the optimal dose is unknown. Aspirin alone is effective in doses ranging from 100 mg¹³ to 975 mg¹⁴ daily; as more than 325 mg daily confers no additional benefit¹⁵ a dose of 150-300 mg is probably reasonable. There is general agreement that dipyridamole is superfluous.¹²

Although aspirin reduces the risk of thrombotic occlusion of grafts, not much can be done to prevent fibrointimal hyperplasia. As late atherosclerosis is related to recognised risk factors such as smoking¹⁶ and hyperlipidaemia¹⁷ these should be corrected. Vigorous attempts to reduce serum lipid concentrations will retard the progression of both graft disease and native coronary diseases.¹⁸

When angina recurs there is an understandable reluctance to make the diagnosis. Chest wall pain is usual, indeed universal, in those in whom the left internal mammary artery has been used. The angina sometimes has a different character, being felt less in the precordium. But gradually realisation dawns, and the diagnosis may be confirmed by exercise testing. Drug treatment should be restarted. There is little point in undertaking repeat angiography until the angina is truly limiting. Only occasionally is there a stenosis that invites

angioplasty, and then the results are not encouraging.¹⁹ A second operation is certainly possible: other veins (the other saphenous vein and arm veins) and arteries (such as the gastroepiploic) may be used. The results are less satisfactory with a higher mortality (for example 6.9% compared with 2% in one series²⁰) and greater morbidity. But despite the higher threshold for recommending repeat operations, these now comprise a sizable component of the work of most cardiac surgical units.

Coronary artery bypass surgery should be reserved for those who need it: those with limiting angina and severe coronary disease. Current surgical practice may produce better results than that of 10 years ago,²¹ but even so patients should be warned that their angina will recur some time in the future. Often, however, this is a better prospect than the alternative.

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Showing the green card

New surveillance scheme to monitor the effects of pesticides on health

Many patients believe that their health has been damaged by pesticides or other toxic chemicals. How can their doctors decide whether they are right?

When the BMA's Board of Science and Education prepared its report *Pesticides, Chemicals and Health*, it found that little was known about the effects on the general population of exposure to pesticides.¹ Others have also drawn attention to the need for more information. The World Health Organisation has recommended that "every effort should be made to perform epidemiological studies and to improve understanding of the effects of pesticides on the public health."² The House of Commons agriculture committee and the medical and toxicology panel of the advisory committee on pesticides want better coordination of existing systems for monitoring poisonings due to pesticides and full investigation of serious poisonings and major incidents.^{3,4} The British Agrochemicals Association and the Green Alliance have jointly called for the establishment of a scheme to monitor incidents involving

pesticides to replace the four existing schemes for reporting such incidents.⁵

To obtain data on exposure to pesticides and suspected adverse effects on health the BMA working party on pesticides recommended setting up a "green card" reporting system. This was intended as an early warning system, analogous to the yellow card system for reporting adverse drug reactions, which would enable better monitoring of exposure to pesticides. The working party believed that doctors, particularly general practitioners, were ideally placed to alert other agencies to cases of suspected pesticide poisoning.

The Health and Safety Executive, with the encouragement of the Department of Health and the BMA, has funded the West Midlands Poisons Unit to conduct a pilot scheme in the West Midlands and Trent regions. This three year scheme will investigate the frequency and severity of acute pesticide poisoning in these regions; it will run parallel to rather than

replace existing systems for collecting data. Part of its remit is to assess these data critically and to collate them in a useful form. The pilot scheme should identify deficiencies in the existing mechanisms and improve reporting rates of suspected adverse reactions to exposure to pesticides; current levels of underreporting were noted with concern by the chief medical officer in a circular earlier this year.⁶ The benefits of the green card scheme will be strengthened by clinical and toxicological support provided by the poisons unit. Detailed clinical audit of reported cases is planned for the second and third years of the pilot scheme, which should help distinguish confirmed cases of pesticide poisoning from reported incidents that are not confirmed by clinical follow up.

The green card, which requests information on the suspected pesticide and the reactions and details of the patient, has been designed to be as user friendly as possible. Since the scheme was launched in June cards have been sent to 5000 general practitioners and 50 accident and emergency departments in the West Midlands and Trent regions. Doctors returning green cards will be contacted by staff at the poisons unit, who will provide guidance about symptoms and their possible connection with exposure to a pesticide. In addition to providing immediate specialist advice by telephone (the "pesticide hotline") on diagnosing and managing pesticide poisoning, the new scheme offers general practitioners background information on specific chemicals and reactions when appropriate.

Some questions raised by *Pesticides, Chemicals and*

Health—for example, how dangerous is long term exposure to low doses of pesticides?—will remain unanswered by the new scheme. But the increase in information on the effects of pesticides on health should be substantial. No room for complacency exists while our knowledge is so incomplete: as Geoffrey Rose said in a recent lecture on environmental health to the Royal College of Physicians' regional conference (Bristol, 1990), "Important effects on health could easily be missed, and 'have not noticed' must never be mistaken for 'is not there.'"

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Lipoprotein(a)

Thrombotic and atherogenic

In 1963 Berg described a lipoprotein antigen, which he called lipoprotein(a) (Lp(a)).¹ Numerous studies since then have found that plasma Lp(a) concentrations above 0.3 g/l (of total Lp(a) mass), which are present in one in five people, are associated with an increased risk of coronary heart disease^{2,3} and stroke.⁴ Important milestones in Lp(a) research were the elucidation of the primary structure of apo(a) and of apo B100, the two protein components of Lp(a).^{5,6} A flurry of recent research has contributed greatly to understanding the biosynthesis and degradation of Lp(a) and its role in thrombogenesis and atherogenesis. Two studies in this week's issue add to this knowledge (pp 675, 694).^{7,8}

Lp(a) contains one (or two) molecules of apo(a) linked to apo B100 by a disulphide bridge.^{2,3,6} Apo(a) is related to plasminogen, from which the enzyme plasmin that hydrolyses fibrin blood clots is released by tissue plasminogen activator. The apo(a) molecule is composed of an N-terminal variable repeat of plasminogen kringle (a disulphide bonded domain shaped like a Danish cake) IV, a single kringle V, and the plasminogen protease domain.

Plasma Lp(a) concentration varies from almost undetectable to over 1.0 g/l, but differs little with sex, body mass index, or age in adults.^{2,3,9,10} Concentrations are, however, reported to increase during infancy.⁹ Black people have substantially higher levels than white people, surprisingly without increased coronary heart disease.^{2,9} The size of apo(a) varies between about 280 and 830 kD.^{2,3} The 20 or more size isoforms are inherited in Mendelian codominant fashion and result from variation in the number of kringle IV repeats in the gene.¹¹ The Lp(a) plasma concentration is inversely correlated with allele size²; the size polymorphism accounts

for more than 40% of the variability in Lp(a) concentrations.¹² Other sequence differences in the apo(a) gene, which presumably change mRNA or protein processing, may also substantially alter Lp(a) plasma concentrations.¹¹

Lp(a) is produced in the liver,²³ where it is presumably linked to apo B100 in the endoplasmic reticulum. In the endoplasmic reticulum and later in the Golgi apparatus apo B100 is loaded with triglyceride for secretion as very low density lipoprotein. Although the density of most Lp(a) falls between the densities of low and high density lipoproteins, Lp(a) can circulate with triglyceride rich lipoproteins and is presumably secreted as such.^{9,13}

Plasma Lp(a) concentrations are influenced by metabolic and endocrine factors and by drugs that affect hepatic production of very low density lipoprotein in the same direction. Hepatic disease and excessive alcohol consumption decrease Lp(a) concentrations.¹⁴ Lp(a) is increased in diabetics with proteinuria⁸ and in albuminuric renal disease.¹⁵⁻¹⁸ It is decreased by treatment with nicotinic acid, which blocks the supply of non-esterified fatty acids to the liver.¹⁹ Fish oil also appears to lower Lp(a) plasma concentrations, and fish oil decreases secretion of very low density lipoprotein.^{4,20} The production of very low density lipoprotein is regulated entirely by post-translational mechanisms, partly by sorting apo B100 between intracellular degradation and secretion.²⁰ Most probably the production of Lp(a) is similarly controlled once apo(a) and apo B become linked in the endoplasmic reticulum.

The pathways of Lp(a) clearance from the circulation are uncertain. Studies, particularly with transgenic mice that overexpress the low density lipoprotein receptor, suggest that