This was shown in the survey referred to earlier as well as in Dr Tomlin's study.

With the routine use of ventilators the use of low-flow rebreathing systems with carbon dioxide absorption appears to be diminishing. The higher gas flows employed are adding to the pollution. In addition flowmeters and vaporisers often remain open in anaesthetic rooms long after the patient has gone back to the ward via the operating theatre.

The problem of pollution is perhaps well recognised now. The current shortage of anaesthetists is putting more stress on the available people and perhaps forcing them to face the pollution for longer periods. It must be even more so in Birmingham!

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Should the indications for prenatal chromosome analysis be changed?

SIR,—The question posed by the title of the paper from Copenhagen by Professor John Philip and others (29 October, p 1117) begs an answer, which we suggest should be in the negative.

Close scrutiny of the data presented by the Copenhagen group (see table) reveals that the low overall frequency of chromosome abnormality in their high-risk group is accounted for by the unusually low number of abnormalities detected in pregnancies in mothers aged 35-39 years (0·2%). This low figure is of considerable interest but disagrees with our experience in Edinburgh and with that of the other major studies quoted in the paper. The explanation for the difference in incidence of chromosome abnormality is not obvious, but it is of interest that almost all women over 35 years in the Copenhagen population appear to have had diagnostic amniocentesis. One explanation advanced for the finding of a much higher than expected number of fetal chromosome anomalies in the second trimester of pregnancy compared with the incidence at birth[2] is that unknown selection factors may affect the population of older mothers having antenatal diagnosis performed.[4]

However, continued availability of facilities for antenatal diagnosis for older mothers is in our opinion essential. Antenatal diagnosis fulfils a dual role—primarily to reassure the majority of individuals tested that the fetus has a normal chromosome constitution and secondly by providing a smaller number of individuals, when chromosome abnormality is detected, with the offer to terminate the pregnancy. Pregnancies in women over 35 years are currently accorded "high-risk" status, and the removal of one risk (chromosome abnormality) is beneficial to the patient, by reducing one source of anxiety, and to the clinician, who has an extremely useful additional piece of information available if faced with difficult decisions on management in later pregnancy. Serious handicap associated with chromosome abnormality in infants of women over 35 years would be reduced, the reduction of Down's syndrome infants in the Danish population by screening all pregnant women aged 35 and over being estimated at 25%.[5] Such a policy has obvious benefits for the parents involved, and is generally reckoned to be cost-effective.[5 6]

Chromosome abnormalities in pregnancies in women aged 35-39 years

Canadian study[1]	1·6%
Glasgow[2]	1·5%
European study[3]	1·2%
Edinburgh	1·4%
Copenhagen	0·2%

Two main problems in this field remain at present: firstly, to ensure that prenatal diagnosis is readily available to the older woman, and, secondly, to evolve a method of detection of younger women who may have a higher-than-average risk of a chromosomally abnormal fetus. It has been calculated that only 12% of patients over 40 in south-east England have diagnostic amniocentesis performed.[4] Responsibility for increasing the number of older women screened lies with health workers caring for pregnant women, since Professor Philip and his colleagues emphasise that the acceptance rate among women offered amniocentesis is high. Unfortunately, using age as the sole criterion of risk for chromosome abnormality, the precise age (in the 35-39-year age group) where transition from low to high risk occurs is not yet defined. We therefore intend to continue our current policy, which is to offer amniocentesis to patients of 38 years or over and to make the procedure available on request to those aged 35-37.

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Treatment of echinococcosis

SIR,—We were interested to read the paper by Dr A Bekhti and others (22 October, p 1047) in which they reported encouraging results with mebendazole in the treatment of human echinococcosis. This drug had already given good results in the treatment of experimental echinococcosis in mice.[1] Unfortunately, however, the compound proved to be toxic for rat fetuses and has been withdrawn from the market.[2]

Its derivative fluoromebendazole is endowed with a broad spectrum of activity and high efficacy. Results obtained in treating diffuse mice echinococcosis show promise.[3] No side effects have been reported as yet.[4]

We have tested this compound in three cases of human echinococcosis at a dosage of 2 g a day for 10, 6, and 12 months respectively. Clinical and biological tolerance has been excellent. The first patient was a 25-year-old woman in whom rupture of a cyst had occurred during surgery for echinococcosis of the liver. No secondary localisation has been observed. The second patient was a 20-year-old man with disseminated abdominal echinococcosis contraindicating surgery. Considerable clinical and radiological regression has been observed; in particular a giant pelvic cyst compressing the bladder and ureters has almost completely disappeared. In the third patient, a 28-year-old man, rapid progression of diffuse lung echinococcosis has been halted.

Despite the small number of observations, in view of the fact that there is no known medical treatment for disseminated echinococcosis, which has a very poor prognosis, we think that fluoromebendazole might be a useful drug and deserves further study in that field.

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Iodine and the thyroid

SIR,—In your leading article on this subject (17 December, p 1566) it is stated that hyperthyroidism is common in Iceland. In a survey on Graves's disease in Iceland from 1938 to 1967[1] the annual incidence was found to range from 0·097 to 0·138 per 1000 inhabitants and toxic nodular goitre was virtually unknown. From Denmark,[2] the Soviet Union,[3] and West Scotland[4] an incidence of thyrotoxicosis ranging from 0·22 to 0·50 per 1000 has been reported.

It is well known that an increase in iodine intake in areas of endemic iodine deficiency is associated with an increase in the incidence of thyrotoxicosis, but there is no evidence that a chronic high iodine intake will permanently increase the incidence (or prevalence) of thyrotoxicosis. In fact the evidence from Iceland suggests that the opposite may be true. However, further studies on the prevalence of thyroid disease and on the interplay between environmental and genetic factors in populations on different iodine intakes are needed to define the optimal iodine intake.

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Donor blood for neonatal exchange transfusion

SIR,—I read with much interest the letter from Dr J P Lee-Potter (12 November, p 1290) asking for conclusive evidence why the administration of properly tested blood up to four days old for neonatal exchange transfusion should be discouraged. In West Germany we observe an increasing vogue for "warm blood," meaning absolutely fresh

blood straight from a donor and therefore insufficiently tested. "Warm blood" is demanded not only for neonatal exchange transfusion but for practically all cases of emergency transfusion. Its advocates prove uniformly unable to refer to controlled studies suggesting an improved outcome in recipients of "warm blood" compared with those given fully tested stored blood. Before more and more clinicians switch over to this dubious pre-first-world-war procedure, apparently for irrational reasons, careful prospective investigations in this field are urgently needed.

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Cockles of the heart

SIR,—The origin of the expression "warming the cockles of the heart" (12 November, p 1271) is simple: the left atrium or cockle is in close relationship to the oesophagus and when hot liquid passes down the gullet the cockle is warmed. The expression is derived from a common-sense interpretation of anatomy. Using the plural and including the right atrium is allowable poetic licence; cockle (singular) sounds odd.

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Indomethacin in pleurisy

SIR,—Dr K P Goldman's assertion that there is no previous report on the use of indomethacin for relieving pleuritic pain (19 November, p 1353) is inaccurate. Without undertaking an exhaustive literature search I can cite at least two clinical reports documenting successful therapy of acute pleuritic pain with indomethacin.

One report[1] indicates that the drug be administered in substantial amounts, 100 mg every two hours for 4-6 doses. Relief is obtained shortly, usually after the first few days. The drug can then be given in the usual maintenance dosage of 25-50 mg four times a day. Except for minor cases of nausea and euphoria no serious adverse reactions were noted with this regimen even after two years of use.

The second report[2] shows that in a double-blind study satisfactory analgesia was experienced by 84% of 51 patients with acute, severe pleuritic chest pain who received a single suppository containing 100 mg of indomethacin compared with 35% given placebo. Relief of pain started within 30 min in 52% and within 60 min in 85% of indomethacin responders, reaching a maximal effect within 90 min in 67% of the patients. Significant improvements were noted in respect of mechanical lung function, respiratory rate, and the ability to cough effectively in patients experiencing analgesia due to indomethacin. Four of the 25 patients receiving the drug experienced mild to moderate dizziness and two other patients complained of mild nausea.

According to a study by Halt *et al*[3] therapeutic serum levels of indomethacin are reached sooner after rectal than after oral administration of the same dose. In addition, rectal administration of indomethacin has the advantage of not causing gastrointestinal distress and is a useful alternative when oral use is contraindicated in patients with dyspepsia or peptic ulceration.[4]

Although the exact mechanism of indomethacin-induced analgesia in pleuritic pain is not known, the effect might be related to the drug's powerful anti-inflammatory properties,[5] which allow it to interfere in some manner with pain-producing chemical mediators.[7]

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Cooking the turkey

SIR,—Scrutator's indignation (7 January, p 57) about the Departmental advice on the cooking of turkeys is misplaced. In 20 years' experience of the control of infectious disease by far the great majority of outbreaks of food poisoning that I have dealt with have been the result of badly prepared, cooked, or served large turkeys, and it is clear that many catering managers still need to be reminded of good practice in this field.

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Initiation of once-daily pindolol treatment

SIR,—An increasing number of patients with moderate hypertension are now treated with beta-blockers in a once-daily regimen. In Sweden pindolol, metoprolol, and propranolol are now officially approved for administration in this way. Usually the optimum dose of the beta-blocker is reached by a gradual titration.[1 2] For practical reasons it is of course an advantage if the optimum dose can be given once daily from the start of the treatment. For pindolol several studies have indicated the optimum once-daily dose to be 10-15 mg.[3] Against this background a study has been performed with the aim of comparing the tolerability of 15 mg pindolol given once daily and 5 mg administered three times daily.

Twenty ambulatory patients, 15 men and five women of mean age 42, with moderate hypertension, previously untreated, entered the study. The criterion for acceptance was a diastolic blood pressure of $\geqslant$105 mm Hg on at least two different occasions maintained during an initial placebo period of four weeks. The blood pressure was measured in the morning, always before the first tablet intake that day. The patients were divided at random into two different groups, group A being given 15 mg once daily and group B receiving 5 mg three times daily. Double-blind conditions were obtained by using blister-packages.

The mean supine blood pressure and heart rate at the end of the placebo period and after four and 12 weeks of active treatment for the two groups are shown in the table below. There was a significant reduction of the blood pressure after four weeks' active treatment for both groups. There was no difference in the pressure reduction between the groups after either four or 12 weeks' therapy. In three cases side effects were recorded. One woman taking 5 mg thrice daily discontinued treatment after one week owing to fatigue and vertigo; in another case the patient complained of sleep disturbances but continued therapy. One patient on 15 mg once daily noticed vertigo two hours after the tablet intake.

In summary, a gradual titration of pindolol in the once-daily regimen seems unnecessary and the optimum dose can be given directly without increasing the risk of side effects. Thus a simpler regimen can be obtained which may help to keep the patient on the treatment.

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Effects of pindolol treatment 15 mg once daily (group A) and 5 mg thrice daily (group B) on mean blood pressure and pulse rate

	Group A		Group B	
	Blood pressure (mm Hg)	Pulse rate (beats/min)	Blood pressure (mm Hg)	Pulse rate (beats/min)
After 4 weeks' placebo	164/107	74	174/108	76
After 4 weeks' active treatment	147/93	69	149/94	70
After 12 weeks' active treatment	141/85	71	147/88	69

Aid to drug compliance

SIR,—It is well known that patients, even when well motivated, often fail to take their prescribed drugs correctly. Obviously this is most likely to occur when aged patients are on multiple drugs; however, even a single course of an antibiotic may be taken incorrectly.

All drugs could be packed in "calendar-packs" with one tablet to be pushed out each marked day for four weeks and a space on each pack to mark, say, morning, noon, and evening. Then if the dose were two tablets thrice daily six such packs would give one month's supply. Some drugs are already available in this way—for example, contraceptive pills, certain iron preparations, Lasix+K, and Tenormin. Doubtless manufacturers are financially inhibited from changing to such packaging. However, in many countries it is already a legal requirement for drugs to be dispensed in an "original pack"; it would be possible for the Department of Health and Social Security to allow drug manufacturers to retain extra profits to cover this once-and-for-all increase in expenditure. This would result in a worthwhile increase in drug efficacy and safety.

A useful and simple interim measure would be to issue a small card with all medicines, including syrups and ointments. This would have