been designed and conducted with adequate power to compare maximum doses of nebulised and intravenous β agonist. It shows without doubt that for some patients who do not respond to nebulised treatment intravenous treatment should be considered in future. Such treatment would not have been considered formerly because much of the work was poor.¹

I am surprised that Dr Crompton deems 15 mg of nebulised salbutamol in two hours to be a small dose; should we, as he seems to suggest, have given 20 or 30 mg in the same period? I know of no other unit giving such doses.

I also agree that ipratropium bromide is useful in severe asthma,² but I note that O'Driscoll and Cochrane showed that most informed clinicians were not using both ipratropium and a β agonist: only 57% used both drugs routinely in severe asthma.³

We think that it is somewhat narrow minded to condemn a treatment which will benefit some severe asthmatics. Intravenous aminophylline is not without hazard, and many deaths have been reported with its use. Perhaps we should consider intravenous β agonists not for the routine treatment of severe asthma but for the more difficult cases.

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Several problems arise in drawing pharmacokinetically and pharmacodynamically sound conclusions from the study of Dr B Cheong and others (13 August, p 448) on treating acute asthma with intravenous salbutamol.

The β_2 selectivity is greatly reduced when the drug is given intravenously and unwanted cardiovascular effects are inevitably more of a problem. Their exclusion of patients with cardiovascular disease introduces a dangerous bias in ignoring those most likely to be at risk from the unwanted β_1 agonist effects of systemic salbutamol. In addition, two young patients were withdrawn from the study because of these very β_1 cardiac toxic effects. Even with 5 mg of nebulised drug arrhythmias may be a problem,¹ and fatalities with this treatment are not unknown.²

Patients entered the trial only after receiving 5 mg of nebulised salbutamol. The response of individual patients to this dose is variable and prolonged,^{3,4} so there may well have been a carry over of increasing effect into the trial period as the pharmacodynamic effect of inhaled salbutamol is unlikely to be complete at 30 minutes, when the patients were randomised.

The speculation that mucus plugs account for the poor effect from the inhaled drug is hard to follow as plugged airways will prevent ventilation whether the distal airways are dilated or constricted. The most obvious defects of this study, even under these very difficult clinical circumstances, are the failure to measure the resulting plasma concentrations in the individual patients to whom these variable arbitrary doses were given and to provide some reassurance that the differences in response between the two groups were valid. Even with nebulised salbutamol in doses as low as 3 mg the drug is detectable in plasma.⁵

We are concerned that the danger of death from asthma treatment is not yet safely separated from death from the disease and that this unsatisfactory

trial might influence treatment to increase this danger.⁶

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- 1 Higgins RM, Cookson WOCM, Lane DJ, John SM, McCarthy GL, McCarthy ST. Cardiac arrhythmias caused by nebulised beta-agonist therapy. *Lancet* 1987;ii:863-4.
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The selection bias beast has struck again! He is one of those wily demons that infest medical publications, distort clinical measurements, disrupt protocols, and cloud the processes of logic.¹ Although common, he usually is detected with great difficulty. No one is immune. His latest victims are Dr B Cheong and colleagues (13 August, p 448), whose commendably clear presentation enabled me to spot him.

Dr Cheong and colleagues set out to compare the efficacy of inhaled and intravenous β agonists in severe acute asthma. First they had their ill patients with asthma inhale a β agonist. Some responded to this, but we do not know how many. Those who failed to improve were entered in the trial and randomised to receive more of the same drug by inhalation or intravenously. The outcome is predictable, I think.

It is remarkable under the circumstances that intravenous treatment (25% increase in peak flow rate) was not found to have a more decisive advantage over the inhaled treatment (14% increase). I suspect that in fair competition, with randomisation before any treatment, the inhaled route might have emerged the winner.

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General practitioners' responsibilities

Unfortunately Dr Michael Whitfield and Ms Romola Bucks did not address the problem of managing long term disability or disabling disorders (apart from rheumatoid arthritis) (6 August, p 398). The general practitioners should have an important role in providing primary care for individuals with such disorders.^{1,2}

We are conducting a community study of adults aged 16-64 with appreciable handicap such that they are independent in self care only with assistance from a helper, aids, or adaptations and who appear on the Harrow social services register of handicap. Home interviews with 42 consecutive individuals showed that 17 had not seen their general practitioner in the past two years. The main diagnosis for these patients were cerebrovascular disease (4), rheumatoid arthritis (4), multiple sclerosis (2), secondary cerebral tumour (1), ankylosing spondylitis (1), osteoarthritis (1),

paraplegia (1), back pain (1), cerebral palsy (1), and poliomyelitis (1). Of the remaining 25, nine had been seen at home and 16 in the surgery. Nineteen patients had had four or more visits annually. Most of these doctors used a demand system relying on a patient's request for a consultation. There was no difference in the level of disability between those who saw their doctor regularly and those who did not as measured by the Barthel score. Almost all subjects had limited walking ability. Although the numbers were small, most consultations were related to chronic airways disease and diabetes (rarely the cause of disability). Thus emotional and social needs may not have been met.⁴ Half the patients were seen in hospital clinics but often for only one facet of their disease such as incontinence.

Griffiths suggested that general practitioners should be the lynchpin of all services for the community care of physically disabled people.⁵ Our pilot study shows that regular medical supervision of this group is limited and supports findings in younger handicapped adults.⁶ The general practitioner becomes even more important in the management of severe handicap.⁷ It appears that this responsibility has failed to achieve prominence in the eyes of the profession, and as a result those with physical disability may remain deprived of available resources to improve their quality of life.¹

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Screening tests for HBsAg in transfusion centres of developing countries

Dr Vaskar Saha and others (30 July, p 334) concluded that enzyme linked immunosorbent assay (ELISA) is the most cost effective method in averting possible transfusion associated hepatitis B infection. Although I agree with their conclusions, I do not agree with their mathematical calculations.

The risk that a unit is "infective" (assuming ELISA to be 100% sensitive as they have in their calculations) is 0.07. The risk that a transfusion of 1 unit might have an infective outcome is $0.07 \times$ (the risk that a recipient is susceptible) $= 0.07 \times 0.508 = 0.036$. This probability is poorly worded in their table as: "Risk of uninfected recipient receiving HBsAg if he or she receives 1 unit, etc" (my emphasis). For one unit this risk is 0.07 (the probability that the unit is positive for hepatitis B surface antigen). They go on to calculate that the risk from a 3 unit transfusion is three times the risk from a 1 unit transfusion. This is not the case. The risk is $1 -$ (the probability that a 3 unit transfusion is not infective) $= 1 - (0.93)^3 = 0.196$. The chance of a 3 unit transfusion causing possible infection is $0.196 \times$ (percentage of donors susceptible) $= 0.196 \times 0.508 = 0.099$ (not 0.108 as stated). Completing the calculations gives a cost per averted potential infection of \$60.37 for ELISA, \$101.04 for reverse passive haemagglutination, and \$141.52 for