there are few published data to support these claims. In a prospective randomised trial in 140 patients that compared laparoscopic and open appendicectomy Tate *et al* found no significant differences between the groups in pain score, analgesic requirement, hospital stay, or time to return to work.² The only significant finding was that the operating time was nearly twice as long in the laparoscopic group. In addition, conversion to an open operation was necessary in a fifth of the patients undergoing laparoscopy.

Further prospective randomised trials are needed to establish the place of laparoscopic surgery. Without such data the current enthusiasm for laparoscopic surgery may be unfounded.

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Management of asthma in general practice

Question patients about occupation and hobbies

EDITOR,—Duncan Keeley correctly addressed the issues concerning treatment of asthma in general practice once the condition has been diagnosed, including the questions to ask during routine consultations to gauge the severity of the disease.¹ However, general practitioners need to ask all asthmatic patients one important question before consigning them to lifelong treatment: What are your occupation and leisure interests? Over 200 agents have been proved to cause occupational asthma, ranging from high molecular weight proteins such as bakers' flour, animal fur, fish proteins, and detergent enzymes to low molecular weight isocyanates and glutaraldehyde.

Initially patients with occupational asthma do not associate symptoms directly with work, but they wake at night coughing after exposure. Once they have become sensitised they produce specific IgE or IgG antibodies, which cause a more immediate response. During the next long term phase the difference in symptoms at home and work is not obvious. At this stage an absence of symptoms on holidays may be the only clinical clue. Smoking and atopy are variable risk factors depending on the causal agent.

The "single" allergen causing occupational asthma is a fascinating model for natural asthma. Prompt removal from exposure is likely to cure the asthma. Delay in removal and continued antigenic challenge results in cross sensitisation to other household allergens and chronic asthma. The implications for children initially allergic to one type of pet animal are obvious.

Serial peak flow measurements are the best method of diagnosis² but require careful interpretation. Results can become confused by treatment with β agonists or inhaled steroids.

Herein lies the great opportunity for general practitioners to "cure" a chronic condition that has substantial costs for individual patients and the NHS. New causes and old examples of occupational asthma are always present in general practice.

The final diagnosis of occupational asthma requires specialist help from an occupational physician or chest physician but general practitioners have an important role in the diagnostic chain. They are best equipped to suspect the

diagnosis because they know the patient, his or her family, and local industries.

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Difficulty with spacer devices

EDITOR,—Duncan Keeley provides a common-sense and comprehensive approach to the problems of managing asthma in general practice.¹ He makes the mistake, however, of extrapolating the advantages of spacer devices to elderly people, claiming that such devices are "easily used by . . . elderly patients (except those with weak or arthritic hands)."

Though clinical experience might support this view, there has been controlled evaluation of inhaler technique with large volume spacers in elderly patients. Newman *et al* studied nine patients with a wide age range, only two of whom were over 70, and confirmed increased lung deposition with a single actuation in all patients including the elderly patients.² Chu *et al* studied 53 patients aged 65 to 88 using metered dose inhalers and Nebuhalers. Although the patients found the Nebuhaler more convenient, there was no difference in percentage reversibility with the Nebuhaler.³ The patients' technique was not assessed.

In my clinical experience, most very elderly people find large volume spacers easy to use.

Many, however, experience difficulty in inserting the metered dose inhaler into the spacer, and others have an uncorrectable tendency to actuate the inhaler repeatedly before inhalation. A controlled study of elderly patients' technique is under way in my department.

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Neuroleptic malignant syndrome

May be caused by other drugs . . .

EDITOR,—M F Bristow and D Kohen state that the neuroleptic malignant syndrome may occur in response to the sudden cessation of dopamine agonists as well as in patients treated with neuroleptic drugs.¹ But the syndrome has also been reported after the administration of non-neuroleptic drugs, including lithium, metoclopramide, carbamazepine, antidepressants (including dothiepin and amoxapine), tetra-benazine, and metirosine.²⁻⁴

The authors emphasise that the pathogenesis of the syndrome is unknown and mention several possible central mechanisms. Although dopaminergic hypofunction in the basal ganglia seems the most likely cause of the rigidity and tremor, peripheral mechanisms may give rise to the other features. Sustained rigidity and tremor are likely to produce considerable heat as a result of muscle

metabolism, and this could account for the fever. Fever and metabolic changes secondary to rhabdomyolysis could contribute to autonomic dysfunction and clouding of consciousness, the two remaining key features of the syndrome. The beneficial effect of dantrolene, a skeletal muscle relaxant, in reducing the duration of the syndrome⁵ supports the importance of muscular mechanisms in pathogenesis. Central abnormalities may also play a part—in particular, decreased activity in dopaminergic pathways in the hypothalamus may lead to fever.

Awareness of the epidemiology of the neuroleptic malignant syndrome may help alert clinicians to early cases. The male to female ratio among patients is 2:1, and 45% of patients are aged between 20 and 39, although the condition occurs at all ages.² Ninety per cent of cases begin within 10 days of the start of treatment with a neuroleptic drug, though not necessarily for the first time, and a rapid increase in the dose during this period is usual. Although all neuroleptic drugs have been implicated, half of all reports have concerned haloperidol.⁵

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. . . and other diseases

EDITOR,—M F Bristow and D Kohen acknowledge that psychiatry is not the sole domain of the neuroleptic malignant syndrome.¹ The syndrome has been described in patients with advanced cancer² and AIDS.³ Malnutrition and severe debility may be precipitating factors in susceptible patients. Outside psychiatry the diagnosis may often be missed as three of the four standard diagnostic criteria (fever, autonomic instability, and altered consciousness) may be seen as evidence of advancing malignant or other disease. All of these factors will contribute to an underestimation of its true incidence.

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Don't confuse with anticholinergic intoxication

EDITOR,—In their editorial on the neuroleptic malignant syndrome M F Bristow and D Kohen refer to the four main signs (fever, rigidity, autonomic instability, and altered consciousness), noting that incomplete varieties are encountered.¹ In their brief discussion of the differential diagnosis, however, they do not mention the clinical resemblance between this condition and anticholinergic intoxication.

Anticholinergic intoxication causes fever, autonomic instability, and altered consciousness and is likely to occur in patients with rigidity induced by neuroleptics.² Patients with severe psychiatric illness are not uncommonly treated with escalating doses of one or more neuroleptic drugs with anticholinergic properties. Moreover, such

patients may also be taking an antidepressant with anticholinergic properties and, almost routinely, receive an anticholinergic drug such as procyclidine to prevent or alleviate rigidity.

Though some patients with anticholinergic intoxication will be "hot as a hare, blind as a bat, red as beetroot, and mad as a hatter," in psychiatric practice they will more probably be noticed to have a fever and will be diagnosed as having the neuroleptic malignant syndrome. Patients considered to have this syndrome should always be examined for the physical hallmarks of anticholinergic intoxication, particularly pupillary dilatation and dry skin and mucous membranes. The investigation and treatment of this condition are considerably less enigmatic than those of the neuroleptic malignant syndrome and have been well described by Lipowski.³

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Injection immunotherapy

EDITOR,—In A J Frew's article on injection immunotherapy one of the display panels states that insect venom immunotherapy is not recommended in patients with a history of chronic perennial asthma.¹ Such advice would be widely accepted when applied to allergen immunotherapy for rhinoconjunctivitis, but I believe it is unnecessary to extrapolate this advice to people allergic to insect venom.

Since 1977 I have been associated with the insect venom allergy clinic at Guy's Hospital, where we have successfully and safely treated many asthmatic patients as well as those with hypertension and even ischaemic heart disease. When anaphylaxis follows either injections or stings asthma is an important risk factor. Most of the deaths reported in young patients receiving injection immunotherapy for inhaled allergens before 1986 were due to acute severe asthma.² This makes it imperative for asthmatic patients to be desensitised to venom if they have had generalised reactions to stings. The benefit:risk ratio for immunotherapy is higher in patients who have risk factors such as cardiovascular disease or asthma because of the risk of a sting or of unsupervised adrenaline administration in such patients.

Obviously, it is important to take careful account of the asthmatic status of patients undergoing this treatment. In our clinic all patients have their peak expiratory flow rates measured before the injections and before they are allowed to leave after their mandatory period of medical supervision. Patients who come to the clinic with an exacerbation of their asthma are not given their next injection until the exacerbation has responded to treatment. In the case of children I consider that venom immunotherapy should be recommended only for those who are asthmatic. The only child dying from an anaphylactic reaction to a bee sting of whom I have personal knowledge was known to be asthmatic.

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- 1 Frew AJ for British Society for Allergy and Clinical Immunology Working Party. Injection immunotherapy. *BMJ* 1993;307:919-23. (9 October.)
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Ultrasound dating subject to bias

EDITOR,—Mark Wilcox and colleagues used ultrasonography to determine fetal age and reported a stronger correlation between birth weight and gestational age at term than has been observed previously.¹ We believe that their approach is subject to bias.

Dating methods based on ultrasonography do not take into account the natural variability of fetal size early in pregnancy. Thus a relatively large fetus at any given time will be assessed as being older and a relatively small fetus of identical gestational age will be assessed as being younger.² If we assume that fetuses tend to keep their relative size throughout pregnancy then among newborn infants of exactly the same true gestational age but different sizes there would be a correlation of weight with ultrasonographically determined gestational age: the largest would have the longest gestation and the smallest would have the shortest. This could account for the authors' finding that, among term births, the curve showing birth weight by gestational age was steeper than that derived from datasets based on the last menstrual period. Using the last menstrual period has its own limitations, but this particular bias is not among them. For all its merits, ultrasonography is still not the gold standard.

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Avoidable factors in stroke

Smoking, drinking, and hypertension

EDITOR,—J N Payne and colleagues identify shortcomings in the care of patients dying of diseases related to hypertension.¹ I carried out a survey of modifiable risk factors in 70 consecutive young patients with stroke (aged under 55) admitted to hospital over five years.

The main modifiable risk factors identified (table) were hypertension, current cigarette smoking, and excessive alcohol intake (confirmed by macrocytosis and raised γ glutamyl transferase activity). Ten patients had had hypertension diagnosed previously but were not taking antihypertensive drugs at the time of the stroke. Seven patients in whom hypertension had not been diagnosed had raised blood pressure and electrocardiographic evidence of longstanding hypertension (left ventricular hypertrophy). Of the 37

Modified risk factors in 70 young people with stroke

	No
No risk factor	10
Hypertension	33
Current treatment	16
No current treatment	10
? Undiagnosed	7
Cigarette smoking	45
Excessive alcohol intake	19
Diabetes mellitus	5
Atrial fibrillation	3

normotensive patients, 27 were current smokers or had an excessive alcohol intake, or both.

In up to 44 of the 70 patients in this series modifiable risk factors may have been managed inadequately. The reasons for this were not addressed by the study, but there are obvious lessons regarding the reduction of stroke in this age group.

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Consider carotid endarterectomy

EDITOR,—It was depressing to note that avoidable factors may have contributed to the death of 44% of those patients with hypertension who died in J N Payne and colleagues' survey of avoidable factors in deaths from stroke and hypertensive disease.¹ In a study of 168 general practitioners in Leicestershire only 21% were aware of the results of the European and North American carotid surgery trials.²

Over 2900 patients have been recruited to the European carotid surgery trial, of whom about half were hypertensive, with a diastolic blood pressure ≥ 90 mm Hg, at the time of randomisation. The trial has shown a reduction over five years of over 20% in ischaemic stroke in the ipsilateral hemisphere in patients who had carotid endarterectomy compared with patients who had no surgical treatment as prophylaxis against stroke; it also showed nearly 10% benefit for surgery when all strokes, including deaths during surgery, were considered after five years. In other words, carotid endarterectomy confers a clear benefit over best medical treatment alone in a patient who has a tight carotid stenosis ($> 82\%$), provided it is symptomatic. At present, in Britain fewer than half of the people who would benefit from carotid endarterectomy undergo it.

Thus it seems that at primary care level an alarming number of patients are dying of stroke or disease related to hypertension that might have been prevented; only a small number of general practitioners are aware of the benefits of surgery for patients with a symptomatic tight carotid stenosis; hypertension may well be associated with carotid stenosis in a patient with stroke; and most eligible patients are denied a valuable method of preventing stroke—that is, carotid endarterectomy.

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Screening for breast cancer

Randomised trials testify to benefit

EDITOR,—Recent letters have criticised screening for breast cancer by mammography,^{1,2} which is the only method of screening for malignancy that has been shown to be of value in rigorous randomised trials. Harold Hewitt incorrectly states that there is no evidence that detection of breast cancers by screening eliminates dissemination.¹ There is clear evidence that screening detects less aggressive cancers, which are less likely to have disseminated.³

Although Bruno Barmus presents data on