Some reports have suggested that triglyceride concentration may be a more important risk factor in women than men, but this seems to be true only in univariate analyses. Most studies that adjust for high density lipoprotein cholesterol and other lipids do not support an independent association between serum triglyceride concentrations and coronary heart disease in women.^{6,11}

What, then, can one fairly conclude? Has measurement of triglyceride concentrations a role in preventing cardiovascular disease? Despite the numerous studies, the use of triglyceride concentration in screening or in guiding lipid lowering treatment must still be seen as experimental. Precise measurements will be needed if triglyceride concentration is to be used to help identify people at high risk of coronary heart disease, but any such use seems limited—because of the greater convenience and predictive accuracy of measurements of high density lipoprotein cholesterol. Possibly measurements of triglyceride will identify people who would benefit from aggressive cholesterol lowering treatment or point to the best class of drugs for treating patients with hypercholesterolaemia. Both of these uses for measurement of triglycerides are speculative, however, and in both cases the test needs to be done only in someone found to have a raised cholesterol concentration.

As far as screening is concerned, measuring triglycerides is less convenient than measuring high density lipoprotein cholesterol or total cholesterol, and current evidence suggests that its value in risk classification would at best be limited. Even if the test gave additional information about risk it would not necessarily lead to better treatment decisions. Despite the many clinical trials of reducing raised concentrations of cholesterol, the application of total and low density lipoprotein cholesterol to treatment decisions remains controversial.¹⁴ There is far less evidence supporting the use of triglyceride concentrations.

Concern about resources for health care has raised the standards of evidence required for any general screening

strategy. The useful screening test—as is well known—has to be safe, convenient, inexpensive, and to discriminate between those who do and do not benefit from further diagnostic evaluation or treatment. Further evidence may someday enable triglyceride concentration to meet these standards, but not yet.

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Reducing the use of benzodiazepines in general practice

Explain the likely duration of treatment (short) before prescribing the first dose

See paper on p 27

Benzodiazepines are the most commonly used psychotropic drugs.^{1,2} When introduced they were embraced with enthusiasm by the medical profession and public alike, although since then a backlash has developed against them, which has culminated in legal actions against their manufacturers. The use of benzodiazepines has fallen steadily since the 1970s.³ Adverse effects have been highlighted, including the chance of a discontinuation syndrome after patients stop taking the drugs.⁴

Doctors have been exhorted not to prescribe these drugs and to try to stop their long term use.⁵ The exhortations have worked: a community survey in this week's journal does not confirm earlier popular notions of long term use of benzodiazepines (p 27).⁶ Benzodiazepines are now often regarded as suitable only for short term use, if they have a use at all. (This ignores their appropriate longer term use by some patients.⁷) The development of newer anxiolytics and hypnotics and roles for some newer antidepressants as anxiolytics may further alter patterns of use of benzodiazepines.

Educating the public about the risks and benefits of these drugs is the key to reducing their use. Educational programmes can be supplemented by written material and

counselling during medical consultations. An educational programme directed at prescribers, people providing care, and patients (who also received training in relaxation) halved long term use of benzodiazepines among elderly residents in care.⁸ A study of 200 long term users found that more than half were using benzodiazepines as hypnotics and had done so for a median of 15 years. Use fell by almost a third after a simple mailing encouraged patients slowly to reduce then stop their drugs.³ Some of the patients may have been receiving the wrong treatment—insomnia may be a symptom of depression, which is better treated with antidepressants than benzodiazepines.

The appropriate use of benzodiazepines depends on a careful diagnosis and clear instructions regarding the drugs' use.⁹ For many patients general health advice; supportive counselling; and information on sleep, relaxation, and behavioural strategies, including cognitive behavioural therapy may suffice. These techniques can be learnt, and every practitioner should be able to provide them. They do not necessarily require long consultations and may be used over several brief consultations. Active participation in treatment reinforces the patients' responsibility for their health. Patients

should be told which benzodiazepines to use and why, whether to take them short term or intermittently, and what effects (including adverse effects) to expect. The likely duration of use should be explained before the first dose is taken. If, on starting treatment, patients expect that it will be of short duration they find it easier to reduce the dose later and then to stop the treatment.¹⁰

Patients using benzodiazepines long term should be reviewed to see whether they continue to need them. When no justification exists patients should be introduced to the idea of stopping the drug. Do not threaten patients with abrupt cessation of a drug that they associate with keeping them well: explain that the original need for treatment may no longer apply; recommend slow reduction; and explain the possibility of a short term, self limiting, discontinuation syndrome. This avoids such symptoms being prematurely misinterpreted as indicating a return of prior insomnia or anxiety.

General practitioners should be aware of the negative effects of not prescribing benzodiazepines. Sedative tricyclic antidepressants, antihistamines, and neuroleptics are more toxic. Untreated, or inadequately treated, patients remain chronically disabled. Furthermore, they may try to relieve persisting distress with alcohol or other agents that have worse short and long term adverse effects.

Some people seek benzodiazepines for non-medical purposes—last week's letters pages provide several examples (p 1709).¹¹ Such behaviour should be recognised and strategies adopted for the safe use of prescribed drugs. Doctors should not prescribe benzodiazepines for patients they don't know unless genuine clinical indications exist—in which case only

small amounts should be prescribed. Alternatives to drugs should be offered.¹²

Doctors should avoid stigmatising people with mental illness by implying that everybody should be able to overcome mental distress without the need for drugs. The principles for reducing use of benzodiazepines in general practice apply to drugs for any condition; this is not exclusively an issue for people with psychiatric problems.

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Bone marrow transplants from peripheral blood

Set to transform medical oncology

Treating malignant disease with very high dose chemotherapy, often with total body irradiation, has become established during the past decade, particularly for lymphomas and leukaemias. Reinfusion of some of the patient's bone marrow (collected before high dose chemotherapy) has improved the outcome of these very intensive regimens. These autologous bone marrow transplants (autografts) entail about four weeks' pancytopenia,¹ and despite improvements in supportive care this procedure is associated with substantial morbidity and a 5-10% mortality, mainly due to myelosuppression.

Normal bone marrow contains enough undifferentiated stem cells to allow long term reconstitution (engraftment), but it seems to lack those more committed progenitors that would lead to engraftment within two or three weeks. In the past few years it has become possible to collect such committed progenitor and stem cells not from within the bone marrow cavity but from peripheral blood. The use of peripheral blood stem cells as autografts has changed much of haematological practice and will transform medical oncology within the next few years.

Until 1984, the stem cell content of either bone marrow or peripheral blood could be estimated only indirectly by in vitro colony forming assays. Since then a monoclonal antibody, now called CD34, which reacts with a haemopoietic progenitor cell surface antigen, has become available.² Cells positive for CD34 constitute only 0.1% of mononuclear cells in blood—one tenth the proportion found in bone marrow.³

Because of these low proportions, collecting sufficient cells for an autograft proved too difficult for routine use.^{4,5}

Nearly 20 years ago populations of stem and progenitor cells were found to increase in peripheral blood during the recovery phase from intensive chemotherapy,⁶ and the first attempts to explain this phenomenon (by collecting such "mobilised" blood progenitor cells) were made in 1984.⁷ More recently, the administration of haemopoietic growth factors, such as granulocyte colony stimulating factor and granulocyte macrophage colony stimulating factor, after chemotherapy was found to increase the number of circulating CD34 positive cells up to 100-fold to a number far exceeding the yield from bone marrow harvesting.⁸ Enough progenitor cells to ensure rapid and stable engraftment can be collected from one to three sessions of aphereses on consecutive days.⁹ Such autografts of peripheral blood stem cells have been used for many hundreds of transplants with the unexpected and dramatic benefit of a reduction in the duration of neutropenia and, especially, thrombocytopenia to less than two weeks, leading to shorter hospital stays and lower procedural costs.^{4,10} This accelerated recovery is thought to be due to reinfusion of larger numbers of progenitors more mature than their marrow counterparts; these therefore develop into functional blood cells more quickly.

Initial concern that collection of peripheral blood stem cells might not be sufficient for long term reconstitution of the function of bone marrow has not been confirmed.¹⁰ The more