and who acquired δ subsequently. The possibility of an ethnic (genetic) factor in δ pathogenicity must also be considered.

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1 Smedile A, Verme G, Cargnel A, *et al.* Influence of delta infection on severity of hepatitis. *Lancet* 1982; ii:945-7.
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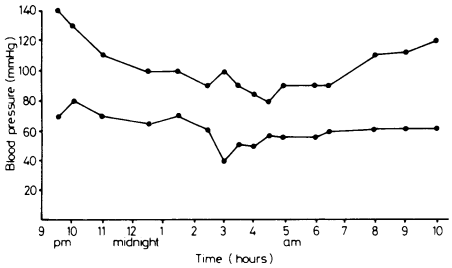
First dose hypotensive effect of captopril

SIR,—Dr G P Hodsman and others (12 March, p 832) concluded that the degree of hypotension caused by the first dose of captopril was related to the pre-existing level of hypertension rather than to the dose of captopril given. They also suggested that the safest form of treatment of severe hypotension caused by captopril was a graded infusion of angiotensin II. Of some bearing on these conclusions is this report of the first recorded self poisoning attempt with captopril.

A fit 18 year old man took six 25 mg tablets of captopril (prescribed for his mother) at 8 10 pm on the evening of admission. He was registered in casualty at 9 20 pm with a blood pressure of 140/70 mm Hg, looking and feeling completely well. An intravenous line was inserted and heparinised, he was washed out, but no obvious tablets were recovered; he was admitted to hospital for observation. His blood pressure fell to 80/50 mm Hg 7 hours 20 minutes after ingestion of captopril (see figure), and he reported feeling faint on several occasions through the night.



Blood pressure in an 18 year old man after oral captopril 150 mg.

The National Poisons Information Centre had no information on the toxic effects of a single dose of 150 mg captopril, but we decided to nurse the patient head down and to infuse quickly with normal saline should his blood pressure fall precipitously; it did not. There were no other toxic effects and he was discharged home the next morning.

This case supports the conclusion of Dr Hodsman and others that the initial hypotensive effect of captopril is related to existing hypertension rather than to the dose of captopril given and that it is possible for a healthy young person to take up to 150 mg of captopril without a profound fall in blood pressure, as one would expect in a subject with (presumably) normal blood volume and sodium and renin concentrations.

I conclude that in a district general hospital where junior medical staff manage acute medical emergencies a safe and adequate treatment of the first dose effect of captopril in patients who were previously normotensive is simple routine medical management of hypotension rather than primary use of angiotensin II infusion.

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SIR,—Dr G P Hodsman and others (12 March, p 832) suggest that "smaller incremental dosage increases in the range 1-5 mg should be explored." Because of the unpredictability of response to captopril in patients with renovascular hypertension we introduced incremental low dose treatment to our unit three years ago. We give such patients, on an inpatient basis, an initial dose of 1 mg and monitor their blood pressure every quarter hour for four hours. On the second day we continue with 3·125 mg captopril, increasing incrementally according to response. Eighteen patients have been treated in this way and only one of these required specific corrective measures for treatment of an acute hypotensive episode after a 1 mg dose of captopril. We therefore endorse the authors' suggestion of exploring further such an approach to treatment.

To give these smaller doses we have formulated our own 1 mg and 3·125 mg capsules. A 6·25 mg scored tablet, however, would be useful for two reasons. Firstly, the smaller dose would increase awareness of the potentially powerful hypotensive effect of this drug and, secondly, dose titration would be made easier.

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Smoking, lung function, and body weight

SIR,—Dr B Nemery and others (22 January, p 249) reported that the lower weight of smokers in a working population aged 40-55 was attributable to the group with ratios of forced expiratory volume in one second (FEV_1) to vital capacity (VC) lower than 66·6%. In trying to interpret these results they excluded the possibility that body weight could affect FEV_1/VC since no relation was found among non-smokers.

We analysed in the same way as Dr Nemery and others data recorded for 1049 men examined in 1972, aged 41 to 74 years, who had all been working and examined 12 years earlier—that is, in 1960.[1] In this population we had previously noticed that chronic phlegm was related to lower body build index, independently of age, smoking, or peptic ulcer, but we did not look at spirometric values in this respect.

Body build index (weight (kg)/height (m)²) according to FEV_1/VC level. Values are means ± SD

	FEV_1/VC		
	≥66·6%	<66·6%	
Non-smokers	26·2 ± 3·2 (101)	26·2 ± 3·3 (27)	
Ex-smokers	27·0 ± 3·5 (168)	27·2 ± 4·0 (78)	
Moderate smokers (15 ≤ g/day)	26·9 ± 3·7 (184)	25·5 ± 3·4 (90)	p < 0·01
Heavy smokers (>15 g/day)	26·3 ± 3·1 (187)	24·8 ± 3·9 (83)	p < 0·001

Numbers in parentheses = number of men.

The table shows that our results are in complete agreement with those of Dr Nemery and others. There was no difference in body build index among subjects with or without airflow obstruction who had never smoked or who were ex-smokers; for moderate and heavy smokers those with airflow obstruction had a significantly lower body build index. Values for smokers without airflow obstruction were similar to those of non-smokers. The differences observed in the two groups of smokers persisted when those with a history of peptic ulcer were excluded. The correlation coefficients between FEV_1/VC and body build index were 0·06 for non-smokers, 0·05 for ex-smokers, 0·22 for moderate smokers, and 0·21 for heavy smokers. The last two were highly significant. Because all four groups of men with airflow obstruction were significantly older than those without obstruction in their respective smoking categories we calculated partial correlations, taking age into account. The values were then 0·03, 0·09, 0·23, and 0·22 respectively. Partial correlations on current amount of smoking or pack years of smoking did not change the values appreciably (for pack years, r = 0·06 for ex-smokers, 0·22 for moderate smokers, and 0·21 for heavy smokers).

Whether or not a low body build index was a risk factor for decline in FEV_1 was considered in Fletcher *et al's* and our own longitudinal studies.[2 3] Fletcher *et al* found a weak negative correlation between weight and decline in FEV_1, but the correlation disappeared after adjustment for smoking and was attributed to the fact that non-smokers and ex-smokers were heavier than smokers. Similarly, in our study there was no relation between decline in FEV_1 and body build index. Nevertheless, in neither study was any attempt made to look at the possible relation within smoking categories. Doing this on our longitudinal data, and restricting the analysis to those who did not change their smoking habits over the 12 years, it seems that body build index is not a risk factor for decline in FEV_1 for any smoking category. This confirms in another way the conclusion of Dr Nemery and others, and, as they say, two hypotheses remain: weight loss in smokers may be the consequence of impaired lung function, or among susceptible smokers cigarette smoking acts on both the respiratory tract and metabolism.

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Dihydrocodeine for breathlessness in "pink puffers"

SIR,—Dr M A Johnson and others (26 February, p 675) reported some interesting findings with dihydrocodeine in dyspnoeic patients. Our recent studies on breathlessness induced by exercise have shown the advantages of describing the effects of drugs in terms of the relation between the intensity of breath-

lessness and ventilation.[1-3] On this basis, we have seen two types of drug effect.

Promethazine in normal subjects did not affect the ventilatory response to exercise but breathlessness was slightly reduced; thus the relation between breathlessness and ventilation was depressed towards the ventilation axis.[1] Codeine, on the other hand, caused statistically significant reductions in ventilation and in breathlessness such that the relation between these measures was unaffected.[3] The complete analysis of our study on codeine has now been published[3] and shows a more complex picture than that referred to earlier. Both drugs have only small effects and there is some interest in seeking agents with greater activity which might be helpful to the dyspnoeic patient. The more attractive profile would be that of an agent which dissociates breathlessness from the control of breathing.

The report by Dr Johnson and others on the effects of dihydrocodeine on breathlessness in patients with the "pink puffer" syndrome and their earlier study[4] do not explore the relation between breathlessness and ventilation. Thus we do not know if the reduction in breathlessness went hand in hand with effects on ventilation or whether there was a proportionally greater effect on breathlessness. We wish to suggest that such an analysis would help understanding of how dihydrocodeine produces its effects and would facilitate comparison with the effects of other drugs, including other opiates.

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1 Stark RD, Gambles SA, Lewis JA. Methods to assess breathlessness in healthy subjects; a critical evaluation and application to analyse the acute effects of diazepam and promethazine on breathlessness induced by exercise or by exposure to raised levels of carbon dioxide. *Clin Sci* 1981;**61**:429-39.
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BCG vaccination

SIR,—We welcome your article on BCG vaccination (12 March, p 876) and endorse the statement: "A prevaccination tuberculin test is necessary in all age groups except newborn infants, and only those people with negative reactions should be offered vaccination."

We should, however, like to make the following observations. Where the multipuncture test (Heaf or Tine) has been used in prevaccination tuberculin testing it has been our practice to vaccinate only those who are completely tuberculin negative—that is, grade 0. The tuberculin reaction, which is an expression of tuberculin hypersensitivity, is generally weak,[1] grade 1, or grade 2 after BCG vaccination and among our own patients a grade 1 reaction to the Heaf or Tine test after vaccination is very common. It would follow that a grade 1 reaction to the multipuncture tuberculin test is indicative of an acquired immunity against disease from tubercle bacilli. In those subjects whose prevaccination tuberculin test results in a grade 1 reaction BCG vaccination in our opinion is not therefore recommended.

We agree that strict adherence to the recommended test procedure is essential in all the tuberculin tests. The manufacturer's recommendations for reading the Tine test, however, are out of date. Any palpable induration should be regarded as positive and equivalent to a reaction of at least 5 mm induration to the standard Mantoux test (10 IU tuberculin).[2]

With regard to previous BCG vaccination difficulties not infrequently arise in young immigrant families who have recently arrived in this country, have been found to be tuberculin positive, and have what appear to be characteristic BCG scars. In many cases the parents have no knowledge whatsoever of the nature of any injections given to their children in the country of origin. We should like to make a plea for an international form of certification of BCG vaccination similar to that given for smallpox vaccination in the past.

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1 Caplin M. *The tuberculin test in clinical practice.* London: Baillière Tindall, 1980.
2 Rudd RM, Gellert AR, Venning M. Comparison of Mantoux, tine and "Imotest" tuberculin tests. *Lancet* 1982;ii:515-8.

SIR,—I would like to add to the guidelines on BCG vaccination (12 March, p 876). I should prefer the authors to have been more emphatic in discouraging the use of the Tine test. It is not reproducible, and it may give false positive reactions which cause needless anxiety.

In the section on complications after vaccination the treatment of ulcerated lesions is described but not of local or regional gland abscesses. It is important to warn against incising these as a persistent sinus may result. They should be treated by aspiration of the pus through a wide bore needle.

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Buying British

SIR,—Your assistant editor Dr Tessa Richards really must set your contributors a good example. She should check her facts before publishing them. "The first major medical textbook to be written in English ... was William Osler's *Principles and Practice of Medicine*," she writes, published "a little over half a century" after William Cullen wrote *Synopsis Noslogiae Methodicae* in 1769 (26 March, p 1027). Not so, Osler's book was first published almost a century and a quarter after Cullen's in 1892. (The last edition, the sixteenth, of this masterpiece of English medical prose was published as recently as 1947.) The first major medical textbook after Cullen's was in fact not Osler's but Sir Thomas Watson's famous *Practice*. This was first published in 1843 and ran to many editions over the next 40 years throughout the English speaking world.[1]

Moreover, in no way can Osler's book be said to contribute to "Britain's longstanding reputation for producing medical textbooks of quality." His book had been written at Harvard and was in its fifth or sixth edition before Sir William Osler came to Oxford University as regius professor of medicine. Osler was a Canadian and the *Principles and Practice of Medicine* was published by Appleton in the USA throughout its 50 years. The only English about it is the beautiful language.

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1 McGehee Harvey A, McKusick VA, eds. *Osler's textbook revisited.* New York: Appleton-Century-Crofts, 1967:1.

Medical sense and nonsense in biography

SIR,—Interpretation of symptoms of organic disease by non-medical writers or historians may certainly be subject to errors, especially in "permissive biographies," for which factual data are not available. But Mr Milo Keynes's evident approval of Dr Edward Larkin's facile criticisms of Lady Antonia Fraser's biography of Oliver Cromwell[1] (26 March, p 1023) is singularly inappropriate and uninformed. I admire Antonia Fraser's intuitive and wholly convincing understanding of Cromwell's spiritual crisis combined with puzzling physical symptoms when in 1628 he first consulted Dr John Symcotts of Huntingdon and then Sir Theodor de Mayerne in London; the latter's case book describes the mental state of his patient as "valde melancholicus." This was not what we would call today a nervous breakdown but a profound mystical experience combined with transient irrational behaviour, perhaps aggravated by physical illness.[2]

As far as factual medical information on Cromwell's last illness and death is concerned, it was Antonia Fraser who first among the modern historians pointed out that the story of his "bastard tertian ague," diagnosed by Dr George Bate, must not be interpreted as true malaria infection. The suggestion of septicaemia of biliary or urinary origin was first made by Mr Dickson Wright in 1937 and supported by Dr Chalmers Davidson of Edinburgh, whom Antonia Fraser consulted.[3] Confirmation of this probable diagnosis, based on the report of Cromwell's necropsy and other considerations, will be found in a recent paper.[4] Nevertheless, any diagnosis of presumed disease made today from vague and equivocal symptoms described 350 years ago as "hot and cold fit, distemper, flux, imposthume, etc" is bound to be conjectural and I doubt if medically qualified writers are more reliable in this respect than erudite and conscientious historians.

With regard to Mr Keynes's emphasis on the supremacy of professional psychologists over writers "stuffed with intuition and understanding," I wonder if Shakespeare's mere amateurish knowledge of deepest human emotions is not preferable to many ponderous and intricate theses of professionals trying to explain the tragedies of Hamlet, Shylock, Othello, or King Lear.

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