ventilator. Humidifiers were filled with 0.02% chlorhexidine and the respiratory tubes autoclaved every 24 hours. However, the rate of colonisation of the trachea in these patients was similar to that previously found in patients in whom these measures were not undertaken. The lack of a protective effect could be accounted for by contamination of the trachea by secretions of the oropharynx. Atherton and White³ found similar organisms in the gastric contents and trachea of a series of patients who had intermittent positive-pressure ventilation and they proposed the stomach as a source of bacteria colonising the respiratory tract. It seems anatomically more likely that secretions of the mouth and pharynx are the source of bacteria for both trachea and gastric contents.

The hazard of bacterial spread from the oropharynx to the trachea in ventilated patients emphasises the importance of oral hygiene, oropharyngeal suction, and the difficult problem of avoiding contamination of feeds and fluids. If leakage occurs frequently around the cuffs of endotracheal tubes, much more attention will have to be paid to these aspects of patient care in intensive therapy units.

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¹ Freeman R. In: de Louvois J, ed. *Selected topics in clinical bacteriology*. London: Baillière and Tindall, 1976:1-20.

² Casewell M, Phillips I. *Br Med J* 1977;iii:1315-7.

³ Casewell M, Phillips I. *J Clin Pathol* 1978;31:845-9.

⁴ Teres D, Schweers P, Bushnell LS, et al. *Lancet* 1973;ii:415-7.

⁵ Atherton ST, White DJ. *Lancet* 1978;ii:968-9.

A further hazard of ventilation

SIR,—We were interested to read the short report of aspiration around a high-volume, low-pressure endotracheal cuff (7 November, p 1220). We would like to report a further hazard we have encountered with two patients in this unit.

Both patients were ventilated via an 8-mm Shiley tracheostomy tube with a Cape ventilator. The cuffs of both tubes were inflated correctly and there were no audible leaks. The peak inspiratory pressures were 38 cm H₂O in the first case and 40 cm H₂O in the second. End-expiratory pressures were atmospheric. In each case an oesophageal temperature probe (Light Laboratories, Type 10ES) was inserted via the nasopharynx. The

Chest radiograph showing oesophageal temperature probe in right main bronchus of patient with tracheostomy tube.

probes have a diameter of 3 mm. It was noted on chest radiographs done soon after insertion that the probes were in the right main bronchus of each patient (figure).

The hazards of this complication are pulmonary infection and false temperature readings. With the introduction of fine-bore nasogastric feeding tubes, which could also conceivably pass around the low-pressure cuff, a further and more serious complication can be envisaged. We feel that a chest radiograph or direct laryngoscopy should be performed in all patients who have oesophageal tubes passed while they are being ventilated.

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Megadose vitamin C and metabolic effects of the pill

SIR,—Some years ago we reported¹ that women taking oral contraceptive pills containing oestrogen plus progestogen had lower than expected levels of ascorbic acid in their leucocytes and platelets. This finding was confirmed by several other studies.²⁻⁵ More recently, Dr D J Back and colleagues (9 May, p 1516) have shown that the plasma concentration of ethinyloestradiol is significantly higher in oral contraceptive users receiving 1000 mg ascorbic acid daily than in the same women not receiving a vitamin C supplement. The bioavailability of ethinyloestradiol is only about 40%,⁶ owing to extensive formation of sulphates during absorption and first pass through the liver. The interaction with ascorbic acid may be due to competitive inhibition of this sulphation, for ascorbic acid is also sulphated in the gut wall during absorption. The net effect of megadose vitamin C is therefore to increase the bioavailability of ethinyloestradiol. We have conducted a small study to determine whether this interaction has biological consequences.

Twelve healthy young women (18-23 years), non-smokers, who had used low-dose oral contraceptives (Triquilar, Schering; Triphasil, Wyeth; Nordette, Wyeth) for at least six cycles, were randomised between two vitamin C supplements in a double-blind manner. One supplement contained 50 mg and the other 1000 mg ascorbic acid. The women were instructed to take the vitamin capsule at the same time as their oral contraceptive pill. During the second cycle the women were switched to the alternative vitamin supplement. Blood was collected from fasting subjects on the last day of oral contraceptive taking in each cycle. Plasma was separated and analysed for high-density lipoprotein cholesterol, fibrinogen, coagulation factors VII and VIII, sex-hormone-binding globulin, and caeruloplasmin. Analytical methods are described elsewhere.⁷ A comparison of mean values for each

Biochemical findings in oral contraceptive users receiving vitamin C supplements

Test	Units	Mean $\pm$ SD	
		50 mg vitamin C	1000 mg vitamin C
HDL-cholesterol	nmol/l	1.30 $\pm$ 0.10	1.41 $\pm$ 0.09
Fibrinogen	mg/l	3.7 $\pm$ 0.8	4.6 $\pm$ 0.7
Factor VII	% control	101 $\pm$ 8	119 $\pm$ 9
Factor VIII	% control	109 $\pm$ 21	151 $\pm$ 23
Sex-hormone-binding globulin	nmol/l	68 $\pm$ 12	95 $\pm$ 14
Caeruloplasmin	g/l	0.51 $\pm$ 0.11	0.79 $\pm$ 0.13

Conversion: SI to traditional units—High-density lipoprotein cholesterol: 1 nmol/l $\approx$ 38.6 mg/100 ml.

of these measurements with the two levels of vitamin C supplementation are shown in the table. Results obtained during the high-dose vitamin C supplementation are significantly different from results during the low-dose supplement.

We conclude that the use of megadose vitamin C by oral contraceptive users enhances the effect of contraceptive steroids on important plasma proteins, and may increase the risk of cardiovascular disease. The overall effect of the large vitamin C supplement is to convert a low-oestrogen pill into a high-dose pill.

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¹ Briggs MH, Briggs M. *Nature* 1972;238:277.

² Rivers JM, Devine MM. *Am J Clin Nutr* 1972;25:684-9.

³ Kalesh DG, Mallikarjunerwara VR, Clemetson CAB. *Contraception* 1972;4:183-5.

⁴ McLeroy VJ, Schendel HE. *Am J Clin Nutr* 1973;26:191-6.

⁵ Wynn V. *Lancet* 1975;ii:561-4.

⁶ Back DJ, Breckenridge AM, Crawford FE, et al. *Contraception* 1979;20:263-73.

⁷ Briggs MH, Briggs M. *J Steroid Biochem* 1979;11:425-8.

Effect of supplementary food on suckling patterns and ovarian activity during lactation

SIR,—The paper by Professor P W Howie and others (19 September, p 757) showed that in Scottish women the introduction of supplementary feeding was associated with a reduction of nursing and the resumption of ovarian activity. These women were essentially substituting artificial feeding for breast feeding, whereas in many developing countries women introduce supplementary foods while still maintaining intense lactation and prolonged amenorrhoea.¹ Clearly, under the latter circumstances supplementation per se does not automatically lead to the resumption of ovarian activity.

The distinction between the substitution of artificial foods for breast milk and the mere supplementation of additional foods while intensive breast-feeding is maintained is important, since it would be unfortunate if the findings of this excellent Scottish study were to be incorrectly generalised to a Third World setting, and policy makers assumed that lactating women were at risk of conception as soon as they introduced supplements.

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¹ Paul AA, Muller EM, Whitehead RG. *Trans R Soc Trop Med Hyg* 1979;73:686.

Therapeutic embolisation

SIR,—In his leading article "Therapeutic embolisation" Mr A E Young mentions the burgeoning specialty of interventional radiology" (31 October, p 1144). An increasing part of this is percutaneous angioplasty, in which arterial stenoses and, in some cases, occlusions can be treated by catheterisation. I should like to draw attention to another technique which radiologists can offer in arterial disease. In conjunction with Dr Kjeld Nielsen of Copenhagen, I am assessing the value of intra-arterial carbon dioxide in-

sufflation in peripheral vascular disease. The gas, from 100 to 400 ml, is injected directly via an arterial catheter, the site depending on the angiographically demonstrated arterial supply to the limb.

I have reserved the method mainly for those who are not suitable for angioplasty and in whom surgery is not contemplated. Twenty-one such patients, with generally severe and widespread disease, have been treated. Eight had rest ischaemia with threatened limb loss; objective evidence of reversal of ischaemia and complete symptomatic relief were obtained in five. In a follow-up period of up to seven months there were two recurrences, at three months and one month respectively, the latter patient being relieved by repeat insufflation. Three of the eight patients had no significant benefit. There were 13 patients with intermittent claudication—five with complete symptomatic relief, five with partial improvement, and three with no effect in a follow-up period of up to six months.

The mode of action is unknown. In physiological studies in which small amounts of various gases were injected in the brachial artery of volunteers¹ temporary vasodilatation was found, without satisfactory explanation. In the cases reported here, the vasodilatation appears to be longer lasting, presumably at least sufficient to allow collaterals to develop. Alternatively, there may be a change in tissue metabolism. These aspects are being investigated and will be subsequently reported.

I appreciate that the method as yet has little scientific basis, and that in the group with claudication there is no objective evidence of benefit. However, until more definitive information can be provided, it is suggested that the method is at least worth trying in the category of patients described, for whom no reconstructive procedure, either by surgery or by percutaneous angioplasty, can be offered. Apart from the fact that it involves arterial catheterisation, the method appears to be perfectly safe. Minor discomfort in the limb may occur, with patchy mottling of the skin; but these are only transient effects.

It is generally appropriate for the radiologist to carry out the procedure, as catheterisation of the most appropriate vessel (depending on the disease distribution) ensures optimum delivery. It can be performed at the time of the diagnostic angiogram if criteria for its use have previously been agreed locally.

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¹ Dove F, Greenfield ADM, Whelan RF. *Clin Sci* 1954; 13:365-76.

Azathioprine-induced shock

SIR,—We read with interest the report of Dr T Cunningham and others (26 September, p 823) about azathioprine-induced hypotension in two patients with rheumatoid arthritis who both had upper gastrointestinal disturbance. An acute drug hypersensitivity was implicated but the mechanism remains unexplained.

Pancreatitis induced by azathioprine is well reported,¹ but to our knowledge not in rheumatoid arthritis. The above report does not include serum amylase estimations.

We have recently observed a 65-year-old patient with seropositive rheumatoid arthritis

treated with longstanding diclofenac 50 mg thrice daily, who developed nausea, vomiting, and mild diarrhoea on 100 mg while taking azathioprine. This was associated with tachycardia but no significant hypotension. His serum amylase concentration was raised to 530 IU/l (normal 70-300 IU/l) and both symptoms and serum amylase settled on drug withdrawal. Rechallenge with 50 mg azathioprine reproduced his symptoms and a significant rise in serum amylase, which returned to normal when the drug was withdrawn. The oral cholecystogram, barium meal findings, and serum calcium were normal.

We would suggest that pancreatitis may be implicated in such azathioprine-induced reactions in rheumatoid patients.

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¹ Sturdevant RAL, Singleton JW, Deren JJ. *Gastroenterology* 1979;77:883-6.

Do drug dependence clinics work?

SIR,—Dr T Webb (31 October, p 1185) follows principles which operate unfortunately throughout the modern British system of treating drug addicts—namely, (a) when attacking critics avoid the questions they raise and (b) make no constructive suggestions.

Instead of discussing what I said in my article (26 September, p 857) Dr Webb invents something I did not suggest (that is, undercutting the market in controlled drugs) in order to criticise it. It would be more interesting to know what he thinks about the questions I really did raise concerning the large and growing black market in drugs, the failure of our present curiously rigid system to perform the task for which it was constructed, and the consequent rise in drug-related crime.

In his calculation of the enormous profits (233.3%) made by addicts selling their drugs he reveals a common erroneous belief—namely, that addicts do not themselves need or take drugs. This belief, translated into treatment and prescribing policies, keeps addicts away from clinics and drives them on to the streets and to private doctors.

It is news to me, though it does not surprise me, that patients from London sell drugs in the West Midlands. But why can Dr Webb not influence their doctors? I am sure that virtually every doctor, given convincing evidence that a patient was selling his drugs in the West Midlands or anywhere else, would immediately stop prescribing for that patient.

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***We sent this letter to Dr Webb, who replies below.—Ed, *BMJ*.

SIR,—I did not attempt to discuss Dr Dally's suggestions—firstly, for the sake of brevity and, secondly, because I agree with the majority of the points she makes. I chose instead to point out the one major danger of any doctor, private or NHS, attempting to "treat" addicts without the benefit of a back-up team of some description.

Dr Dally is wrong to say that I invented the

suggestion that we should undercut the market in controlled drugs. To quote her article, "Private treatment means about a tenth of the cost, and only a minute proportion of the time needed to maintain a drug habit on the blackmarket." It is for this very reason that any system is so open to abuse unless it is rigidly controlled.

The only way of reducing the problem is to impede the blackmarket suppliers effectively, preferably at source. I think we must accept that *all* methods of treatment of and supply to addicts are less successful than we would like. Therefore until more effective means of dealing with the problems are available we are left to using the system which is least open to abuse.

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Tricyclic antidepressant poisoning and prolonged external cardiac massage during asystole

SIR,—I was interested to read about the two patients with imipramine poisoning reported by Drs D A Orr and M G Bramble (24 October, p 1107). The first patient had a generalised convulsion prior to developing a ventricular tachycardia and the second patient two generalised convulsions before circulatory arrest. At no time was an anticonvulsant administered to either of these patients.

My impression has been that intravenous phenytoin, given on admission, to patients with severe tricyclic antidepressant poisoning prevents convulsions. It theoretically may also prevent ventricular dysrhythmias. I would be interested to hear the views of the authors on these points.

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***We sent this letter to the authors, who reply below.—Ed, *BMJ*.

SIR,—Before we comment on the possible use of phenytoin in preventing convulsions induced by a tricyclic antidepressant the cardiovascular effects of this drug need to be closely examined as tricyclic antidepressants have a quinidine-like effect on the myocardium when taken in overdosage. Quinidine is a class Ia antiarrhythmic agent, which may of itself produce serious ventricular dysrhythmias by prolongation of the Q-T interval. Prolongation of the Q-T interval is virtually pathognomonic of tricyclic antidepressant poisoning^{1 2} and it has recently been suggested that phenytoin may be contraindicated in such cases as it is also a class I antiarrhythmic agent (31 October, p 1187). The situation is more complex than this, however, as phenytoin is a class Ib antiarrhythmic agent, which in contrast to quinidine does not increase the duration of the action potential. Nevertheless, the effectiveness of this drug remains unproved and it may be deleterious in atrial tachycardias.³ Studies using lignocaine (another class Ib antiarrhythmic agent) in tricyclic antidepressant poisoning have shown that it may be useful in controlling simple ventricular ectopic beats, but its ability to prevent serious cardiac arrhythmias remains doubtful.⁴ Phenytoin may also exacerbate the hypotension due to tricyclic antidepressant-mediated afterload reduction.²

In view of the uncertainty which surrounds