What to do in atheroma

‘What to do in atheroma’ was the title of a two-day conference held at the Royal College of Physicians in July 1990. The object of the meeting was to provide a forum for a cross-disciplinary exchange of ideas between basic scientists and clinicians in different specialties who treat the varied manifestations of atheromatous disease.

Basic science

Dr N. Woolf (Middlesex Hospital) opened the meeting with a succinct review of atheromatous pathology, emphasising the dynamic interplay between smooth muscle proliferation, lipid accumulation, plaque cracking and thrombosis—a theme frequently recapitulated throughout the meeting [1].

Dr M. J. Mitchinson (Cambridge) discussed the effects of oxidation of polyunsaturated fatty acids on macrophage function and the breakdown of atheromatous plaques [2]. If his concepts are valid, it will be important to ensure that high polyunsaturated to saturated fat ratio diets contain adequate quantities of biological antioxidants.

Dr S. Humphries (Sunley Research Institute/Charing Cross) elegantly demonstrated the use of molecular biology techniques to study the function of individual cells in the atheromatous plaque responsible for the secretion of cytokines or lytic enzymes.

Dr J. Scott (Northwick Park) discussed the molecular biology of apolipoprotein B—an extremely large protein which is a major component of chylomicrons, VLDL and LDL lipids [3]. It occurs in both a ‘full-length’ form, APO-B100, made exclusively in the liver, and a ‘short’ form, APO-B48, made in the intestine and principally concerned with chylomicron transport. Scott and coworkers have shown that APO-B100 and APO-B48 are actually made from the same gene, but in the intestine; the APO-B in RNA is ‘edited’ to convert a codon for glutamine to a codon meaning ‘stop’—thus truncating the protein [4]. There are several APO-B polymorphisms, but their role in common abnormalities of lipid metabolism is still undetermined. APO-B production is under complex metabolic control involving, among others, thyroid hormones.

Coronary artery disease

Professor D. de Bono (Leicester) described the distribution of coronary stenoses in coronary arteriograms from different patient populations. Patients presenting with stable angina had more stenosed segments and a higher proportion of multivessel disease than patients presenting with a first acute myocardial infarction. Within the ‘stable angina’ population, subgroups could be identified with ‘isolated stenosis’ or ‘diffuse’ patterns of disease—the latter including a high proportion of patients with diabetes mellitus.

Dr J. Shepherd (Glasgow) discussed the evidence that coronary atheroma can be made to regress by vigorous treatment of hyperlipidaemia. The evidence from quantitative coronary angiography is now convincing, and the crucial factor appears to be a high ratio of HDL to total cholesterol [5,6]. Numbers are as yet too small to link regression, or at least lack of progress, of atheroma with reduced mortality but the effects are concordant with other trials having clinical endpoints.

Dr S. R. Underwood (National Heart Hospital) reviewed non-invasive ways of imaging atheroma. Magnetic resonance can be used to measure aortic diameters accurately and so to time pulse-wave velocity, giving a measure of aortic compliance and thus, perhaps, an indication of atherosclerotic burden; it can also distinguish between calcified, fatty and fibrous tissue in aortic or iliac plaques [7], though the problems of movement and resolution have not yet been sufficiently solved to image coronary atheroma.

Dr V. Fuster (Mount Sinai Hospital, New York) presented two major challenges for coronary disease in the 1990s—the regression of atheroma, and the prevention of restenosis after coronary angioplasty. Echoing Dr Shepherd, he emphasized the potential for preventing progression of coronary atheroma using strategies for lowering total cholesterol and raising HDL cholesterol. On the basis of animal experiments, Dr Fuster is convinced that post-angioplasty restenosis is a reaction to local thrombosis at the angioplasty site. Conventional antithrombotic or antiplatelet agents have been unimpressive in preventing restenosis but are much less effective in preventing platelet adhesion as opposed to aggregation. New agents are also becoming available which are much more potent and specific inhibitors of thrombin than those hitherto available. He suggested that the potentially deleterious systemic effects of powerful antithrombotic agents could be minimised by ‘targeting’ them specifically to the damaged vessel wall.

Dr D. C. Cumberland (Sheffield) talked of developments in coronary angioplasty. On the one hand conventional balloon angioplasty (POBA—‘plain old balloon angioplasty’) has, despite its conceptual crudeness, become increasingly successful with increasing operator skill. On the other hand, ‘high tech’ solutions including laser angioplasty, atherectomy and, to some extent, coronary stenting had so far been less successful in preventing restenosis than initially anticipated [8].

Professor D. Wheatley (Glasgow) discussed the current role of coronary bypass grafting. Technical developments in anaesthesia and increasing use of the
internal mammary artery as a conduit had made coronary grafting both safe and effective. In terms of survival, patients who had most to gain were those with extensive (three-vessel) coronary disease and some impairment of left ventricular function, despite a somewhat higher initial operative mortality in this group. Both Professor Wheatley and Dr Cumberland saw coronary angioplasty and bypass grafting as complementary rather than competitive, at least in the UK context of limited resources.

Peripheral vascular disease

Dr F. G. R. Fowkes (Edinburgh) presented preliminary data from the Edinburgh Artery Study on the risk factors associated with peripheral arterial disease in a community setting. Major risk factors included smoking, total cholesterol (but not triglyceride), diabetes mellitus or impaired glucose tolerance, and hypertension. The association between smoking and symptomatic claudication appears to be even stronger than between smoking and ischaemic heart disease.

Dr A. M. Henney (Sunley Research Institute) described work in collaboration with the Department of Surgery at Charing Cross Hospital on the genetics of abdominal aortic aneurysm. Although traditionally described as 'atheromatous' there is a significant family association, and other risk factors for peripheral vascular or coronary disease are often absent. There is a significant association with a particular phenotype of haptoglobin, which in turn may be a marker for increased proteolytic enzyme activity in the aortic wall [9]. Although altered proteolytic enzyme activity alone does not cause the aneurysms it may interact with age-related atherogenesis to result in increased incidence and earlier presentation of aneurysms.

Dr D. C. Cumberland (Sheffield) discussed peripheral artery angioplasty [10], and Professor P. R. F. Bell (Leicester) the role of the vascular surgeon. Again, emphasis was placed on a collaborative and complementary approach. The highest success rate with both percutaneous and surgical approaches was in proximal stenoses but, even if peripheral disease could not be tackled, dilation or bypass of a proximal stenosis would often improve peripheral flow by increasing effective arterial pressure. Laser and atherectomy devices had more scope and more success in dealing with long lesions in femoral or iliac vessels than in the heart. Professor Bell emphasised that the establishment of a peripheral vascular service had been shown to reduce the need for amputations for peripheral vascular disease, and made pleas both for the early referral of patients with incipient gangrene and that amputation should not be undertaken without a vascular surgical referral [11,12].

Dr R. G. Gosling (St Thomas’s Hospital) described developments in non-invasive imaging of peripheral vascular disease. Duplex ultrasound scanning is informative but time-consuming, and a combination of Doppler ultrasound with a computerised videoscanner system has been useful as a screening procedure for selecting patients for more time-consuming or invasive studies.

Cerebral vascular disease

Dr P. Sandercock (Edinburgh) discussed a cost-benefit analysis of different ways of investigating patients with TIAs.

Table. What to do in atheroma

| Heart                      |           |                          |                          |
|----------------------------|-----------|--------------------------|--------------------------|
| Now:                       | Don’t smoke | Aim for low total cholesterol/HDL ratio | Aspirin                  |
|                            |           |                          |                          |
| Future:                    | Different thresholds for treating risk factors in diabetics, Asians? | New antithrombotic agents |                          |
|                            |           |                          |                          |
| Peripheral vascular disease|           |                          |                          |
| Now:                       | Don’t smoke; aspirin; exercise; ultrasound assessment prior to angiography | Angioplasty/surgery for severe claudication or limb salvage |                          |
|                            |           |                          |                          |
| Future:                    | Genetic predisposition to aortic aneurysm and other peripheral vascular disease? |                          |                          |

Cerebrovascular disease

Now:                       Treat hypertension

Don’t smoke

Aspirin

Duplex ultrasound assessment of patient with TIAs

Future: Role of carotid endarterectomy to be clarified by current trials
suspected carotid disease. Screening of asymptomatic patients is definitely not cost-effective; the 'best buy' in symptomatic patients is probably duplex ultrasound in combination with angiography [13].

Dr C. P. Warlow (Edinburgh) pointed out that, although transient ischaemic attacks were highly predictive of subsequent stroke, only 10–15% of patients with stroke had preceding transient ischaemic attacks. The evidence that control of hypertension would reduce the incidence of stroke was clearcut. Aspirin seemed effective in reducing overall mortality by about 25% in virtually any group of patients with atheromatous disease—whether the initial presentation was with cardiac, peripheral, vascular, or cerebral symptoms. The role of carotid endarterectomy remained uncertain: both European and American trials comparing carotid endarterectomy with medical therapy were still recruiting, but there had been a steep overall decline in the rate of carotid endarterectomy in the United States.

Discussion

Was it a worthwhile conference? In terms of attracting large numbers, no—though whether that was due to competition from Henley, Wimbledon, and summer holidays or to a prejudice that nothing new would be said is debatable. In the event, there were plenty of new data, most of the clinicians were intelligible to the basic scientists (and vice versa), and perhaps the abiding impression, to borrow a phrase from Denis Noble’s Oliver-Sharpney lecture which followed, was of a field crying out for an integrative approach. With the increasing flight from general medicine into specialisation, there is a danger that knowledge about, for example, the vascular system becomes fragmented. One solution would be to follow our continental cousins and establish ‘angiology’ as a specialty; another would be to keep holding this sort of meeting!

Finally, what should one do in atheroma, now and in the future? The table says it all.

References

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