visit. Should the first level be above 7 mmol/l (270 mg/100 ml) or any subsequent value exceed this figure, then the pill should normally not be commenced or continued. But even where there are no facilities for such analyses the well-trained prescriber, whether medical or non-medical, and the fully informed user should be able to balance the dangers of the pill against its benefits in each individual case.

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¹ Smith, M, *Journal of Family Planning Doctors*, 1975, 3, 14.

Deaths in asthma

SIR,—Since the "epidemic" of asthma deaths in the 1960s many asthmatic patients have died unnecessarily from this disease and Dr W N Dodds and his colleagues (8 November, p 345) describe another such example. Their patient used an isoprenaline inhaler frequently during her fatal attack and they infer that she might not have died if she had used a drug with more selective β_2 -adrenergic stimulant properties. I sympathise with their concern about this problem but believe that their patient died from asthma and not its treatment and that this is the case with the vast majority of asthma deaths.

It seems fairly certain that the major cause of the increased asthma mortality observed during the 1960s was indeed the introduction of the pressurised metered-dose isoprenaline inhaler, not because of any pharmacological properties of isoprenaline but because of its influence on therapeutic policy. The pressurised cannister inhaler provided, for the first time, an efficient method of delivering an effective bronchodilator drug to the bronchi. This device, because of its undoubted effectiveness, created in the minds of both doctors and patients a feeling of security which sadly proved to be totally unfounded. When the medical profession was alerted to the fact that an increase in asthma mortality had taken place and that at the same time there had been an increase in the use of the pressurised isoprenaline inhalers two major changes in the treatment of asthmatic patients in Britain took place. Firstly, more patients were admitted to hospital,¹ presumably at a nearer stage of the disease, and secondly, there was a national increase in the prescription of corticosteroid drugs.² It is therefore not in the least surprising that these actions were followed by a dramatic decrease in mortality from asthma, since the early administration of corticosteroid drugs and rapid admission of patients to hospital are the only effective ways of preventing death from acute asthma.

The reasons for a patient with severe asthma using a bronchodilator aerosol frequently during a fatal attack are self-evident, since unfortunately most patients who die from this disease do not have immediate access to any more efficient form of treatment. The medical profession has been slow to realise that all patients with asthma are at risk. This risk can be reduced by giving patients prednisolone to be taken on their own initiative at the onset of a severe attack

whenever their bronchodilator aerosol proves to be ineffective and by decreasing to a minimum the time taken to admit patients to hospital.

Asthma can be a rapidly fatal disease, and until we accept this and stop trying to incriminate our often inadequate therapeutic attempts to control it there can be little hope of us decreasing asthma mortality in the future.

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¹ Dollery, C T, *Annals of Allergy*, 1973, 31, 38.
² *Proceedings of the Asthma Research Council Symposium on Evaluation of Bronchodilator Drugs*. London, October 1973. Trust for Education and Research in Therapeutics, 1974.

Management of acute asthma

SIR,—I read with interest your leading article on this subject (11 October, p 65), and was fascinated to note that one object is to correct arterial hypoxaemia by oxygen therapy "to maintain the PaO_2 between 7.95 and 10.59 kPa." I suspect you discovered these interesting numbers by dividing 60 and 80 respectively by the relevant conversion from mm Hg to kPa. Surely you are aware that the lower limit of "safety" for PaO_2 is highly speculative and the higher limit, given presumably to avoid oxygen toxicity, is even more a matter of debate. Would you not settle for a range of 8-10 (or 11, or 12, or 20) kPa? If so there is a possibility that some of your readers might remember what you have written, whereas the range you give will be immediately forgotten, I hope.

Further down you define hypercapnia as characterised by a PaCO_2 greater than 7.95 kPa. Do you really mean this?

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* * This illustrates the sort of difficulty that is bound to arise during the transition period when people are still thinking in traditional units but dutifully converting their values into SI units. The reason for the rather curious values given in kilopascals in our article would have been made clear had we not inadvertently omitted to give the values in millimetres of mercury too. In answer to Dr Saunders's further query a PaCO_2 persistently above 7.95 kPa (60 mm Hg) is, in our view, frequently an indication for assisted ventilation.—ED, *BMJ*.

Rabies

SIR,—The attention drawn to the importance of rabies in man by your recent excellent leading article (27 September, p 721) accompanying the article on treatment by Mr L Klenerman and others (p 740) and followed by some interesting correspondence has been a welcome addition to the publicity given by the mass media to the importance of keeping rabies as a disease of animals out of the United Kingdom.

However, in my opinion, the various contributors may have placed in the background the first decision with which a medical ad-

viser will be faced on being informed that a patient has been bitten by a dog while on holiday in a country in which rabies occurs or is endemic. Indeed such a case was spotlighted recently by Scottish television. As modern vaccines such as the duck embryo vaccine have been shown to be safe and relatively free of pain on injection it seems to me that there must be one answer only, and that is to embark on post-incident vaccination with the use of antirabies serum or human immunoglobulin when available. There is well-documented case evidence to show that if one waits until the fate of the dog is known before starting vaccination the patient may die. In fact patients have died even when vaccination has been started immediately.

One of the patients who died in London this summer had been bitten on the lower lip, causing significant haemorrhage, by a stray puppy apparently playful and normal. This patient had received medical advice immediately after the incident to the effect that as the puppy had appeared normal there was no need to treat the wound or to vaccinate against rabies. This occurred in a country where rabies is endemic in the canine population, but any medical adviser in Britain may be faced with a similar decision by a tourist returning overnight from such a country having been bitten by a dog the previous day.

Finally, may I use the courtesy of your columns further to appeal to the medical profession to supplement the continuing efforts made by the customs officers and veterinarians to detect any dog, cat, or other animal imported illegally into Britain? This dreadful practice is known to occur at least 100 times each year and has sometimes been detected by a conscientious neighbour or even given away by the confident boast of the perpetrator, not necessarily over a drink!

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Drugs for addicts

SIR,—I was very interested in the letter from Dr A H de C Freed (20 September, p 703), as he so exactly expresses views which I have held for a long time. Although in no way an expert on drug addiction and treatment, I have discussed the subject with many who are. They always leave me with a feeling of vague disquiet.

To the question, What percentage of cures do you achieve? one often gets a guarded answer. "It's difficult to give a definite figure, but we seem to do quite well. Some move away and we lose sight of them; but we do have a lot of successes." How many can be considered absolutely permanent? "Well, many keep off drugs for six months or even a year, but of course some do revert." How many revert? "It's difficult to say, but probably quite a few do." Of course it's all very difficult, but it seems to me that the statistics tend to be very inaccurate.

Certain questions and points should be kept in mind about addicts, at any rate those on heroin or other hard drugs: (1) Is our kindly system of dealing with these people by prescribing their drugs on the NHS a really effective one? It does probably reduce

black market dealings, but it does not stop them. (2) Does it cure? In my humble opinion, No. And I doubt if it ever will. It does lead to trading of NHS drugs. (3) Is it a good thing for us to let them receive sick pay and supplementary benefits, and stay at home on their drugs? (4) These people are a potential hazard to others. They have an "infectious," almost incurable, and very dangerous disease which will probably cause many early deaths. (5) Anyone who spreads addiction, sorrow, early death, for personal gain is far worse than someone who kills in the heat of the moment. They merit the most severe penalty. It must be made impossible for them ever to do this again. (6) Other forms of treatment: Although "patients" they must be restricted by law and treated as compulsory inpatients until the severe withdrawal symptoms are past. They should then be sent to hostels, work camps, etc, where the regimen would have to be kind but strict, administered by a dedicated staff who could not be "bought." No contact with the outside world would be allowed, no parcels, no unopened letters, visitors very rarely, and strictly supervised, only, say, a quarter of the inmates being visited at any one time.

This re-education in the broadest sense would have to continue for quite a time, and when patients were allowed to go home a kindly but strict and frequent supervision would have to be kept over them until they were considered completely and permanently cured. I realise how difficult all this would prove, and how expensive to institute, but not much less would be effective. Dedicated people are hard to find nowadays and they would be likely to have to face vilification by folks of small understanding in the outside world and vituperation from those inside. The possibility of litigation could not be ruled out. They would need wholehearted and firm backing by the law. If *real* cures, *permanent* cures, resulted, perhaps this difficult and expensive treatment would prove worth while.

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Toxic megacolon in Crohn's disease

SIR,—Your leading article on the above subject (27 September, p 723) refers to a recent report from this institution.¹ Our preferred method of primary surgical treatment for toxic megacolon is that of loop ileostomy and decompression blow-hole colostomy.² In a group of 49 patients recently reported³ there was one death, a mortality of 2%. All patients in the group detoxified and decompressed following this procedure, the average hospital stay being 18 days. Two patients required early colectomy during the original hospitalisation for persistent colonic haemorrhage. Colectomy was subsequently performed on 41 of these patients at a mean interval of six months, and in eight patients an ileorectal anastomosis was able to be performed. Pathological examination of the colectomy specimens showed a 2:1 predominance of transmural colitis 66% to mucosal ulcerative colitis 29%, with 5% being in the non-specific group.

On the basis of these results we feel that less than colectomy is indicated in the surgical management of the toxic megacolon

phase of inflammatory bowel disease, and that total proctocolectomy can hardly ever be justified in this condition. It seems logical to us to perform a comparatively simple and effective operative procedure in an acutely ill patient, and in this way to prepare the patient for colectomy at a time when the acute illness has passed.

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- 1 Farmer, R G, Hawk, W A, and Turnbull, R B, *Gastroenterology*, 1975, **68**, 627.
- 2 Turnbull, R B, et al, *Surgical Clinics of North America*, 1970, **50**, 1151.
- 3 Fazio, V W, *Gastrointestinal Emergencies*. Philadelphia, W B Saunders. In press.

Serum α -fetoprotein in cystic fibrosis

SIR,—Professor R K Chandra and others (29 March, p 714) reported significantly increased levels of α -fetoprotein (AFP) in the serum of patients with cystic fibrosis (CF), in the parents of the patients, and in some of their siblings in Newfoundland, Canada. These findings were confined by Dr J A Smith (17 May, p 392) in the United States for both homozygote and heterozygote carriers of CF genes. In contrast to Professor Chandra, Dr D J H Brock and others in Scotland and Dr J C Wallwork and others in England (17 May, p 392) were unable to detect an increased serum concentration of AFP in any of their CF patients or their relatives. So far as we know, serum AFP levels have not been measured in homozygote and heterozygote carriers of CF genes in central Europe.

Over the past four months we have examined the sera of 38 patients (aged 2 to 18 years) with CF of various severity of the disease for the presence of raised serum levels of AFP. Except for one Turkish boy, all patients with CF were of German origin. The diagnosis of CF was based on both clinical symptoms of pulmonary and pancreas involvement and sweat sodium-chloride levels above 80 mmol/l on pilocarpine iontophoresis. All patients with CF except one 7-year-old boy had normal values of SGOT, SGPT, and the other liver-specific serum enzymes.

The determination of AFP in the serum was carried out by radioimmunoassay with ¹²⁵I-labelled AFP in the double antibody technique. The first antibody was a rabbit anti-human AFP-serum, the second antibody a goat-anti-rabbit- γ -globulin. The test was carried out in 0.1 M borate buffer containing 0.5% beef albumin as described by Nishi and Hirai¹ and Ishii.² Incubation periods were always 24 hours for the first antibody, the radioactive labelled AFP, and the second antibody. ¹²⁵I-labelled AFP and the antisera were obtained from Dianabot-Laboratories, Tokyo, Japan. Crystalline AFP, isolated as described by Lehmann,³ 4 was used as standard by Mancini's radial immunodiffusion technique. The concentration of crystalline AFP (local standard) was 90 μ g/ml in the International Standard Preparation 72/225 of the World Health Organisation (Lyon, France).⁷ The normal range was calculated from the values of 62 healthy adults: the mean value of AFP in the serum was 4.52 ng/ml, the standard deviation 1.92 ng/ml, the upper limit of the 2.57- σ -range, including 99% of all values, 9.45 ng/ml.

The serum AFP levels in our 38 patients with CF were not different from those in healthy adults. The average serum AFP level of all patients with CF was 3.08 ng/ml (range 1-10 ng/ml). The standard deviation was 2.27 ng/ml. In infants and children the

normal range of the serum AFP levels is even higher than in healthy adults. Therefore the serum AFP levels in our patients with CF are within the normal range for healthy children of the same age. In addition, the sera of all 38 patients with CF were examined both by electroimmuno-osmophoresis with anti-human AFP-serum (limit of sensitivity 3.6 μ g/ml) and by double diffusion (limit of sensitivity 10 μ g/ml) as described by Lehmann and Lehmann.⁵ Our findings correspond with those of Dr Wallwork and others and of Dr Brock and others. These authors also, in contrast to both Professor Chandra and others and Dr Smith, have been unable to detect an increased serum concentration of AFP in any of the CF patients.

There is no explanation for this discrepancy, as Professor Chandra and his colleagues have apparently used the same rabbit antiserum and standards as Dr Brock and others. In our opinion, genetic differences cannot explain the different results concerning the serum AFP levels in patients with CF. The majority of the ancestors of the patients with CF who have been tested in the USA and in Canada may have their origin in central Europe and the north-western part of Europe.

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- 5 Mancini, G, et al, *Colloquium on the Protides of the Biological Fluids*, 1965, **11**, 370.
- 6 Lehmann, F-G, and Lehmann, D, *Zeitschrift für klinische Chemie und klinische Biochemie*, 1973 **11**, 399.
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Whooping-cough vaccine

SIR,—The statement by the Joint Committee on Vaccination and Immunisation (20 September, p 687) concerning the continued use of whooping-cough vaccine is important, if only for the data it contains. These show that as in previous epidemics mortality from whooping cough in the 1973-4 epidemic occurred almost entirely in infants under 12 months. Current DHSS inoculation policy leaves this age group relatively or completely unprotected by direct vaccination, and any benefits of the inoculation programme appear to depend on herd immunity promoted among children in whom mortality from pertussis has always been much less. The success of this recently modified inoculation policy operating in the context of an increasing proportion of parents born after systematic pertussis inoculation was introduced, and who probably do not now have significant protection against pertussis,¹ remains to be seen.

It is not possible to judge from the committee's data the extent to which the promotion of community protection may be offset by the hazard from a severe encephalopathic reaction in an inoculated child past the age of maximum hazard from the natural