Correspondence

Histological changes in venous grafts

We read with interest the recent paper which provided some data regarding the histological changes in "failed" aortocoronary saphenous vein grafts,¹ but feel that some points merit further consideration.

No data were provided in the article as to the exact length of time these grafts had been in situ. This information would have been of interest, because the features of atherosclerosis in coronary vein grafts are unusual before a period of five years. It has also been suggested that the atherosclerotic process in vein grafts may be intrinsically different from that seen in the native coronary system.² Native coronary atherosclerosis is usually focal, with eccentric plaques which have a fibrous cap overlying a core of lipid debris. Saphenous vein graft atherosclerosis, on the other hand, is typically diffuse and concentric, it does not usually have a fibrous cap, and may have a heavy inflammatory infiltrate with lipid containing giant cells.³ These differences may influence the management of these patients as the friable lesions in vein grafts are prone to embolisation, and recent reports suggest that the presence of a late stenosis in a vein graft to the left anterior descending coronary artery is an indication for reoperation, even in the absence of severe symptoms.² It would have been interesting to see if these histological features had been particularly conspicuous, and at what time they became so.

The authors "did not see any of the acute changes due to the endothelial damage caused by the preparation of these grafts." Endothelial damage is indeed a well recognised feature of vein preparation, but the process of re-endothelialisation after implantation into the arterial system is generally very efficient.⁴ Obviously the rate depends on the extent of damage incurred, but even a 5 cm length of damage will re-endothelialise by six weeks.⁵ Admittedly, in the presence of severe damage, a fully confluent endothelial layer may not be achieved in all areas, but it would have been surprising if the authors had been able to detail this in this particular series of grafts. They also suggest that perfusion of the vein before surgery, using low pressure and anticoagulated blood, will result in less intimal thickening and longer graft survival. There is indeed experimental evidence which suggests that techniques of vein preparation may influence long term patency, but this is by no means established. More recent evidence than that cited by the authors has shown that intimal hyperplasia occurs to the same extent in veins which have been implanted undistended with a complete endothelial layer, compared with veins implanted after distension to 600 mm Hg.⁶ This suggests, as is commonly accepted, that the process of intimal hyperplasia in vein grafts is complicated and multifactorial in aetiology. More importantly, no clinical trial has ever been performed which suggests vein preparation techniques may influence the long term outcome of coronary artery bypass grafting. We agree, however, that changes in pressure and blood flow may be important in the genesis of intimal

thickening, and believe that more detailed studies of "failed" coronary saphenous vein grafts may provide further insight into this complex phenomenon.

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Dr Charles comments:

We thank Drs Underwood and Coumbe for their interest in our paper.

We were interested in the changes seen in veins as a response to pressure. As the pressure in the veins of the lower leg is nearly the same as that in aortocoronary vein grafts,¹ we looked at both to compare the histological changes, as well as veins at different sites and therefore at different pressures. The grafts had all been in for more than a year, and most for more than three years. We did not expect any acute changes to have been present. The atheromatous plaques tended to involve the whole circumference of the vein, but usually somewhat asymmetrically.

We were interested to learn, however, that raised pressure alone does not cause the lipid rich atheromatous plaque seen in the graft, as these are not seen in varicose veins.

We agree that many factors are involved in the pathogenesis of atherosclerotic plaques in grafts, but we feel that endothelial preservation is important. This may be most relevant in early graft occlusion, as suggested in the paper cited,² where there were large increases in occluded grafts in the distended veins, although these were not analysed further. It is also noted that these were in normocholesterolaemic pigs followed up for up to 43 weeks and no atheroma was present. The discussion notes the importance of cholesterol in late graft occlusion, and cholesterol deposition may be enhanced by distension.

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Apocrine metaplasia: a new type of Müllerian metaplasia

I read with interest the article by Allan *et al.*¹ The authors note in their discussion that, "this type of metaplasia may give rise to a primary apocrine carcinoma in Müllerian derivatives which has yet to be described". One is reminded of the paper by Laerum² in which the author addresses that group of conditions under several headings including "Diseases which have not yet occurred but will be discovered at some time in the future, sooner or later". Citing possible examples, Laerum mentions moondust poisoning and renal podocytomas. The suggestion by Allan *et al.* for a potentially new carcinoma arising in the ovary of course raises great possibilities. I must, therefore, chastise the authors for failing to cite this seminal paper which deals with hitherto undescribed, albeit awaiting to be described, entities.

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Use of low molecular weight heparin during pregnancy

I wish to thank the members of the Working Party of the Haemostasis and Thrombosis Task for their comprehensive and most informative article, Guidelines on the prevention, investigation and management of thrombosis associated with pregnancy.¹ I would also like to document my personal experience with the use of low molecular weight heparin during pregnancy.

I have used low molecular weight heparin (Fragmin) in five pregnant women for prophylactic anticoagulation. All five had a history of deep venous thrombosis (two during the previous pregnancy) without any known thrombophilic abnormality. Their age ranged from 25 to 34 and their weight from 55 kg to 68 kg. Fragmin treatment was started between 15 and 18 weeks of gestation, at 2500 U (two patients) or 5000 U (three patients) daily. One patient developed a heparin induced skin reaction at the injection sites, so treatment had to be stopped.² The other patients continued treatment without any untoward side effects, until 24 hours before delivery. Because of the paucity of information concerning the secretion of Fragmin in breast milk, postnatal anticoagulation was continued with unfractionated heparin (12 hourly) for four weeks.

As the low molecular weight heparins are relatively new, there is little experience of their use during pregnancy.¹ The main reasons for using low molecular weight heparin in the above patients were the convenience of once daily injection and the theoretical advantage of the lower dose causing less bone demineralisation.

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