aprotinin is excreted renally lower doses are recommended in renal failure. No studies have yet been published examining the potentially increased risks of postoperative thromboembolic disease and loss of graft patency that may occur with any agent modifying perioperative haemostasis. Until full risk benefit analyses have been performed aprotinin should be used with caution. If, however, these studies indicate little risk, then current studies of aprotinin's use in paediatric and "low risk" cardiac surgery, liver transplantation, and vascular surgery suggest that aprotinin may have wide applications in reducing perioperative bleeding. Its efficacy suggests that the importance of fibrinolytic activation in the pathogenesis of perioperative bleeding has previously been underestimated.

BEVERLEY J HUNT

Senior Research Fellow, Research Haematology Group, Harefield Hospital, Harefield, Middlesex UB9 6JH

MAGDI YACOUB

British Heart Foundation Professor of Cardiac Surgery, National Heart and Lung Institute and Royal Brompton Hospital, London SW6 8HP

1 Russell GN, Peterson S, Harper SJ, Fox MA. Homologous blood use and conservation techniques

for cardiac surgery in the United Kingdom. BMJ 1988;297:1990-1.

2 Royston D, Bidstrup BP, Taylor KM, Sapsford RN. Effect of aprotinin on need for blood

transfusion after repeat open-heart surgery. Lancet 1987 (ii: 1289-91).

Kraut E. Frey EK. Werle E. Uber die Inaktivierung des kallikrein. Hoppe-Scyler's Physiological Chemistry 1930:192:991-1007.

4 Tanaka K, Takao M, Yada I, Yuasa H, Kusagawa M, Deguchi K, Alterations in coagulation and fibrinolysis associated with cardiopulmonary bypass during open heart surgery. *Journal of Cardiothoracic Anaesthesia* 1989;3:181-8.

5 Dubber HC, McNicol GP, Uttley D, Douglas AS. In vitro and in vivo studies with Trasylol, an

anticoagulant and a fibrinolytic inhibitor. Br J Hacmatol 1968;14:31-49.

6 Hunt BJ, Cottam S, Segal H, Ginsburg R, Potter D. Inhibition by aprotinin of t-PA mediated

fibriolysis during orthotopic liver transplantation. Lancet 1990;336:381

7 Fritz H. Wunderer G. Biochemistry and applications of aprotinin, the kallikrein inhibitor. Drug Res 1983;33:479-94.

8 Espana F, Estelles A, Griffin JH, Aznar J, Gilabert J. Aprotinin is a competitive inhibitor of activated protein C. Thromb Res 1989;56:751-6.

activated protein C. Thromb Res 1987;36:771-6.

Tanaka K, Wada K, Morimoto T. The role of the protein C-thrombomodulin system in physiological anticoagulation during cardiopulmonary bypass. ASAIO Trans 1989;35:373-5.

Harker LA, Bleeding after cardiopulmonary bypass [Editorial]. N Engl J Med 1986;314:1446-7.

Bidstrup BP, Royston D, Sapsford RN, Taylor KM. Reduction in blood loss and blood use after

cardiopulmonary bypass with high dose aprotinin. J. Thorac Cardiovasc Surg 1989;97:364-72. 12 van Oeveren W. Jansen NJG, Bidstrup BP, Royston D, Westaby S, Neuhof H, et al. Effect of aprotinin on haemostatic mechanisms during cardiopulmonary bypass. Ann Thorac Surg

13 McGowan EB, Yeo K-T, Detwiler TC. The action of calcium-dependent protease platelet surface glycoprotein. J Biochem Biophys 1983;22:287-301.

14 Murphy WG, Moore JC, Warkentin T, Kelton JG. Aprotinin inhibits calpain-induced proteolysis

of GPIb on the platelet surface. Schwerz Med Woschenschr (in press). de Smet AAEA, Joen MCN, van Oevern W. Roozendaal KJ, Harder MP, Eijsman L, et al.

Increased anticoagulation during cardiopulmonary bypass by aprotinin, $\mathcal J$ Thorac Cardiovasc Surg 1990;100:520-7.

16 Hunt BI, Segal H, Yacoub M. Guidelines for monitoring heparin by the activated clotting time when aprotinin is used during cardiopulmonary bypass. J Thorac Cardiovasc Sing (in press).

17 Carrel T, Bauer E, Laske A, von Segesser L, Turina M. Low dose aprotinin for reduction of blood

loss after cardiopulmonary bypass. Lancet 1991;337:673.

Coronary bypasses 10 years on

About two in five will occlude

The return of angina comes as a bitter disappointment to patients who have had coronary artery bypass surgery. Ten years ago they believed that they were cured. Their doctors may have had reservations, but they did not know how long the grafts would last. Now we know better, thanks to some prospective studies.

Fitzgibbon and his colleagues from the National Defence Medical Centre in Ottawa have a "compliant" population of military staff, 222 of whom have undergone repeated elective coronary angiography. Rates of occlusion of vein grafts at 1 month and 1, 5, 7.5, and 10 years were 8%, 13%, 20%, 40%, and 41% respectively. The jump at 7.5 years is due to the unplanned inclusion of a group of patients studied again for clinical rather than routine reasons - that is, their angina had returned. Similar results have been obtained in Montreal by Bourassa and colleagues, who reported rates of 3.4% at 2-3 weeks, 10% at 6-18 months, 19% at 5-7 years, and 37% at 10-12 years.2 Graft occlusion occurred 2.5 times more commonly after six years than before. Similarly, Lytle et al from the Cleveland Clinic found that 36% of grafts were occluded 7.3 years after surgery.3 These authors also report the development of graft stenoses: early studies suggest an incidence of 5-10%, often at the distal anastomosis, but some narrowings are seen in 38% of grafts at five years and 75% at 10 years.1 Few vein grafts escape disease, but the pathological findings vary with the age of the graft. Early occlusion is usually due to thrombus, probably resulting from technical problems with the vein, particularly at the distal anastomosis. Fibrointimal hyperplasia occurs next, and conventional atheroma is superimposed some years later.

The main manifestations of these developments are recurrent angina, myocardial infarction, and death. It should be emphasised that surgery improves the 10 year survival of patients at high risk - that is, those with extensive coronary disease and poor left ventricular function. Mortality in the

surgical groups tends, however, to accelerate after 5-7 years, so that if patients with less severe disease are included no overall benefit is demonstrable. If perioperative myocardial infarction is excluded the rate of subsequent heart attack is lower in the surgical group until five years. Thereafter the incidence rises to 2.4% a year, compared with 1.4% in a comparable group treated medically.8 The infarcts, however, are smaller9 and less commonly fatal8—no doubt because the grafts and long standing coronary disease have encouraged the development of a mature collateral circulation. Subsequent reinfarction, however, is more likely. Patients presenting with recurrent angina commonly do so with an episode of rest pain some seven years after their operation, a familiar experience that might be termed the seven year glitch.

So what should we do about all this? Firstly, we should remember that surgery for degenerative disease never cures. Bypass surgery should be postponed in those with mild to moderate coronary disease and good left ventricular function. If the coronary arteriogram does not show significant left main stem or three vessel disease medical management can safely be encouraged: extra effort spent on exercise and diet, together with prophylactic nitrates and maintenance β blockade, can be surprisingly successful. We should think twice about surgery for certain patients. Women fare less well, probably because of their smaller stature and vessels10; younger men, although an apparently deserving group, will have clinically important atherosclerosis of the graft five years later. 11 Buying time with angioplasty may therefore be preferable. As for the operation itself, using the left internal mammary artery for the anterior descending graft is clearly desirable because its long term patency is superior (92.5% at 10 years).3 Aspirin also reduces the rate of graft occlusion, halving it at one year in a recent study.12 Ideally aspirin should be started within hours of surgery, although not before because of the increased risk of bleeding. Despite the many studies of the benefits of aspirin

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.19

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

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.

M C PETCH

Consultant Cardiologist, Regional Cardiac Unit, Papworth Hospital, Cambridge CB3 8RE

- Fitzgibbon GM, Leach AD, Kafka HP, Keon WJ. Coronary bypass graft fate: long-term angiographic study. J. Am Coll Cardiol 1991;5:1075-80.
 Campeau L, Enjalbert M, Lesperance J, Vaislic C, Grondin CM, Bourassa MG. Atherosclerosis
- and late closure of aortocoronary saphenous vein grafts; sequential angiographic studies at 2 weeks, 1 year, 5 to 7 years, and 10 to 12 years after surgery. Circulation 1983;68(suppl II):1-7.

 3 Lytle BW, Loop FD, Cosgrove DM, Ratliff NB, Easley K, Taylor PC, Long term (5 to 12 years)
- serial studies of internal mammary artery and saphenous vein coronary bypass grafts. J Thorac Cardiovasc Surg 1985;89:248-58.
- Bourassa MG, Fisher LD, Campeau L, Gillespie MJ, McConney M, Lesperance J. Long-term fate
 of bypass grafts: the Coronary Artery Surgery Study (CASS) and Montreal Heart Institute
 experience. Circulation 1985;72 suppl V::71-8.
 Veterans Administration Coronary Artery Bypass Surgery Cooperative Study Group. Eleven-year
- survival in the Veterans Administration randomized trial of coronary bypass surgery for stable angina. $N\ Engl\ \mathcal{J}\ Med\ 1984;311:1333-9.$
- 6 Varnauskas E, and the European Coronary Surgery Study Group. Twelve-year follow-up of survival in the randomized European coronary surgery study. N Engl J Med 1988;319:332-7.
 7 Alderman EL, Bourassa MG, Cohen LS, Davis KB, Kaiser GG, Killip T, et al. Ten-year follow-up
- of survival and myocardial infarction in the randomized Coronary Artery Surgery Study (CASS). Circulation 1990;82:1629-46.
- Peduzzi P, Detre K, Murphy ML. Thomsen J, Hultgren H, Takaro T, and the Veterans Administration Coronary Artery Bypass Surgery Cooperative Study Group. Ten-year incidence of myocardial infarction and prognosis after infarction. Circulation 1991;83:747-55.
 Wiseman A, Waters DD, Walling A, Pelletier GB, Roy D, Theroux R. Long term prognosis after
- myocardial infarction in patients with previous coronary bypass surgery. J Am Coll Cardiol 1988;12:873-80
- 10 Loop FD, Goldehg LR, Macmillan IP, Gosgrove DM, Lytle BW, Sheldon WC, Coronary artery rgery in women compared with men: analysis of risks and long-term results. J Am Coll Cardio

- 11 Fitzgibbon GM, Hamilton MG, Leach AJ, Kafka HP, Markle HV, Keon WJ. Coronary artery disease and coronary bypass grafting in young men: experience with 138 subjects 39 years of age and younger. J. Am Coll Cardiol 1987;9:977-88.
- 12 Gavaghan TP, Gebski V, Baron DW. Immediate postoperative aspirin improves vein graft patency
- early and late after coronary artery bypass graft surgery. Circulation 1991;83:1526-33.

 13 Lorenz RL, Schacky CV, Weber M, Meister W, Kotzur J, Reichardt B. et al. Improved aortocoronary bypass surgery patency by low-dose aspirin (100 mg daily). Lancet 1984;i:1261-4.

 14 Brown BG, Cukingham RA, De Rouen T, Goede LV, Wong M, Fee HJ, et al. Improved graft patency in patients treated with platelet-inhibiting therapy after coronary bypass surgery. Circulation 1985:72:138-46.
- 15 Goldman S, Copeland J, Moritz T, Henderson W, Zadina K, Ovitt T, et al. Saphenous vein graft patency I year after coronary artery bypass surgery and effects of antiplatelet therapy. Circulation
- 16 FitzGibbon GM, Leach AJ, Kafka HP. Atherosclerosis of coronary artery bypass grafts and smoking. Can Med Assoc J 1987;136:45-7.
 17 Campeau L, Enjalbert M, Lesperance J, Bourassa MG, Kwiterovich P, Wacholder S, et al. The
- relation of risk factors to the development of atherosclerosis in saphenous-vein bypass grafts and the progression of disease in the native circulation. $N\ Engl\ \mathcal{J}\ Med\ 1984;$ 311:1329-32.
- 18 Blankenhorn DH. Nession SA. Johnson RL, Sanmarco ME, Azer SP, Cashin-Hemphile L. Beneficial effects of combined colestipol-niacin therapy in coronary atherosclerosis and coronary venous bypass grafts. JAMA 1987;257:3233-40.
- 19 Webb JG, Myler RK, Shaw RE, Anwar A, Mayo JR, Murphy MC, et al. Coronary angioplasty after coronary bypass graft surgery: initial results and late outcome in 422 patients. J Am Coll Cardiol 1990:16:812-20.
- 20 Salomon NW, Page US, Bigelow JC, Krause AK, Okies JE, Metzdorff MT. Reoperative coronary surgery. 7 Thorac Cardiovasc Surg 1990;100:250-60.
- 21 Cameron EWJ, Walker WS. Coronary artery bypass surgery. BMJ 1990;300:1219-20.

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. 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." 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.34 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.

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

> BMJ volume 303 21 SEPTEMBER 1991