Medical Association* 2007; **298**: 1652-60.

### **Simple inguinal hernias can be safely left alone**

The first large clinical trial comparing immediate surgery with watchful waiting concludes that if an uncomplicated inguinal hernia causes little pain or inconvenience it can be safely left alone. Researchers randomised 364 men to watchful waiting. Two years later, they had no more pain or functional incapacity than the 356 randomised to standard open surgical repair. Only 2 patients in the former group developed hernia incarceration, one with bowel obstruction, during the 4 years of follow up, a rate of 1.8 per 1000 patient years. The risk was considerably lower than the risk of surgical complications associated with prophylactic repair (22%). About a quarter of patients had surgery before the end of the trial at four years. They were no more likely to have surgical complications or a recurrence than patients who had surgery earlier. *Journal of the American Medical Association* 2007; **295**: 285-92.

### **Management of atopic eczema in children aged up to 12 years: summary of NICE guidance**

The National Institute of Clinical Excellence (NICE) in the UK has given guidance on how to manage atopic eczema in children aged up to 12 years. Recommendations are given on diagnosis and assessment, categorisation of physical severity, stepped care approach to management, education and information, and indications for referral for specialist dermatological advice. Adopting a holistic approach to assessing the child's atopic eczema is recommended taking account of the physical severity of eczema and its impact on quality of life, which may range from no impact to severe limitation of everyday activities and psychosocial functioning. This assessment should guide treatment decisions. In management, identify and manage trigger factors. Stepped care approach is recommended for management, tailoring treatment according to severity and stepping up or down according to clinical response. Emollients are the basis of management and should be used even when the skin is clear, adding other treatment when required. Using topical steroids is recommended, with mild potency steroids for mild eczema, moderate potency steroids for moderate eczema and potent steroids for severe eczema. *British Medical Journal* 2007; **355** : 1263-4.

### **Fat children are more likely to get heart disease as adults**

In a cohort study of more than 276 000 Danish school children, risk of heart disease in adulthood rose in line with adjusted body mass index (BMI) at ages 7-13 years. For example, each extra unit of BMI z score (equivalent to a weight increase of 6.3kg) in a 13-year old boy was associated with 24% increase in the risk of fatal heart diseases in adulthood and 17% increase in the risk of non-fatal events. The risks associated with being overweight in childhood went up with age but were detectable and significant even at 7 years for boys and 9 years for girls. A higher BMI z score was riskier for boys than for girls at all ages. *New England Journal of Medicine* 2007; **357**: 2329-37.

### **Baclofen helps alcoholic liver disease patients stop drinking**

A small placebo controlled trial suggests that baclofen can reduce alcohol cravings and help people stop drinking without doing any further damage to the liver. Over 70% of the 42 Italian adults who took baclofen for 12 weeks managed to stop drinking completely, compared with only 29% of the 42 who took placebo. The baclofen group had significantly more drink-free days, significantly lower scores on a validated measure of alcohol craving and significantly fewer relapses. Baclofen is excreted by the kidneys, unlike other drug treatments for alcohol dependence, and should be safer for patients with advanced liver disease.

An accompanying editorial welcomed the results as promising enough to justify bigger, longer and more diverse trials of baclofen. *Lancet* 2007; **370**: 1915-22.

## Ongoing regulation of generic drugs in USA

Today generic drugs account for 63% of all US prescriptions for drugs whereas in 1984 only 18.6% were written for generic products. Since generic drugs sell at substantially lower prices than their brand name counterparts, they save consumers, and purchasers of prescription drugs billions of dollars annually. Before 1984, generic makers were obliged to conduct the same efficacy and safety tests that were required for the original brand name manufacturers. In 1984 the new drug act required the generic drug manufacturers to only establish bioequivalence to the active ingredient of the original drug and demonstrate adherence to FDA approved manufacturing processes to receive FDA approval. This provision obviated the necessity to conduct clinical trials, reducing the cost of development of generic products. The law also allowed the generic drug manufacturers to apply for FDA approval and conduct testing for bioequivalence before relevant patents expire. This law has increased the use of generic drugs as well as law suits, and modifications to this law are being discussed now. *New England Journal of Medicine* 2007; **357**: 1993-4.

It is worth noting that in USA two-thirds of the prescriptions are for generic drugs, which have been shown to be bioequivalent to patented branded products.

## Faith in vitamin E, beta-carotene and estrogen endures despite evidence of lack of efficacy from randomised controlled trials

Throughout 1990s many scientists, doctors and patients believed that vitamin E could help prevent heart disease as large observational studies found clear evidence of benefit. Since then, large and more convincing randomised controlled clinical trials have found the opposite. However, belief in the protective properties persists. A close look at the scientific articles citing the early observational studies showed that half were still arguing in favour of vitamin E as late as 2005, five years after a landmark trial overturned these observational studies findings.

Belief in the anti-cancer potential of beta-carotene has endured even longer. The notion that beta-carotene prevents cancer was discredited by randomised trials published in 1996. In a citation analysis, two-thirds of the citations were still favourable to the original observational work 10 years later. Most of the articles simply ignored the later evidence. Results were similar for the more recently discredited idea that estrogen protects the post-menopausal women against dementia. In the vitamin E analysis, articles in the specialist journals were more likely than articles in general journals to defend the protective properties of vitamin E. *Journal of the American Medical Association* 2007; **298**: 2517-26.

The use of vitamin E, beta-carotene and estrogen for prevention of heart disease, cancer and dementia should be discouraged in the light of evidence.

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