Drug treatment of hypercholesterolaemia

Establish diagnosis before treatment

EDITOR,—Jane Patmore and colleagues' lesson of the week raises many issues on the diagnosis and current management of lipid disorders.¹ Firstly, several consensus guidelines recommend that a lipid diagnosis should be established before drug treatment is started and that the lipid profile should include measurement of the high density lipoprotein cholesterol concentration.^{2,3}

Secondly, the case reported was complicated by many confounding factors known to influence total and high density lipoprotein cholesterol concentrations, including the administration of β blockers, prednisolone, and high dose oral hormone replacement treatment and the coexistence of renal disease (the patient had received a transplant). These factors would confuse any diagnosis of a primary hyper- α -lipoproteinaemia. The authors measured the apolipoprotein A1 concentrations, but other apolipoproteins (apolipoprotein A2 (present in high density lipoprotein) and apolipoprotein (a)/B₁₀₀) are independent risk markers for ischaemic heart disease in patients with both normal and abnormal renal function.⁴ The role of measurements of apolipoprotein in clinical practice is unclear,^{4,5} and satisfactory reference ranges have not been established in patients with renal disease. Coadministration of immunosuppressive drugs—in this case azathioprine—may also affect liver function.⁵ Any increase in liver transaminases could potentially make monitoring of adverse biochemical effects of fibrates and statins difficult.

We consider that drug treatment should be withheld from all patients for whom a lipid profile has been obtained but high density lipoprotein cholesterol has not been measured. All necessary investigations should be undertaken to establish the cause of the underlying dyslipidaemia. Ignoring a request for measurement of the high density lipoprotein cholesterol concentration in patients with hypercholesterolaemia is a false economy as the long term costs of drug treatment far outweigh the cost of this measurement; it will also commit some patients to inappropriate drug treatment and potential side effects.

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- 1 Patmore J, Coyle S, Jones R, Wieringa G. Hypercholesterolaemia: not all cases warrant treatment. *BMJ* 1993;307:1125-6. (30 October.)
- 2 Betteridge DJ, Dodson PM, Durrington PN, Hughes EA, Laker MF, Nicholls DP, et al. Management of hyperlipidaemia: guidelines of the British Hyperlipidaemia Association. *Postgrad Med J* 1993;69:359-69.

Priority will be given to letters that are less than 400 words long and are typed with double spacing. All authors should sign the letter. Please enclose a stamped addressed envelope for acknowledgment.

- 3 European Atherosclerosis Society. The recognition and management of hyperlipidaemia in adults: a policy statement of the European Atherosclerosis Society. *Eur Heart J* 1988;9:571-600.
- 4 Grundy SM, Vega GL. Role of apolipoprotein levels in clinical practice. *Arch Intern Med* 1990;150:1579-81.
- 5 Webb AT, Reaveley DA, O'Donnell M, O'Connor B, Seed M, Brown EA. Does cyclosporin increase lipoprotein(a) concentrations in renal transplant recipients? *Lancet* 1993;341:268-70.

Determine cardiac risk

EDITOR,—Jane Patmore and colleagues highlight the fact that not all cases of hypercholesterolaemia warrant treatment.¹ There are several further lessons to be learnt. Both the European Atherosclerosis Society and the British Hyperlipidaemia Association have recently published updated guidelines on preventing coronary heart disease and managing hyperlipidaemia.^{2,3} These differ from previous recommendations in emphasising that treatment of hyperlipidaemia should not be based primarily on a specific cholesterol concentration but that the degree of cardiac risk should determine the concentration at which treatment is started and the appropriate goal to aim for.

In patients with proved coronary heart disease drug treatment should be considered in cases resistant to diet in which the total cholesterol concentration remains above 5.2 mmol/l or the low density lipoprotein cholesterol concentration remains above 3.4 mmol/l. If lipid lowering drugs are being considered at least one and preferably two fasting samples should be taken for the measurement of total cholesterol, triglyceride, and high density lipoprotein cholesterol concentrations. This rule should apply whatever the total cholesterol concentration. Knowledge of the full lipid profile not only safeguards patients from inappropriate drug treatment but ensures that the optimal class of hypolipidaemic agents will be selected.

We wish to sound a note of caution for laboratories that use a computer to request measurement of high density lipoprotein cholesterol and triglyceride concentrations automatically only for samples with moderate hypercholesterolaemia. Patmore and colleagues realised that their patient had hyper- α -lipoproteinaemia only after she had been treated unnecessarily with two lipid lowering drugs. Taking 6.5 mmol/l as the lower limit for measurement of high density lipoprotein cholesterol will miss many patients with proved coronary disease. In a recent audit of over 400 patients admitted to our coronary care unit the mean total cholesterol concentration (measured within 24 hours of an event) was 5.8 mmol/l. Although analysis of high density lipoprotein cholesterol and triglyceride concentrations is more time consuming and expensive than measurement of the total cholesterol concentration alone, the "costs" of inappropriate or suboptimal treatment are much greater. If selective lipid analysis is undertaken this should be based on the clinical details of the patient rather than arbitrary cholesterol concentrations. Fasting lipid profiles should be obtained for all patients in whom lipid lowering drugs are being considered.

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- 1 Patmore J, Coyle S, Jones R, Wieringa G. Hypercholesterolaemia: not all cases warrant treatment. *BMJ* 1993;307:1125-6. (30 October.)
- 2 European Atherosclerosis Society. Prevention of coronary heart disease: scientific background and new clinical guidelines. *Nutrition, Metabolism and Cardiovascular Diseases* 1992;2:113-56.
- 3 Betteridge DJ, Dodson PM, Durrington PN, Hughes EA, Laker MF, Nicholls DP, et al. Management of hyperlipidaemia: guidelines of the British Hyperlipidaemia Association. *Postgrad Med J* 1993;69:359-69.

Review criteria for cholesterol tests

EDITOR,—Contrary to Jane Patmore and colleagues' assertion, their lesson of the week shows the danger of not viewing each patient with hypercholesterolaemia as at high risk of coronary heart disease.¹ Had the authors pursued a policy of measuring the high density lipoprotein cholesterol concentration in all patients at high risk (that is, with a total cholesterol concentration >7.8 mmol/l), the woman who was the subject of the case report would have avoided unnecessary treatment.

In my laboratory we measure high density lipoprotein cholesterol in all patients with a total cholesterol concentration >6.5 mmol/l rather than excluding all those who are in the highest risk group (total cholesterol >7.8 mmol/l) as Patmore and colleagues did. Over 3% of samples in our laboratory, and a similar proportion of patients referred to our lipid clinic, have a total cholesterol concentration >7.8 mmol/l with a high density lipoprotein cholesterol concentration >2.0 mmol/l. Most of these patients would be classified as not in a high risk group. The European Atherosclerosis Society has recommended that drug treatment should be based on low density lipoprotein cholesterol concentrations.² Patmore and colleagues provide the users of their service with calculated low density lipoprotein cholesterol concentrations, but not those most likely to require treatment (with a total cholesterol concentration >7.8 mmol/l). Why?

Finally the authors conclude that by standardising their criteria for assaying high density lipoprotein cholesterol they identified the patient with hyper- α -lipoproteinaemia. I disagree: they missed the patient in the first place because of their criteria and should now alter those criteria to minimise the chance of missing more cases.

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- 1 Patmore J, Coyle S, Jones R, Wieringa G. Hypercholesterolaemia: not all cases warrant treatment. *BMJ* 1993;307:1125-6. (30 October.)
- 2 European Atherosclerosis Society. Prevention of coronary heart disease—scientific background and new clinical guidelines. *Nutrition, Metabolism and Cardiovascular Diseases* 1992;2:113-56.

Authors' reply

EDITOR,—The main message that we wished to convey in our lesson of the week is that a raised high density lipoprotein cholesterol concentration may be the sole cause of a raised total cholesterol concentration and in such cases potentially dangerous and expensive drug treatment is not required. The British Hyperlipidaemia Association's survey found that only three quarters of the