Advanced cardiological practice

‘Advanced cardiological practice’ was the title of a one-day conference held at the Royal College of Physicians in October 1993. All the speakers work or have worked at the Hammersmith Hospital in London.

Endocarditis

Professor C Oakley (Hammersmith Hospital) opened the meeting and described the diversity with which endocarditis presents, the pitfalls in diagnosis and treatment, and the complications that may occur. Symptoms and signs are the result of infection, a heart disorder, immunological activation, and embolism. Patients may therefore initially present to any one of a wide variety of medical specialties. A high index of suspicion and repeated examination of the patient are necessary to make an early diagnosis. A murmur frequently develops but may not do so in right-sided endocarditis, when presentation may be with respiratory infection. Transient neurological signs may be missed if the patient is not regularly examined; CT scans of the brain may be helpful. It is important to seek a cardiological opinion at an early stage. Echocardiography should always be carried out by experienced operators who have been alerted to the possible diagnosis; but even then, vegetations are not always seen. Treatment with antibiotics should be started immediately after blood cultures have been taken and not be delayed until culture results are available. Early diagnosis and treatment reduces complications and the need for surgery. The indication for surgery is clear in the presence of native and bioprosthetic valve destruction, an unstable prosthetic valve, refractory heart failure related to valvular dysfunction, abscess formation, and resistant organisms; surgery for large mobile vegetations is more controversial. Mortality in 24 patients treated at the Hammersmith Hospital was 12.5% in the surgical group and 18.5% in those in whom surgery was not advisable. Prosthetic valve endocarditis carries a higher mortality than native valve endocarditis and different infective agents may be responsible.

Disordered action of the heart

Although Dr H J Dargie (Glasgow) described angiotensin converting enzyme (ACE) inhibitors as
'the biggest advance in heart failure in the past 20 years', the improvement in survival brought about by these drugs can be measured in months rather than years. Transplantation is more successful in prolonging survival but is only possible in a small number of patients. Preliminary studies suggest that survival can be prolonged by lowering the pulmonary wedge pressure to 16mmHg, often with high doses of vasodilators.

Sudden cardiac death remains a problem. A recent meta-analysis suggests that amiodarone confers protection, but confirmation from further studies is awaited. Beta blockers may have a particular role after acute myocardial infarction, but are not tolerated by all patients. Digoxin withdrawal from patients in sinus rhythm reduces their exercise capacities, and while there is some improvement in exercise tolerance with amlodipine there is not enough conclusive evidence to date to support its routine use. The patient's suitability for non-pharmacological methods—revascularisation, valve surgery, automatic implantable cardioverter defibrillators (AICD), pacing cardiomyoplasty, and transplantation—must be considered, together with adequate control of blood pressure, weight, and cholesterol, cessation of smoking, reduction of alcohol, and counselling. However the reduction in survival may be small and demonstrates the conflict between improving quality of life at the expense of an increase, albeit a possibly small increase, in mortality. Some drugs can improve the quality of life but at the cost of an increase in mortality, particularly at higher doses.

Heart failure is a common problem with considerable morbidity, mortality, and economic cost, particularly from repeated hospital admissions. Treatment must be tailored to each patient after appropriate assessment.

Professor Sir M Yacoub (Royal Brompton National Heart and Lung Institute, London) reviewed previous and current experiences of, and future hopes for, cardiopulmonary transplantation. The main indication for transplantation is heart failure. Not only do patients live longer but they also have a better quality of life; persisting limitation to exercise capacity may be improved by rehabilitation programmes, possibly as a result of their effects on skeletal muscle. Late death is mainly a result of immunological responses or immunosuppressive therapy. Cyclosporin improves survival, and other immunosuppressive drugs are evolving among which the macrolide drugs appear to be particularly important. Donor supply is limited but xenograft transplantation and artificial hearts with biventricular support may become possible.

Dr P Curry (Guy's Hospital, London) described the development of electrophysiological (EP) investigations in the past 15 years. They have led to a better understanding of the mechanisms and anatomy of arrhythmias, of interpreting the electrocardiogram (ECG), and to the more appropriate use of drug therapy, pacemakers and related devices, ablation and surgery. Other investigations for patient assessment should not be forgotten, however, such as event recorders which are underused. Twenty-four hour tapes and exercise tests are of value and signal averaged ECGs help to stratify the risk of potential malignant arrhythmias. Low variability of the R-R interval after myocardial infarction is associated with a two- to four-fold increase in mortality. EP studies need more sophisticated equipment and trained personnel. For the patient’s benefit it is important to reduce the duration of EP studies, which has been aided by advances in catheter design. To date the implantation of an AICD has always been preceded by electrophysiological evaluation although this may not be strictly necessary if other measurements, such as persistently high left ventricular end diastolic pressure, suggest a high risk of sudden death. The role of amiodarone in preference to such a device is not yet defined.

Dr E Rowland (St George’s Hospital Medical School, London) turned our attention to the role of ablation in the treatment of arrhythmias. It was at first limited to DC ablation of the His bundle in atrial fibrillation with an uncontrolled ventricular response despite medical therapy; but ablation, and in particular radiofrequency ablation, is now becoming an important treatment, possibly the treatment of choice, for symptomatic Wolff-Parkinson-White syndrome, concealed accessory pathways, and AV nodal reentry tachycardias. ECG mapping has located the source of atrial flutter to a narrow isthmus between the tricuspid annulus and the inferior vena cava and has been treated with some success by ablation, although experience is still limited. Ablation has a role in the management of ventricular tachycardia but mainly in the otherwise normal hearts in which the site of origin is small. Tachycardia associated with coronary heart disease, ventricular dilation, or congenital artery disease is less amenable because there is more widespread electrical damage. Dr Rowland warned against the development of too many laboratories with ablation facilities. A multicentre European study is now in progress, and while the complication rate is low (0.5% on average), it is highest in small centres performing few procedures. Ablation should be confined to specialist centres where expertise can be maintained.

Coronary disease

Professor M J Davies (St George’s Hospital Medical School) gave a comprehensive and well-illustrated description of the fibrolipid plaque. A plaque is composed of a lipid core separated from the lumen by a fibrous cap made up of a collagen lattice containing macrophages and smooth muscle cells. Advanced plaques do not necessarily encroach on the lumen but may eventually lead to symptoms either as a result of primary growth with smooth muscle proliferation, collagen production and lipid accumulation, or as a result of secondary complications, in particular throm-
bosis, at a site of injury. Superficial injury from endothelial denudation is common and its occurrence bears no relationship to the degree of stenosis subtended by the plaque in question. Superimposed thrombosis may be minor and asymptomatic, or major with acute and subacute obstruction of the coronary artery. Similarly, plaque fissuring and subsequent thrombosis vary in magnitude. Fissures occur in response to an increase in cap stress and a reduction in cap strength. Cap stress increases with an increase in core size, reduced cap thickness, loss of the internal collagen core, possibly hypertension, and when stenosis is minimal. Cap strength is reduced when collagen and aminoglycan concentration is low, the normal collagen architecture is lost, and when the density of monocytes is increased and that of smooth muscle cells decreased. Further insights into the structure of arterial plaques came from a study of the composition of plaques in the aorta. Ulcerated plaques contain a higher concentration of cholesterol esters and total lipid than intact plaques; they also have a higher percentage of monocytes and a lower percentage of smooth muscle cells. Smooth muscle cell proliferation, which occurs in response to platelet activation at a site of thrombosis, is a protective healing mechanism. Minor thrombosis does not lead to symptoms but smooth muscle cell proliferation may increase the degree of stenosis and symptoms of chronic stable angina. The pharmacological inhibition of smooth muscle proliferation may be inadvisable as it may inhibit the healing of ulcerated plaques.

Professor A Maseri (Catholic University of Rome) discussed endothelial dysfunction and the response of atherosclerotic coronary arteries to substances such as acetylcholine, substance P, and sodium nitroprusside. He presented evidence for an inflammatory and acute phase response in unstable angina. Patients with unstable angina whose plasma C-reactive protein (CRP) remained low (< 3) recovered without complications or invasive therapeutic manoeuvres; those in whom the CRP reached the mid-range (3 to 10) were more likely to require a revascularisation procedure, and those in whom the CRP rose above 10 were more likely to suffer fatal or non-fatal myocardial infarction or require revascularisation. Myocardial necrosis was not the cause of the inflammatory response as shown by the absence of a rise in troponin T. This not only suggests that an inflammatory element is present in unstable angina but also that the degree of inflammation may predict outcome.

Professor J L Reid (Western Infirmary, Glasgow) discussed hypertension as a risk factor for coronary artery disease. Meta-analysis of recent hypertension trials has shown a linear increase in the relative risk of stroke and symptomatic coronary artery disease with increasing diastolic blood pressure. The highest risk occurs in elderly people who have multiple risk factors; also in diabetics, in people who have renal disease or need renal replacement, people who have suffered symp-
angioplasties are associated with some degree of plaque rupture. More extensive damage with dissection of the media occurs in 3-5% and may result in death, acute infarction, or emergency coronary artery surgery. Restenosis occurs in 50%, with clinical symptoms in 20-30%, and its prevention is the ‘holy grail’ of angioplasty. Smooth muscle cells are no longer contractile but proliferate in response to the excretion of components of the extracellular matrix. This response to balloon injury is seen within the first six months and is unlikely to occur thereafter. Attempts to reduce restenosis have been made with the use of lasers, atherectomy, and stents. Preliminary evidence suggests that stents may be successful, but their thrombogenic properties are a major problem. RITA, a randomised trial of patients with multivessel disease amenable to coronary artery surgery or PTCA, has reported interim results after 2.5 years of follow-up. Neither procedure is superior with respect to increase in exercise tolerance and return to work, or in the rate of acute infarction or death. Patients randomised to PTCA, however, suffer more angina; 31% have had repeat coronary angiography, 20% a further angioplasty, and 20% coronary artery surgery. A randomised trial of PTCA and medical therapy in patients with stable angina and single vessel disease found patients randomised to PTCA had less angina and longer exercise times, but were at higher risk of needing coronary artery surgery. PTCA is an alternative to medical therapy in stable angina and delays or avoids the need for surgery (and eventually delays or avoids the need to redo coronary artery surgery). It may have a role in the early control of unstable angina but it is not a routine management strategy in acute infarction. Its ability to improve survival and prevent infarction is unknown.

Heart muscle disease

Dr M Ryan (Hammersmith Hospital) described the contribution of genetic studies to the diagnosis of hypertrophic cardiomyopathy (HCM). An abnormality occurs in the β myosin heavy chain gene: although there are several different mutations, the same mutation in different patients may not give the same clinical picture; on the other hand different mutations may be clinically indistinguishable. If the carrier status is clinically uncertain during the screening of family members of sufferers, genotyping clarifies the diagnosis. An individual without any clinical signs of HCM has been found to be a carrier and therefore has ‘genetic HCM’. The prognosis for such patients is unknown and raises a number of social, economic and personal implications.

Dr L M Shapiro (Papworth Hospital, Cambridge) considered some of the characteristics of HCM. In two-thirds of patients left ventricular hypertrophy (LVH) is asymmetrical and in one-third symmetrical, either apical or truly symmetrical. Prognosis seems worse in the presence of severe LVH, but is worst in patients who later develop wall thinning and an ejection fraction less than 50%. Patients with HCM universally have diastolic dysfunction, but the degree of dysfunction does not predict electrical instability, the risk of sudden death, or symptoms. Patients with a high pressure gradient across the left ventricular outflow tract may suffer disabling symptoms. They may improve after AV sequential pacing with a reduction in angina, dyspnoea, syncope, and presyncope. Pacing should be reserved for patients who are severely disabled despite medical therapy. Myotomy-nyectomy is an option for those who do not respond to pacing but should only be considered after a trial of pacing for a number of months. Patients with non-obstructive HCM who are very disabled may require cardiac transplantation.

Summary

The conference deserved its title of ‘Advanced cardiological practice’. It dealt with a variety of topics but the programme was well organised and not disjointed. New data were presented and there will be few who did not hear something they had not heard before. A smattering of molecular science was included, but if anybody felt deprived of that, the Bradshaw Lecture* given by Professor P A Poole-Wilson at the end of the meeting, would have remedied this.

*This lecture, on ‘Pump failure in heart failure: cellular mechanisms’, will be published in a future issue of the Journal.