the problems. This discretion should not be exercised unnecessarily, as elderly patients often have visiting grandchildren who could be at risk. A demonstration to patients may be sufficient.

The amount of information required on a label means that unless the container is to be unacceptably large the type size must be small. The use of special label typewriters is preferable to poor handwriting, but is not the complete answer. Supplementary labelling or separate instruction cards may be used, but are not without hazard. Here again the pharmacist needs to be made aware of the problem when a prescription is presented to arrive at the best compromise for each patient. Streamlining a patient's drug regimen and hence reducing the number of containers or doses, or both, may help, and pharmacists can often advise on this too. Many elderly patients do not collect their own prescriptions, so the opportunity for the pharmacist to demonstrate the use of child-proof containers and reinforce directions unfortunately does not arise.

These problems can best be tackled by individual doctors, pharmacists, and community nurses working together on behalf of individual patients. With knowledge of the patient's difficulties and home circumstances, some solution, albeit perhaps a compromise, can often be found. Developments such as the establishment of general practice pharmacies in health centres and perhaps in the future registration of patients with pharmacists could encourage this co-operation, but are by no means essential. With good will from everyone involved, local initiative can, and does, produce considerable improvement.

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Stopping lithium prophylaxis

SIR,—Lithium therapy, like many other forms of chemotherapy, is associated with side and toxic effects and before commencing treatment the possible advantages will need to be weighed against these and the discussion leading to the treatment decision shared with the patient. The timing of the likely cessation of the treatment should be formulated during the process of the decision to institute lithium therapy.

Once an equilibrium has been achieved between lithium and other electrolytes, cellular networks and transmitter units will have been pervaded by lithium. It would not be surprising for the sudden withdrawal of lithium to be followed by an acute confusional state if the cessation of treatment occurred in a setting of electrolyte equilibrium. This could be the explanation of the events described by Dr D G Wilkinson (27 January, p 235).

In general terms, once the recurrent affective illness is held by lithium therapy an attempt should be made to withdraw the medication over a period of six months in those patients who have been on prophylactic therapy for more than a year. In coming to the decision to terminate lithium therapy the following factors can be relevant:

(a) The underlying neurophysiological stratum and an assessment of how near is the cessation of its instability (adolescence, the menopause, and the involution). (b) The length of the periodic cycle of the recurrent affective illness, withdrawal being attempted

when the symptoms have been in remission for twice the duration of the cycle when this is over twelve months or four times the length of the cycle where the latter is less than twelve months. (c) The degree of resolution of any personal problems or conflict—if these persist the withdrawal of therapy is more likely to be unsuccessful. (d) If electrolyte levels fluctuate more than plus or minus 0.2 mmol/l electrolyte equilibrium does not exist, and if there is evidence to suggest that the patient is not complying with the prescription this may be a clear indication to challenge the patient and stop medication if the response is not satisfactory. On the other hand, if steady levels of lithium have been achieved over a period of two to three months then a stage of equilibrium has been reached and it is my experience that a more favourable therapeutic response is likely.

On withdrawal the risks of relapse appear to be higher than the appearance of the withdrawal syndrome described by Dr Wilkinson.

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Fats and atheroma

SIR,—Sir John McMichael argues that dietary intervention is a futile and even hazardous approach to the prevention of atherosclerotic heart disease (AHD). His report (20 January, p 173) is a catalogue of the opinions of the uninformed supported by anecdotal data from inadequately studied populations.

The relationship between the concentrations and component ratios of plasma lipoproteins and the incidence of AHD is well documented.^{1,2} At a cellular level there is evidence that arterial uptake of low-density lipoprotein (LDL) cholesterol is proportional to its plasma concentration³ and that high-density lipoprotein (HDL) reduces binding of LDL to both high- and low-affinity cellular receptors.⁴ Similarly, clinical studies of individuals with precocious manifestation of AHD⁵ as well as individuals with extended protection from AHD⁶ support the conclusion that decreased risk is conferred by both high levels of HDL and decreased concentrations of LDL.

The effect of dietary fatty acids on the plasma lipoprotein spectrum has been the subject of extensive and systematic investigation. That cis-polyunsaturated fatty acids (PUFA) reduce concentrations of plasma total and LDL cholesterol is undisputed. Although an extreme increase in the ratio of dietary PUFA to saturated fatty acid (SFA) may have less desirable effects on the HDL component,⁷ preliminary results suggest that more moderate fatty acid modification (PUFA:SFA, 1:0) may be associated with absolute increases in plasma HDL⁸ and certainly with an increase in the HDL:LDL ratio.⁹

The idiopathic effect of certain vegetable oils on myocardial metabolism, as mentioned by Sir John, is hardly central to the argument. No one is recommending the ingestion of high erucic acid—rapeseed, arachis, or hydrogenated oils—for preventing AHD. Plasma cholesterol-lowering agents including PUFA have been associated with an increased incidence of cholelithiasis.¹⁰ An increase in biliary cholesterol may or may not be an inevitable concomitant of centripetal cholesterol flux. In any case, the morbid consequences of cholesterol gall-stone disease cannot be equated with AHD. Of perhaps greater concern is the possible effect on the risk of colonic carcinoma of any dietary regimen that increases faecal bile acid concentration.¹¹ If the latter is indeed a potentiating factor in lower intestinal carcinogenesis a concomitant increase in dietary fibre might be an appropriate recommendation.¹²

Unequivocal proof that the soundly based and widely accepted recommendations for dietary change will in fact reduce the overall incidence of AHD and its mortality is perhaps an impossible goal. The nature of the disease process is such that the inconsistent results of early trials of secondary prevention can hardly be unexpected.^{13,14} The three major primary prevention trials have, however, all shown a reduction in the signs of AHD not attributable to imperfections in design.^{15–17} A greater effect might be expected with a more rigorous dietary protocol. Sir John's reference to the inadequate outcome of the WHO clofibrate trial¹⁸ is hardly relevant since this drug has a weak therapeutic effect in simple hypercholesterolemia.

Two important "natural" experiments lend support to the dietary fat-AHD hypothesis. These include the reduction in the incidence of AHD that bears a definite temporal relation to the dietary changes and associated decrease in mean serum cholesterol concentration in the United States.¹⁹ Similarly, Joossens *et al*²⁰ have documented a gradual increase in the dietary PUFA:SFA ratio in the north of Belgium. This has been accompanied by a decreased serum cholesterol concentration and reduced mortality from AHD not observed in the south of the country, where similar dietary change has not occurred.

Preventing AHD is a major medical and economic concern. A multiple approach is undoubtedly indicated. Although refinements in our understanding of the relationship of diet to lipoprotein metabolism and atherogenesis can be expected, present information provides sufficient basis for immediate and positive dietary advice.

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¹⁸ Committee of Principal Investigators, *British Heart Journal*, 1978, **40**, 1069.

¹⁹ Walker, W J, *New England Journal of Medicine*, 1977, **297**, 163.

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Leucopenia in association with mianserin treatment

SIR,—We wish to report a case of leucopenia following treatment with mianserin hydrochloride. This has not been previously reported in the literature. It was noted in a 73-year-old woman, a chronic depressive, who had been treated with amitriptyline for two and a half years with no good response. She was previously physically healthy.

The patient was started on mianserin hydrochloride 30 mg daily, increasing to 60 mg daily after 10 days. Over the next two days she developed infected, ulcerative lesions on the left side of her face and neck. All drugs were stopped. Blood samples at that time showed a white blood count

of $2.9 \times 10^9/l$ and a haemoglobin concentration of $10.9g/dl$. Her blood film report was: "Leucopenia. Neutropenia with normocytosis. Platelets adequate. Red blood cells showing anisocytosis and normochromia." On repetition six days later her white blood cells had recovered to $5.3 \times 10^9/l$ and the haemoglobin concentration was $11.5 g/dl$; her film report was "Hypochromia of red cells but white cells and platelets normal." A third blood count seven days later showed her white blood cells to be $6.7 \times 10^9/l$ and her blood film was reported as normal.

At the time of this marked leucopenia her fasting blood sugar, urea, and electrolytes were normal; calcium was lowered at $2.08 mmol/l$ ($8.32 mg/100 ml$); her protein and albumin concentrations were marginally low at 63 and $33 g/l$ respectively. Liver function tests were normal and the serum thyroxine concentration was at the lower end of the range at $65 nmol/l$ ($5 \mu g/100 ml$).

Thereafter she was examined by a consultant physician, but was not considered to be clinically hypothyroid or to show evidence of any serious condition. The patient was commenced on ampicillin when all other drugs were stopped, and following the reported leucopenia this was continued for six weeks. She has now made a full clinical recovery from a discrete episode of leucopenia, apparently following administration of mianserin hydrochloride.

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Creatine kinase MB estimation in myocardial infarction

SIR,—The study by Dr S P Joseph and others (10 February, p 372) on technetium imidodiphosphonate scanning in myocardial infarction was of considerable interest. Additional diagnostic help is undoubtedly needed in the many patients in the coronary care unit who have equivocal electrocardiogram and enzyme results. The incidence of such borderline cases has been estimated to be as high as 20% of admissions to coronary care units.¹

The authors, however, give scant reference in their discussion to the value of creatine kinase MB (CKMB) in such situations. Estimating concentrations of CKMB is a technically much simpler diagnostic method than myocardial imaging and also permits the diagnosis to be made earlier. It is also probably more accurate. CKMB disappears from the serum 36-48 hours after onset of chest pain² (not 24 hours as Joseph *et al* state) and so a serum sample must be obtained within this period, but this should not present difficulties. A further advantage of CKMB estimation is that it can be measured retrospectively in selected cases presenting diagnostic problems so long as serum samples have been kept frozen. Such selected use of myocardial imaging would not be so easy four to five days, say, after admission.

Our group (at the Victoria Infirmary, Glasgow)³ measured CKMB in 38 patients with borderline myocardial infarction. The ECG was non-diagnostic, the total CK concentration was raised but no greater than $400 U/l$ ($n=100 U/l$), and the serum aspartate aminotransferase concentration was no greater than $63 U/l$ ($n=42 U/l$). CKMB estimation diagnosed myocardial infarction in 14 cases and excluded it in 24. Retrospective analysis, taking CKMB concentrations as the yardstick,

suggested that the original clinical diagnosis had been wrong in about 12 cases.

Certainly further diagnostic methods would be helpful in the coronary care unit, but in this capacity CKMB would seem to have advantages over myocardial imaging.

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ABC of Ophthalmology

SIR,—Myopia is the result of inadequate correlation between the converging power of the refractive media (mainly the cornea) and the axial length of the eye. In most myopes the axial length is within the range found in eyes of normal refraction and myopia has occurred because the cornea has failed to flatten sufficiently during growth. Viewed in this light, Mr T Stuart-Black Kelly's claim (20 January, p 198) that myopia is caused by "increased intravitreal pressure" becomes a little implausible. This same fact is the explanation of the alleged influence of hard contact lenses in preventing progress in myopia. Every contact lens practitioner is familiar with the temporary moulding effect of contact lenses on the cornea, but it is equally well known that the effect is transient.

The argument that close work causes myopia wilts before the unassailable proposition that myopia causes close work. A failure to make this distinction in causal relationships has characterised the controversy for well over a century.

When writing for a non-ophthalmological readership, Mr J Stuart-Black Kelly would do well to avoid unqualified statements such as those in the second paragraph of his letter, which, in lumping together those cases of myopia arising from simple dimensional anomaly (the enormous majority) and those having a pathological basis, are likely to cause a great deal of unjustified alarm and perhaps unjustified hardship to young people.

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SIR,—I am grateful to Mr K D Foggitt (17 February, p 489) for giving a correct description of the mechanism for accommodation. However it is described, the important mental picture to possess is that the elasticity of the lens is the major limiting factor and that it is the loss of this and not any "weakness" or "eyestrain" which causes reading difficulties in middle age.

As for colour values, I believe they are subtly altered when visual acuity is improved with glasses. The duochrome test is an example of this. This has, of course, nothing to do with inherited disorders of colour vision.

I applaud Mr Foggitt's comments on myopia. I agree absolutely with his reasoning and conclusions, but would add two further arguments against the proposition that near vision is implicated as a cause. Firstly, non-reading techniques were in use in special

schools for myopes before the second world war for many years. These were abandoned when it became clear that the myopic process was not affected. Secondly, monocular myopia is acquired and progresses very commonly in children, yet reading is normally a binocular activity. What is the nature of the local resistance in one eye which prevents myopia and of its absence in the other eye? Do we fit bifocal lenses to one eye and plain lenses to the other? Perhaps all children of myopic parents should be given bifocals on school entry.

Until large-scale statistically sound evidence is available—and this would be a very complicated exercise indeed, running perhaps for 20 years or more—nearly all is theory. Such hard facts as are available do not indicate any other way forward. It is my belief that children should be spared the role of guinea-pig even though myopia can have disastrous consequences, unless the strongest evidence supports an experiment and that their parents should not be burdened with the fear of irresponsibility if in most cases they ignore the undeniable attractions of the will-o'-the-wisp.

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College of Anaesthetists?

SIR,—The Association of Anaesthetists of Great Britain and Ireland is canvassing support for the Anaesthetists' Academic Foundation with a view to establishing a college of anaesthetists independent of the Royal College of Surgeons.

We are concerned that the council of the association assumes widespread support for an independent college of anaesthetists although no polling has taken place for a number of years. At least in this part of Essex the concept is anathema and we wonder how much active support there is nationally and whether the general body of the specialty is apathetic. The various documents issued by the association office play to a considerable extent on the emotional argument and at times remind one of the party political broadcast. We are particularly concerned about the reporter in *Hospital Doctor* (24 January, 1979) who quotes extensively from an interview with the president of the association, and we must register bewilderment at some of the sentiments stated.

In our view there is no advantage to be gained by change of the faculty status within the College of Surgeons. The faculty acts as an independent body in all important respects. It influences standards by its hospital visiting programme through the Hospital Recognition Committee. It organises educational events and it determines the regulation of the FFARCS examination and itself grants diplomas under the new charter. It has been suggested that examination fees and fellows' subscriptions are paid straight into college funds and that anaesthetists derive little benefit therefrom. Nothing could be further from the truth. The examination is set to a high standard and is expensive to run. The examination hall has considerable overheads and the ratio of candidate to examiner is high (36 candidates and 18 examiners currently each day so that each candidate is independently assessed by five pairs of examiners). Fellows of the Faculty of Anaesthetists enjoy the same privileges within the college as any surgical or dental fellow. The building is prestigious, is in a convenient site for the main railway termini, and houses artistic treasures. There is a fellows' common room and a cafeteria where lunch may be