

This week in BMJ

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Asthma before school

Asthma in children of preschool age is often more severe and less responsive to treatment than asthma in older children. Trials of prophylactic agents (including inhaled steroids, which are of proved value in older children and adults) have produced comparatively disappointing results in children of this age. Children as young as 2 years, however, can use the Nebuhaler, a large pear shaped structure with a one way valve. At p 163 Gleeson and Price report the first trial to show a clear benefit from the use of an inhaled steroid in children under the age of 6 years. When the children were receiving budesonide by Nebuhaler the morning and evening peak expiratory flow rates were substantially higher and the children needed less additional treatment with bronchodilator drugs. No evidence of systemic corticosteroid effects were found after six weeks. A comparatively high dose of budesonide was tested, however, and the possibility of systemic effects after long term administration cannot yet be dismissed. A smaller dose of budesonide than that used in this trial may be sufficient in many cases, and the dose should be the smallest that controls the asthma.

Oxytocin and normal third stage of labour

At the end of the second stage of labour the standard practice in Britain is to inject into the mother a mixture of oxytocin and ergometrine (usually as Syntometrine) in the belief that this reduces the risks of both postpartum haemorrhage and retained placenta. The treatment was introduced many years ago without any formal controlled clinical trials and its value has recently been questioned.

An assay is now available for measuring the plasma concentration of oxytocin, and Thornton *et al* (p 167) have been able to show that when synthetic oxytocin is not given some women produce adequate amounts of natural oxytocin but others do not. They studied only 25 women, but the results suggest that there is indeed a sound basis for current practice.

Risk of suicide in young men

Suicide is one of the commonest causes of death in young adults, and its rate is increasing in many countries. Yet little is known about the precipitating factors. At p 176 Allebeck *et al* describe a unique study from Sweden in which they analysed extensive psychological data collected on over 50 000 young conscripts in 1969-70 as part of the selection procedure for military training. During 13 years of follow up 683 conscripts died, 247 by suicide. Strong correlations between suicide and lower intelligence, poor emotional control, and lack of social maturity were seen, poor emotional control being the most predictive factor. Other relevant factors included contact with the police or welfare authorities, lack of friends, and misconduct at school. No suicides occurred in the few subjects with

schizophrenia or affective psychoses, but a high rate (30/1000) was recorded among intravenous drug users. Although the data cannot be used to predict suicides among the general population because of low specificity, the findings are likely to facilitate the identification of potential suicide victims in services dealing with a high concentration of people at risk.

Flosequinan for heart failure

Of the drugs currently available for treating severe heart failure, the angiotensin converting enzyme inhibitors are probably the most effective. They do not, however, produce improvement in all patients and they may also be limited by side effects.

Cowley and his colleagues (p 169) have investigated a new mixed arteriolar and venous vasodilator, flosequinan, in two groups of patients with severe heart failure. In one group it produced favourable acute changes in central haemodynamics. In the other it improved various measurements, including exercise tolerance, that relate to the symptomatic impairment of patients with severe heart failure. An important finding was that it did not cause reflex neurohumoral stimulation. Flosequinan was investigated under the clinical trial exemption scheme of the Department of Health and Social Security and has yet to be evaluated by the Committee on the Safety of Medicines. Nevertheless, it appears to have the right properties for an alternative drug to angiotensin converting enzyme inhibitors in the treatment of severe heart failure.

Familial hypercholesterolaemia

Familial hypercholesterolaemia is the best defined of the diseases that produce hypercholesterolaemia in humans and was the first genetic disorder recognised as causing myocardial infarction. Heterozygotes have a 50% chance of dying from myocardial infarction before the age of 60, and homozygotes rarely survive to the third decade. Familial hypercholesterolaemia is one of the more common disorders carried on a single gene: it has an incidence of one in 500 and about 100 000 people in Britain are affected.

The disorder results from a defect in the cell surface receptor that normally controls the degradation of low density lipoprotein cholesterol, the main transport lipoprotein for cholesterol in human plasma. The effect of this abnormality is to raise plasma concentrations of low density lipoprotein. Deposits of cholesterol derived from low density lipoprotein are formed in various sites, especially tendons (forming xanthomas) and arteries (causing atheroma).

Treatment of these patients is usually difficult because diet alone is not enough and even the most potent hypolipidaemic agents used singly often fail to produce satisfactory reductions in the low density lipoprotein cholesterol concentration. At p 173 Curtis *et al* report a trial in 18 patients of a combination of cholestyramine and bezafibrate, which showed that the two drugs combined gave better results than either alone.

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Any article may be submitted to outside peer review and evaluation by the editorial committee as well as statistical assessment incorporating the use of published checklists.² This should take four weeks but may take up to six. Manuscripts are usually published within three months of the date of final acceptance of the article.

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Drugs should be referred to by their approved, not proprietary, names, and the source of any new or experimental preparations should be given. Abbreviations should not be used. Scientific measurements should be given in SI units, but blood pressure should continue to be expressed in mm Hg.

Statistical methods should be defined in the methods section of the paper and any not in common use should be

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1 Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *N Engl J Med* 1976;294:687-90.

2 Osler AG. *Complement: mechanisms and functions*. Englewood Cliffs: Prentice-Hall, 1976.

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1 International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. *Br Med J* 1983;296:401-5.

2 Gardner MJ, Machin D, Campbell MJ. Use of check lists in assessing the statistical content of medical studies. *Br Med J* 1986;292:810-2.

3 Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. *Br Med J* 1983;286:1489-93.

4 Gardner MJ, Altman DG. Confidence intervals rather than P values: estimation rather than hypothesis testing. *Br Med J* 1986;292:746-50.