

# Cardiology

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## Introduction

Although cardiology was advancing rapidly in the 1950s it remained, like neurology, primarily a clinical discipline. Diagnosis relied on physical examination with some additional help from the electrocardiogram, chest X-ray and right heart catheterisation. Cardiac imaging was in its infancy. The specialty was led by some remarkable clinicians, notably Dr Paul Wood to whom I was house physician in 1959.

The assessment of patients with mitral valve disease at that time illustrates the importance of clinical skills. Acute rheumatic fever was uncommon but the care of those with rheumatic valve disease remained a major feature of cardiological practice. Mitral valvotomy was already established in the UK but valve replacement awaited the development of cardiopulmonary bypass in the 1960s. Successful outcome from closed valvotomy required the careful selection of patients with mitral stenosis without significant regurgitation and with a sufficiently mobile valve to split along its commissures. Severity of stenosis and mobility of the valve were determined mainly by auscultation. Chest X-rays were examined for signs of left ventricular enlargement, signifying mitral regurgitation, or valvular calcification which made a successful split less likely. The severity of stenosis and any regurgitation was confirmed by analysis of the indirect left atrial pressure wave. If pulmonary hypertension was present the benefits of surgery had to be balanced against an increased operative mortality.

## Investigations

There were rapid developments in investigation during the 1960s, particularly in cardiac catheterisation and angiography. Image intensifiers transformed the foggy appearances on screen to a clean, sharp image. Dark adaption became unnecessary and both patient and operator were exposed to less radiation. Cineangiography replaced slower cut film processes and allowed the recording of images from several angles. Photoelectric oximetry avoided multiple blood sampling when investigating intracardiac shunts. Pre-formed flexible catheters, tailor made for individual procedures and discarded after use, avoided the risk of infection inherent in the former practice of cleaning and sterilisation. By 1970, the left side of the heart and the coronary arteries could be

investigated routinely and safely. Later the use of narrow bore catheters allowed many patients to return home on the day of investigation.

Angiography facilities, however, remained sited mainly in the major surgical centres so that fully trained and competent cardiologists who were appointed outside those units had to refer patients on for invasive studies. This led to clinical delay, wastage of professional skills and much frustration. But the increasing demand for coronary angiography in the late 1980s resulted in the development of angiography facilities in many district general hospitals.

Nuclear scanning of the heart, which is useful in the assessment of coronary disease, remained restricted to relatively few centres so the technique never fulfilled its full potential in the UK. In contrast, the use of echocardiography, allowing detailed study of cardiac structure and function, became widespread throughout the NHS in the late 1970s and 1980s.

The wider availability of investigational facilities and the appointment of cardiac physicians to the majority of hospitals has resulted in a far more equitable access to expert cardiological care across the country than was present even 20 years ago.

Cardiac surgery was also advancing rapidly so that aortic and mitral valve replacement and, in selected cases, valve repair became routine in the 1970s. Of particular significance, given the growing clinical burden of coronary heart disease, was the development of a reliable technique for revascularisation of the heart – coronary artery bypass graft surgery (CABG).

## Coronary heart disease

### Angina

Until the early 1960s, treatment of angina involved restriction of physical activity and the correction of aggravating factors such as obesity, anaemia and hypertension. Patients were generally advised to restrict smoking but not necessarily to stop unless it actually provoked pain.<sup>1</sup> Drug treatment centred on the use of sublingual nitrates although hypothyroidism was occasionally induced in those with more severe angina. Several surgical approaches to revascularisation had been explored but only cardiac denervation through stellate and upper thoracic ganglionectomy, or implantation of the internal mammary artery (IMA) into an area of ischaemic myocardium provided any benefit.

The introduction of beta adrenergic blocking drugs in the 1960s represented a major step in the prevention of angina. Their clinical impact was, I believe, much greater than is now appreciated in the era of revascularisation. Together with the calcium channel blockers beta adrenergic blockers allowed many patients to return to a full and active life.

Although the epidemiological link between hypercholesterolaemia and coronary disease had been recognised for many years, the benefits of lowering blood levels of cholesterol therapeutically were not, particularly in the UK, until publication of the first statin studies in 1994.<sup>2</sup> Everything then changed and the use of these drugs spread rapidly in secondary and primary prevention. Apart from aspirin, many other attempts at prevention, including vitamin E to prevent oxidation of low-density lipoprotein cholesterol, have not survived the test of clinical trials.

Coronary angiography, developed in the 1960s, greatly improved understanding of the natural history of coronary disease. It established the prognostic significance of left main coronary artery stenosis, three vessel disease and left ventricular dysfunction. Throughout the 1970s UK clinicians were frustrated in attempts to acquire sufficient NHS investment in a CABG service commensurate with clinical need. One view was that CABG, although relieving angina, did not improve survival and so development of the service was slow. By the early 1980s, however, evidence was available from trials in the USA and Europe to show that in high-risk cases, as determined by angiography and clinical assessment, survival was indeed improved by revascularisation.<sup>3</sup> The number of CABG operations per annum in the UK rose from around 3,500 in 1979 to nearly 29,000 in 2003. Later, use of IMA grafts extended the duration of benefit because the vessel rarely develops atheroma.

The techniques of angiography led to coronary angioplasty, now usually accompanied by stenting. Used originally as a treatment for angina it is now increasingly employed as a primary treatment in the management of acute myocardial infarction (MI).

## Myocardial infarction

Clinicians were fully aware of the clinical presentation of MI 50 years ago, including electrocardiography (ECG) changes and the significance of a transient rise in serum transaminase levels. Patient care concentrated on effective analgesia, prolonged bed rest and oral anticoagulants preceded by heparin. Anticoagulants protected against the thromboembolic complication of prolonged immobility but early studies had demonstrated a greater reduction in mortality than could be explained by that alone. It was thought that treatment must prevent extension of intracoronary thrombus. Many clinicians continued treatment with coumarin derivatives indefinitely. The use of oral anticoagulants fell from favour in the 1960s but the studies which led to this change of practice were later considered to be flawed. Clinical practice, however, had moved on. Patients were being mobilised early and the benefits of fibrinolysis and antiplatelet drugs became established in the late 1980s leaving no way back for oral anticoagulants.

External defibrillators arrived in the UK in the early 1960s. In combination with chest compression and new ventilation techniques it became possible to resuscitate many patients in ventricular fibrillation (VF). As a result, those with suspected infarction were soon being nursed in areas permitting close observation and immediate resuscitation. These cardiac/coronary care units (CCU), pioneered in particular by Desmond Julian in Edinburgh, became an established feature of hospitals during the late 1960s and 1970s although some scepticism about their efficacy remained.<sup>4</sup> Nurses became proficient at defibrillation so that many patients were resuscitated long before medical staff could reach the unit.

The structure of CCUs varied. At the Birmingham General Hospital the unit was an adapted day room. Possession of a mobile X-ray screening machine allowed us to pace without transferring patients to the radiology department. Some units were simply designated areas of a larger ward, and a few achieved 'pole position' close to the accident and emergency department.

Frank Pantridge, in Belfast, demonstrated that the risk of VF was highest in the early stages of infarction and pioneered a medically staffed ambulance system that brought care into the community. This proved difficult to replicate in much of the UK but later the British Heart Foundation pioneered the provision of defibrillators to ambulance staff and to trained volunteers. This has gone some way towards improving the outcome of cardiac arrest outside hospital.

The early era of coronary care was an exciting time which stimulated a considerable body of research but significant advances in treatment came slowly. There were false dawns of course, notably the use of antiarrhythmic drugs, usually lignocaine, to prevent ventricular fibrillation when 'warning arrhythmias' were detected, but formal trials showed the practice to be associated with an increased mortality.

The introduction of fibrinolytic drugs followed the publication of trials in the late 1980s was a major step forward.<sup>5</sup> It has been claimed that previous, smaller trials should have resulted in the earlier introduction of fibrinolytic treatment but the definitive studies were necessary to clarify the effective route of administration, dosage and duration of treatment. They also established the therapeutic role of oral aspirin. The uptake of treatment was remarkably rapid across the UK, particularly in regions that had been involved in the trials, illustrating the benefit of basing such therapeutic research in the real world.

Earlier mobilisation and discharge from hospital led to the creation of cardiac rehabilitation programmes. They were intended to help patients develop a healthier lifestyle and to increase physical fitness in an environment where they felt safe. Most focused on physical rehabilitation and lifestyle education, others also provided psychological support. Some patients were uncomfortable with the gymnasium-type setting of their programme but most found them of great help and went on to establish cardiac clubs to provide peer support and raise funds for local services. Rehabilitation also provided an excellent opportunity for secondary prevention.

## Heart failure

The care of patients with chronic heart failure in the late 1950s was based on rest, digitalis and salt restriction. A major contribution of the hospital dietetic department was to provide a salt-free diet and to instruct the patient's family in its preparation. The regime was strict, imposing considerable restrictions on social life, but it was effective in alleviating the symptoms and signs of failure.<sup>1</sup> Deviation from the discipline, potentially occurring at Christmas, could be disastrous. Patients became remarkably tolerant of the regimen and not infrequently, when effective oral diuretics became available, found a conventional diet unpalatable.

The only effective diuretics available were the mercurial compounds. These were administered intramuscularly twice weekly, together with ammonium chloride to replace excreted chloride ions. They were of limited value in the treatment of those in life-threatening pulmonary oedema. No oral preparation was available. The first oral thiazide was introduced in 1958 followed by the loop diuretics. The latter had the great advantage of rapid action when given intravenously and revolutionised the treatment of acute left ventricular failure, which had previously relied on morphine, posture, oxygen and reduction of systemic venous return by the application of venous cuffs to the limbs or by venesection. The latter could be remarkably effective. Aldosterone antagonists were a further important development in the treatment of chronic heart failure and had the distinction, many years after their introduction, of being shown to extend survival.

Probably the single most important advance in the management of chronic cardiac failure was the improvement in quality and duration of life by angiotensin converting enzyme inhibitors and their derivatives.<sup>6</sup> Benefits were shown to extend to those with impaired left ventricular function in the absence of symptoms. As a result, detection of impaired function has become one of the major uses of echocardiography.

## Arrhythmias

Fifty years ago the treatment to control heart rate in the presence of atrial fibrillation (AF) was, then as now, digitalis. Physicians also prescribed oral anticoagulants to prevent thromboembolism in the presence of mitral stenosis or after restoration of sinus rhythm by oral quinidine. But in the 1980s it became clear that warfarin also reduced the risk of stroke among those with nonvalvular AF who were at increased risk because of age, hypertension or left ventricular dysfunction. This lesson remains of great importance, given the frequency of AF in the elderly, but many patients are considered to have contraindications to warfarin or to be incapable of complying with the discipline involved. The defibrillator found a vital role in the correction of AF being more effective and safer than the earlier practice of pharmacological conversion using oral quinidine.

Perhaps one disappointment over this period has been the failure to develop effective and safe antiarrhythmic drugs. Several are of limited help but only amiodarone has made a major impact; unfortunately it has significant toxicity.

Heart block carried a life expectancy of around four years before the introduction of pacing; less if it was complicated by syncope (Stokes–Adams attacks). Early implanted pacemakers involved thoracotomy for the attachment of epicardial leads, posing a risk for elderly patients. In the 1960s endocardial pacing via a transvenous electrode became standard practice with the pacing unit implanted subcutaneously. Early pacemakers were bulky and tended to extrude. On arriving in Birmingham in 1966 I was delighted to discover the locally made Lucas unit. This consisted of a small secondary inductance coil attached to the cardiac electrode which could be easily implanted in the thinnest patients. The primary coil was taped to the skin and the battery generator carried on the patient's belt. Of course occasional problems occurred as a result of coil displacement, bathing was restricted and a cool head and steady hand were required to change the batteries. Advances in battery technology resulted in smaller generators and longer battery life. The sophistication of pacing has developed from the earlier fixed rate stimulation of the right ventricle to a process that more closely resembles the physiological condition as described by Michael Gammage.

The pre-excitation tachycardias, notably the Wolff-Parkinson-White Syndrome, have always been difficult to control pharmacologically but developments in intracardiac ECG in the 1970s led to the technique of ablation of accessory pathways which offered potential cure of many patients with these problems.

## Hypertension

An effective drug treatment already existed in the late 1950s for the treatment of malignant stage hypertension. The ganglion-blocking drug hexamethonium, administered subcutaneously, had been shown to improve survival in a condition previously associated with rapid progression to death through renal failure, stroke or heart failure. Although an orally active preparation became available the side effects associated with the drug group, including postural hypotension, impotence, paralytic ileus, and impaired visual accommodation, were such that treatment was reserved for those in the malignant phase.

In succeeding decades there were two parallel developments, the first was a growing recognition that even modest elevation of arterial pressure increases risk of cardiovascular morbidity and death, and the second was the development of drugs which combined efficacy with fewer adverse effects. The early stages of this process were described in detail by Sir George Pickering.<sup>7</sup> Clinical trials have shown that blood pressure reduction among those with levels far lower than were considered to justify treatment during the 1960s and 1970s results in reduced morbidity. Even in the elderly, where a level of hypertension was regarded as inevitable, there is now clinical evidence of benefit in controlling raised blood pressure.

Recent years have seen a more integrated approach to the prevention of cardiovascular morbidity. Clinicians caring for those with hypertension are more likely to take an active interest in coexisting hyperlipidaemia or glucose intolerance. Perhaps the greater involvement of modern general practice may take some of the credit for this development.

## Conclusion

Cardiovascular medicine has changed so dramatically over 50 years that it is impossible to predict the future. The specialty has been dominated by the disease burden of coronary disease. The current revascularisation techniques have improved the well-being of many thousands of sufferers, nevertheless CABG and angioplasty are rather blunt instruments with which to counter a progressive disease. Although more can now be done to prevent progression of atherogenesis, our powers are still limited. Vastly more is now known about the pathogenesis of coronary disease, at both cellular and molecular levels, but as yet this knowledge has had no direct impact on clinical practice. I am sure it will.

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## CURRENT KEY DEVELOPMENTS

### Grown up congenital heart (GUCH) disease: a half century of change

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The incidence of all levels of congenital heart disease (CHD) remains at 7–12/1,000 live births. Despite intrauterine recognition of fetal CHD, very few lesions are now considered incompatible with life. The numbers of adults with CHD now significantly exceeds the paediatric population. The 18-year survival for a child born with complex CHD in the 1960s was 10% whereas a child born with the same complex disease in the 1980s had a 50% 18-year survival. Now 90% survive into adolescence and beyond; the recent Department of Health report has estimated the total number (England and Wales) of grown up congenital heart disease (GUCH) patients in 2000 as 133,190 rising to 158,990 by 2010.<sup>1</sup> The better palliated and natural history of these patients has important implications for long-term care and training of cardiologists in the management of both the natural and unnatural (operated) history of CHD.<sup>2</sup> Coarctation of the aorta was first repaired in 1945 and frequently patients were discharged as ‘cured’. It is now clear, however, that late complications relating to the type of surgical intervention (namely restenosis with end-to-end anastomosis, aneurysm formation with Dacron patch) require continued surveillance. Moreover some patients are prone to premature coronary artery disease, persistent upper limb hypertension (despite relief of the coarctation) and ascending aortic dilatation – probably related to the bicuspid aortic valve present in at least 50%.<sup>3</sup> As a result of the natural and palliated sequelae, late survival is still significantly compromised.<sup>4</sup>

Long-term survival of tetralogy of Fallot (ToF) is already known to be excellent (Fig 1) but many will need further surgery to the right ventricular (RV) outflow tract (RVOT) for free pulmonary regurgitation or RVOT aneurysms (both of which complications are likely to have occurred as a result of the original surgical technique) as well as other interventions (eg implantable cardioverter defibrillator implantation or aortic root surgery). The revolutionary technique of percutaneous pulmonary valve replacement introduced by Phillip Bonhoeffer over the last five years has allowed selected patients to avoid further sternotomies with subsequent improvement in RV function.<sup>5</sup>

Transposition of the great arteries was palliated by the atrial repairs of Mustard and Senning in the mid-1960s. This has permitted good survival for at least 30–40 years but the systemic RV leads to heart failure. Baffle obstructions and leaks are now dealt with percutaneously but considerable morbidity occurs with