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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- 1 Charles AK, Gresham GA. Histopathological changes in venous grafts and in varicose and non-varicose veins. *J Clin Pathol* 1993;46: 603-6.
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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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- 1 Allen C, Johnson S. Apocrine metaplasia: a new type of Müllerian metaplasia. *J Clin Pathol* 1993;46:569.
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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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- 1 Maternal and Neonatal Haemostasis Working Party of the Haemostasis and Thrombosis Task. Guidelines on the prevention, investigation and management of thrombosis associated with pregnancy. *J Clin Pathol* 1993;46:489-96.
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Changes in numbers of epidermal cell adhesion molecules caused by oral cyclosporin in psoriasis

We read with interest the article by Edwards and colleagues,¹ reporting the variable expression of CD54 in active psoriatic plaques which changes unpredictably after cyclosporin treatment. Our current experience of CD54 expression in psoriasis (unpublished observations) is similar in terms of keratinocyte staining, but we have also identified CD54 expression in epidermal dendritic cells. The authors make no comment on CD54 staining of epidermal dendritic cells. The CD54 positivity of contiguous epidermal basal cells at the apex of a rete peg, illustrated in fig 3A, is clearly keratinocyte staining. Fig 1A, however, is unclear, but the CD54 positive cells illustrated are isolated cells without a basal distribution. These features are similar to those of the dendritic cells seen in our study.

The authors express CD18 and CD54 positive cells as cell numbers per unit length of epidermal basement membrane. Keratinocyte staining is logically expressed in terms of numbers of positive cells per total number of keratinocytes. Total keratinocyte number would be a function of epidermal cross sectional area. As keratinocyte staining with CD54 tends to have a wholly basal distribution, the numbers of positive cells could be expressed per unit length of epidermal basement membrane. The number of epidermal dendritic cells is probably not a function of keratinocyte number, and is best expressed as a function of unit epidermal surface length rather than cross sectional area or basement membrane length. The latter could be influenced by the pattern of epidermal acanthosis, which differs in the course of the disease.

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- 1 Edwards BD, Andrew SM, O'Driscoll JB, Chalmers RJG, Ballardie FW, Freemont AV. Changes in numbers of epidermal cell adhesion molecules caused by oral cyclosporin in psoriasis. *J Clin Pathol* 1993;46: 713-7.

Dr Edwards comments:

Payne *et al* wonder whether CD54 staining was present on epidermal dendritic cells in our study. Our definition of what we call dendritic cells is described in the section "Quantitation" and illustrated in fig 1b. As mentioned in the text, these CD18 positive cells stain sparsely for CD54. Thus the cells described as dendritic by Payne *et al* do not fit our definition.

The lack of a gold standard for quantifying the number of cells on an epidermal section is a problem in dermatopathology. We agree that the methods described in their letter are equally valid with our own. We think, however, that because epidermal

cells may vary in size, measuring the basement membrane may be more reproducible. By this method we could semiquantitatively express the number of C18 and CD54 cells in each section.

Book reviews

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(The price and availability are occasionally subject to revision by the Publishers.)

Thrombosis and its Management. Ed L Poller and JM Thomson. (Pp 272; £43.) Churchill Livingstone. 1993. ISBN 0-443-04797-9.

This slim volume is a concise review of the aetiology, pathophysiology, and management of thrombosis. This is, effectively, the proceedings book of the symposium on thrombosis and its management held in Manchester in the summer of 1992 to mark Professor Leon Poller's retirement. Written by a distinguished international panel of authors, edited with commendable speed by Poller and Thompson, and published within a year, it is remarkably up to date. The sections on aetiology and risk factors include authoritative, scientific reviews of the molecular genetics of thrombosis, investigation of the prethrombotic state, thrombophilia, the lupus anticoagulant, the fibrinolytic system, and the role of von Willebrand factor.

Chapters on management and therapeutic approaches occupy two thirds of the book, reflecting the longstanding interests of the editors. These include reviews of the diagnosis and management of thrombosis and prophylaxis in most clinical situations. All the currently available treatment modalities are also reviewed, but there is little reference to newer anticoagulants currently under development, such as hirudin. The pharmacokinetics and relative merits of low molecular weight heparin are particularly well described by several authors.

This is a generally very readable and useful review of the current "state of the art" in thrombosis aetiology and management. Areas of every day clinical concern for every haematologist are covered as comprehensively as is possible in a book of this size. It deserves a place on the shelf of every haematology departmental library.

CRM HAY

Genitourinary tract pathology. A condensed updated version of the Atlas of Genitourinary Tract Disorders (1988). Mark A Weiss, Stacey E Mills. Price:

£99.00. Gower Medical Publishing. 1992. ISBN 1-56375-0260.

All the illustrations in this updated work are in colour, and many of the macroscopic photographs are truly excellent. (There is a slide atlas of the illustrations which can be purchased separately). The photomicrographs, however, are of variable colour intensity (perhaps derived from a pre-existing collection of photomicrographs) and this is a disadvantage, although it does not greatly detract from their educational value. A useful and novel addition is the use of the line diagrams to elucidate and explain many of the microscopic illustrations.

The coverage is wide and encompasses adrenal pathology. There is also an extensive discussion of congenital and developmental abnormalities of the urinary tract. These are topics which some might consider to be the province of the paediatric pathologist rather than the uropathologist—roles which are rarely combined in the United Kingdom.

There are references to each section, but these are grouped together at the end of the book and are not separately mentioned in the text. It is therefore impossible to identify which reference relates to statements made in the chapter concerned. I suspect that these references have originated from a computer disc as in chapter 15, "Non-neoplastic lesions of the testis," three references to sclerosing adenosis of the prostate are included.

Notwithstanding the above, I enjoyed reviewing this book, with its helpful and instructive attempt to match up the clinical, radiological, and pathological features of the conditions considered. It is difficult to know what readership the authors are targeting. It is certainly a useful text for pathologists and urologists in training, but not comprehensive enough to act as a definitive reference book and it does not supplant any of the larger books on this subject which have recently been published.

ID ANSELL

Basic Pathology. 5th edn V Kumar, RS Cotran, SL Robbins. (Pp 772; £29.95.) Harcourt Brace Jovanovich Ltd. 1992. ISBN 0-7216-3732-9.

This is almost exactly a half size version of Robbins's *Pathological Basis of Disease*, which has come to be regarded as a first postgraduate textbook rather than the undergraduate's bible. *Basic Pathology* is a reflection of the editors' recognition that the test of an undergraduate textbook is in its reading by the student body, as opposed to its decoration of their bookshelves.

Nevertheless, the format is similar, with copious diagrams, good quality black and white gross pictures, and occasional photomicrographs. It is unclear whether the paragraphs of morphological description are highlighted to attract or deter the student reader. Thankfully, the book does not descend into the parrot-like series of lists and synopses of the "pocket companion" to Robbins.

After a fairly static period in the undergraduate pathology textbook market an increasing number of attractive options has appeared. The format of *Basic Pathology* is less colourful and cheerful than Underwood's *General and Systemic*