Proceedings of the British Cardiac Society

THE AUTUMN MEETING of the British Cardiac Society was held at the Royal College of Physicians, London, on Thursday and Friday, 9 and 10 November 1972. The President, JOHN GOODWIN, took the Chair at 9.00 a.m. during Private Business. At the Scientific Session which followed, the Chair was taken by A. MORGAN JONES.

Private Business

1 The President reported with deep regret the death of Charles Friedberg, and the meeting stood in tribute.

2 The Minutes of the Annual General Meeting having been published in the British Heart Journal (1972, 34, 959–965) were taken as read and confirmed.

3 The Treasurer reported that Council had approved the appointment of Charles Rippin & Turner to be the Society’s auditors. From being a small inward-looking club the Society was changing into a large and powerful organization with growing influence and importance in British medicine. This change was increasing the expenses and made it essential to have proper professional advice in running the Society’s affairs. Because of rising prices the annual subscription would have to be raised and it was suggested that the figure might be £15, and this would include tea and coffee at scientific meetings. The collection of small amounts of money for tea and coffee had proved to be a very uneconomical business. A subscription of £15 would probably make the Society liable to V.A.T. and the new auditors’ advice would be sought before making the final recommendation. The state of the Society’s investments was generally satisfactory.

4 The Secretary reported that the preliminary notice about the Annual General Meeting in Glasgow on 12 April 1973 had been circulated. Dr. Olav Kerr would be the Chairman.

5 The Secretary reported that the Autumn Meeting of the Society would be held at the Royal College of Physicians on December 13 and 14, 1973, the only available consecutive two days.

6 The Secretary reported that the Annual General Meeting in 1974 would be held in Newcastle on 18 April, and arrangements were already being made.

7 The President said that he felt there was a need for an official channel of communicating between the Department of Health and the British Cardiac Society as representing organized informed opinion on cardiology in the British Isles. Such a channel would provide an essential mechanism for members of the Society to state their views on important problems, and also for the Department of Health to seek the official view of the Cardiac Society on matters of policy. The President reported that he had raised the question of a liaison committee with the Chief Medical Officer to the Department of Health and Social Security and with the President of the Royal College of Physicians; both had agreed with the suggestion, and if the Society approved the President would take steps to implement the proposal and report back at the next meeting.

8 The President said there was a slow but steady increase being made in the number of consultant appointments in cardiology. The principle of two types of cardiological work—pure specialization, cardiology in association with general medicine—was being gradually implemented. The number of senior registrars in cardiology was being carefully kept at a suitable ratio of senior registrars to consultants to avoid a ‘pile-up’ of senior registrars and further difficulty in obtaining consultant posts. The mechanism for the appointment of consultants and of senior registrars was discussed, and the President emphasized that though the number of senior registrars in cardiology throughout the country was probably adequate there was considerable irregularity of distribution. This situation was being gradually improved, but it was important for centres applying for a senior registrar to emphasize the need for training and the adequacy of the training programme available, as these were training posts, and not posts merely to increase the numbers of ‘pairs of hands’ to do specialist work. Where, however, there was a real need for further cardiological services at consultant level, then every request was very carefully considered provided that it was fully and unanimously backed by local opinion and that it had maximum priority in the region concerned.

9 With regard to the Specialist Advisory Committee on Cardiovascular Disease, the President reminded the Society that the training programme had already been drawn up and that a summary had been included in a pamphlet recently published by the Royal College of Physicians on the activities of the Joint Committee for Higher Medical Training of the four Colleges of Physicians. He said that the next problem was to decide the best means of evaluating centres that applied for accreditation for suitability for training cardiologists and said that this matter would require careful thought, with particular attention to the relations between the Specialist Advisory Committee on Cardiovascular Disease and local organizations such as postgraduate Deans’ committees, etc. The Specialist Advisory Committee on Cardiovascular Disease was due to meet the next day
The President reported that the morale of the Society of Cardiological Technicians had been much improved recently owing to the better pay and career structure envisaged under the recommendations of the Zuckerman Committee. New recommendations envisaged that cardiological technicians would have a career structure on a par with other medical laboratory technicians, but emphasized that their promotion and career structure and pay would depend essentially on the training they had received and the examinations they had passed. It was thus essential that there should be training facilities in all areas so that cardiological technicians could pass the necessary examinations.

Oram spoke on the new salary scales which he said were still poor and stopped short of the top physics scale. He felt that this was because the training facilities for cardiological technicians were still very poor and they could not attain the standards which would justify a higher salary scale.

Davison described regional training schemes in Birmingham and Newcastle where training of cardiological technicians was linked with that of physiological measurement trainees. Students working for the O.N.C. went to various hospitals, a fortnight in each, learning the different techniques, with a day and a half release each week for lectures and lecture demonstrations. For this particular course a student needed four 'O' levels, two of which must be in science, preferably one in maths or physics. At the end of the training the student could choose in which department to work. In this way both Birmingham and Newcastle had obtained sufficient students.

Besterman thought that there was widespread ignorance among career advising officers concerning the possibilities of becoming cardiac technicians, and Deuchar felt that the problems of paying technicians higher rates would only come when they had a satisfactory physiological training background so that the cardiac technicians could reach the same academic standard as physics technicians, and he felt strongly that the correct approach was for arrangements to be made for full-time training. The President said that it was up to the technicians to organize a register of approved training posts.

The President warmly thanked Oram and Davison for their hard work in looking into the matter of training facilities. These were clearly extremely patchy and further attempts must be made to improve them. It was agreed that Towers (who had succeeded Oram as the President of the Society of Cardiological Technicians) should, with Oram and Davison and the officials of the Society of Cardiological Technicians, look further into the question of a training programme with a view to compiling lists of training centres which would be available to cardiac departments and to the Society of Cardiological Technicians. The Department of Health should be urged to implement the needs of the training programme.

The President said that fortunately it had been possible to organize the Cardiological Technicians Society's Annual Exhibition at the time of the meeting at the Royal College of Physicians with an overflow in the nearby Regent Centre Hotel. He hoped very much that as many members as possible would find time to attend the Exhibition. The President emphasized the need for a closer relation with the Society of Cardiological Technicians, and hoped that members of the Society would feel it desirable to invite from time to time selected senior or chief technicians to the scientific meetings, particularly when they had contributed to papers that were being read. The President added that he had invited the Chairman of the Society of Cardiological Technicians, Mr. Leslie Goulding, and the Secretary, Miss Norma Millar, to attend the present meeting of the Society, and that they had accepted with enthusiasm.

II Working parties The President said that he had felt the need for some groups to look into certain current problems in cardiology, particularly where further information was needed and where overall data should be made available to members of the Society. He therefore suggested the creation of three working parties with these objects in view. The first of these was to be a working party to examine coronary care in the country, in conjunction with the Cardiology Committee of the Royal College of Physicians, and with representatives of the Department of Health invited as observers.

The second working party, also in conjunction with the Cardiology Committee of the Royal College of Physicians of London, was to be on rehabilitation. Semple had agreed to chair this working party and to suggest the members of it. The working party would look into two main aspects of rehabilitation—first the socioeconomic problems, and second the physiological effects of graded exercise upon cardiac function. It was felt it was particularly important to identify the extent of the need for rehabilitation. As with the working party on coronary care, representatives of the Department of Health and Social Security would be invited to attend meetings as observers.

The third working party would be that of cardiac muscle research. The President said that he had been approached earlier in the year by research workers in the field of cardiac metabolism who were anxious to form a group to learn of each other’s work and to share experiences and problems. The President felt that it was very important that the British Cardiac Society should be closely associated with this and said that he had asked Peter Harris to act as Chairman of a working party to look into the formation of a Cardiac Muscle Research Group and report back to the Society.

12 Young Research Workers’ Award The President said that he felt it would be an important stimulus to young cardiologists and research workers in the field to have a Young Research Workers’ Award for especially important original work. A similar arrangement had been very successful in the American College of Cardiology, and the President said that he had asked Sowton to form a committee to look into the best methods of implementing this suggestion and to report back to the Society at a future meeting.
The Secretary reported that the British Standards Institution had set up a Committee on electrocardiograms, and the Society had accepted an invitation to send representatives to a meeting to be held shortly.

The Society dined together at the Zoological Gardens Restaurant with John Goodwin in the Chair. The guests included Professor and Mrs. Dwight E. Harken and Mr. and Mrs. Norman Barrett.

At the beginning of the Scientific Meeting the President gave the following appreciation of the late Paul Wood:

I did not think that this scientific meeting should start without reminding members and guests that 1972 is the 10th Anniversary of the death of Paul Wood who died in his prime at the age of 55. Paul Wood was essentially a man of his time. He arrived on the scene when cardiac catheterization, pioneered in this country by McMichael and Sharpey Shaffer, was opening up new frontiers of knowledge and when cardiac surgery, under Brock and Holmes Sellers, was developing rapidly. Wood used his talents to develop a discipline of clinical cardiology based on sound physiological principles which has become a model. His impact was enormous. He was a dynamic personality; once met – never forgotten. He had an explosive sense of humour, but he could be abrasive also, and did not hesitate to destroy with mutilating rhetoric a weak argument, sometimes to the discomfiture of colleagues. He thus gained, amid innumerable admirers and friends, some critics. He would, I think, have looked forward eagerly to the programme of this meeting, for he was fond of saying that it was important to anticipate problems and to have the solution ready when the problem presented itself. This would perhaps be a good epitaph for him ten years after his death and not a bad motto for the Society.

Response of renal and femoral vascular beds to experimental myocardial infarction

R. E. Falicov, C. J. Mills (both introduced), and I. T. Gabe

Some of the variability of clinical and haemodynamic findings observed during cardiac failure due to acute myocardial infarction may be the result of reflex or humoral adjustments of individual circulatory beds. In the experimental situation, we have investigated the response of the renal and femoral vascular beds to severe myocardial ischaemia produced by coronary embolization with mercury in 21 closed-chested dogs. The predominant finding in the femoral bed was vasoconstriction. The net renal response, on the other hand, was one of early and persistent vasodilatation. In many instances this was shown by an actual increase in renal blood flow, which occurred in spite of a decline in arterial pressure. The maximal vasodilator response took place within two minutes of coronary embolization (renal vascular resistance fell by $28 \pm 4$ (SEM) %) but renal vasodilatation was still significant after 30 minutes (renal vascular resistance had then decreased by $23 \pm 5$%); at that time, the systemic vascular resistance was conspicuously raised ($39 \pm 14$%). This paradoxical renal vasodilator response to myocardial ischaemia was not abolished after vagotomy, nor was the ability of the renal vessels to constrict in response to noradrenaline impaired after coronary embolization. Thus, while the femoral bed participated in the systemic vasoconstrictive response to myocardial ischaemia, the renal circulation was under the influence of still undefined vasodilator stimuli of early onset but sustained effect.

Mobile coronary care provided by ambulance personnel

D. A. Chamberlain, N. M. White, R. Binning, W. S. Parker, and E. R. Kimber (last four all introduced)

The cost of manning coronary ambulances with medical and nursing staff prohibits their use in most areas. Since July 1971, two coronary ambulances in Brighton have been manned entirely by ambulance personnel who are responsible for monitoring the electrocardiograms of patients in transit, and for defibrillating patients when the need arises. 1497 calls were made on the ambulances, and 882 patients were suspected of having cardiac pain. Fifty-seven patients were in ventricular fibrillation before the ambulance arrived; co-ordinated rhythm was restored in 16 cases, but irretrievable brain damage had occurred in all but one instance. Eight patients developed ventricular fibrillation while being moved to the ambulance or during transit to hospital; one was pulseless with severe cardiogenic shock and died, but the other 7 were defibrillated and reached hospital alive. Five patients survived to be discharged from hospital. Subsequent analysis of electrocardiograms recorded in one ambulance over a 9-month period showed that 86 per cent of all arrhythmias which occurred during transit were diagnosed correctly by the ambulance attendants. We conclude that specially trained ambulance personnel can offer a worthwhile service for the prehospital care of coronary patients.

Salutary effect of methyl prednisolone on viability of heart muscle exposed to anoxia

David E. Jewitt, C. Lynn Skelton, and Edmund H. Sonnenblick (last two introduced)

The development of therapeutic regimens which maintain the cellular viability of heart muscle exposed to anoxia are important for the future management of ischaemic heart disease. In the present study the effect of high concentrations of methyl prednisolone on the mechanical viability of heart muscle during and after anoxia has been studied using isolated isometrically contracting right ventricular papillary muscles of the cat. After equilibration in normally oxygenated ($O_2$ 95%)
and CO₂ 5%) Krebs solution containing 5 mM glucose, muscles were exposed to 90 minutes of anoxia (N₂ 95% and CO₂ 5%) and subsequently reoxygenated.

In 8 control muscles active tension fell progressively during anoxia to 22.8 ± 2.1 per cent of control at 30 minutes and 5.5 ± 1.4 per cent at 90 minutes. Resting tension rose by 1.5 ± 0.25 g/mm² at 90 minutes, indicating the development of contracture. During reoxygenation, active tension rose but only to 26.9 ± 7.5 per cent at 5 minutes and 49.5 ± 7.9 per cent at 60 minutes. Resting tension was still increased by 0.49 ± 0.14 g/mm² after 60 minutes of reoxygenation. These results in control muscles indicate impaired viability. In contrast in 8 muscles to which methyl prednisolone 1 x 10⁻⁶ M was added after 30 minutes of anoxia, the continued fall in active tension was prevented so that active tension was 21.8 ± 3.2 per cent of control at 90 minutes and resting tension had not risen. With reoxygenation, active tension rose to 64.7 ± 8.6 per cent of control at 5 minutes and 101.6 ± 5.7 per cent at 60 minutes. These changes all differ significantly from those in control muscles (P < 0.01).

The results demonstrate that methyl prednisolone exerts a direct effect to sustain viability and recoverability of anoxic heart muscle. This salutary effect of pharmacological concentrations of methyl prednisolone may result from stabilization of the membrane of cardiac lysosomes, so preventing the intracellular release of acid hydrolases.

Effect of propranolol and isoprenaline on ST segment and regional left ventricular blood flow in experimental myocardial ischaemia

Lewis Becker, Rafael Ferreira (both introduced), and Michael Thomas

Propranolol (P) inhibits and isoprenaline (I) exaggerates epicardial ST segment elevation. It has been proposed that these electrical changes relate to alterations in the degree of local ischaemia. To examine this hypothesis further, the effect of these drugs on regional left ventricular blood flow was determined.

Myocardial ischaemia was produced in 18 open-chested dogs by coronary artery ligation. Left ventricular blood flow was measured with 15 μ radioisotopic microspheres 60 minutes later. After intravenous administration of P (0.08 mg/kg) or I (1–5 μg/min infusion), it was measured again. Epicardial electrocardiograms were recorded at multiple sites just before each determination.

After P, raised ST segments were reduced in height (P < 0.01) and isoelectric ST segments became depressed (P < 0.05). Blood flow was unchanged in regions of low flow (< 0.3 ml/min/g) and reduced by 5–15 per cent in higher flow areas. After I, the height of raised ST segments increased (P < 0.001) and isoelectric ST segments became raised inside, but not outside, the margin of cyanosis. In spite of this, blood flow was unchanged in the outer half, and increased in the inner half of the ventricular wall in regions of low flow (< 0.5 ml/min/g). In higher flow areas there was an increase in flow in both halves.

Thus P inhibits ST elevation while blood flow is unchanged or reduced; I exaggerates ST elevation despite unchanged or increased flow. The effect of these drugs on ST segments must therefore be related to factors other than blood flow.

Circumstances attending 100 sudden deaths in men from coronary disease by coroner's necropsies

A. Myers (introduced), H. A. Dewar, and D. R. Appleton (introduced)

The exact circumstances in which these deaths took place were elicited from the nearest relative within 2 weeks of demise, and in such a way as to show whether they were likely to be coincidental or causal. The background of atherogenic factors was also obtained. A standard technique by the same two pathologists showed the relative proportions of coronary thromboses, of myocardial infarcts, of neither or both.

Significant factors were (1) the time of day and probably the day of the week, (2) exercise which was only occasionally violent or unusual, (3) preceding emotional stress, (4) a meal within one hour of death, (5) recent consumption of alcohol, (6) change from cold to warm environment.

Factors without significance were (1) season of the year, (2) the nature of the last meal and postprandial hyperlipaemia, (3) cigarette smoking in the hour preceding death, (4) change from warm to cold environment.

The pathological findings did not bear a close relation to the circumstances except that those who died in the 3 hours after taking alcohol were less likely to have fresh thrombi than the remainder; they did not display an unusual incidence of pulmonary oedema.

In only 23 per cent could the most efficient coronary ambulance service have had the opportunity of attempting resuscitation.

Surgery for acute coronary insufficiency

Alan Harris, Aubrey Leatham, David Wheatley (introduced), and Keith Ross

The objectives of vein bypass grafts for stenosis of coronary arteries are to abolish ischaemic pain and to prevent irreversible necrosis of heart muscle.

Bypass vein grafts have been performed in 5 patients with ischaemic pain increasing over a period of 1 to 4 weeks with or without preceding pain. In no case was there evidence of infarction. There was no mortality, no infarction at operation, and all 5 patients immediately lost their ischaemic pain. The results of restudying coronary and graft circulation were shown.
Normal electrocardiogram in severe angina pectoris requiring coronary venous bypass graft

Wolfgang Burian, Michael Petch, Richard Sutton (all introduced), and Lawson McDonald

Of 70 patients who underwent coronary venous bypass graft surgery because of grossly incapacitating angina pectoris, 10 showed a normal resting electrocardiogram: 9 were men; 1 was a woman. Their ages were 30 to 63 years. Four had suffered from previous myocardial infarctions, but no residual myocardial damage was present in the electrocardiogram.

Left ventricular angiography and cardiac catheterization revealed normal left ventricular function and end-diastolic pressures in all patients. In one case there was slight mitral regurgitation.

Coronary angiography demonstrated severe disease of one, two, or all major coronary arteries, with a predominance of disease that affected three vessels. It was a consistent feature that collaterals supplied the distal part of the diseased vessels.

Depending on the arterial disease that was present, patients had one to three vein grafts implanted. There have been so far no early or late postoperative deaths. Postoperative catheterization of 7 patients one to seven months after the operation showed 7 out of 15 grafts open.

The significance of a normal resting electrocardiogram in severe angina pectoris with respect to left ventricular function, the pattern of coronary arterial disease, operative treatment, and the follow-up of these patients were discussed.

Coronary artery bypass graft haemodynamics

Anthony Rickards, John Wright (both introduced), and Raphael Balcon

Measurements of blood flow in coronary artery bypass grafts have been shown to provide prognostic information about their long-term patency. However isolated measurements may be misleading as bypass graft flow depends on a large number of factors.

A series of measurements of coronary artery bypass graft flows have therefore been made in 24 grafts in 16 patients at the time of operation. In 12 patients aortic, ventricular, and atrial pressures have also been recorded.

The response of the variables to clamping the graft, and injections into the graft of nitroglycerin and papaverine have been determined.

Any individual vessel may or may not respond to the three interventions of ischaemia, nitroglycerin, and papaverine. However a response to one intervention is accompanied by a response to the others. Nitroglycerin and papaverine both increase graft flow providing arterial hypotension does not mask the response. Little effect of the interventions has so far been found on ventricular performance, but both vasodilators may profoundly affect the rate of ventricular relaxation (dp/dt min).

The significance of these observations and their relation to coronary anatomy were discussed.

External assessment of left ventricular function after coronary vein bypass graft surgery

Ricardo Seabra-Gomes, Winston Oh, Richard Sutton (all introduced by Lawson McDonald)

Systolic time intervals, left ventricular ejection time (LVET), pre-ejection period (PEP), and PEP/LVET ratio, measured externally from phonocardiograms, have been shown to reflect left ventricular function. Twenty patients with severe ischaemic heart disease were investigated before coronary venous bypass graft surgery with phonocardiography, left ventricular angiography, and selective coronary angiography. Postoperatively phonocardiography was performed on all patients at one week and at three months. Fourteen of these patients have been re-investigated postoperatively with left ventricular angiography and selective coronary and vein graft angiography in addition. The results show that at one week after operation systolic time intervals indicate a decrease in left ventricular performance; but at three months improvement over preoperative values was recorded. This improvement correlated well with vein graft patency and the findings at left ventricular angiography. Its relation to haemodynamic findings was discussed. Thus, external assessment of such patients is a clinically useful, repeatable, and atraumatic technique.

Natural history of slight mitral regurgitation

Howard Allen (introduced), Alan Harris, and Aubrey Leatham

A long-term follow-up has been completed in 62 patients believed to have isolated slight mitral regurgitation as manifest by a systolic murmur rising to a crescendo in late systole. The phonocardiographic day-books at the National Heart Hospital and St. George's Hospital were searched and all patients included in whom a phonocardiogram had been recorded between 1950 and 1963. They were excluded if the mitral regurgitation was thought to be more than slight as shown by left ventricular hypertrophy on the electrocardiogram or left atrial enlargement on x-ray, or if there was evidence of cardiac infarction. From 5 to 18 years later, in 1968, 58 of the 62 cases were traced and all those alive were re-examined and the electrocardiogram and x-ray were repeated. Four cases were lost, but death had not been recorded at Somerset House. The survivors were requestioned again by post in 1972, giving a follow-up varying from 9 to 22 years though the history of a murmur was usually much longer. In 1968 the follow-up revealed 3 deaths, one from cerebral haemorrhage, one from bacterial endocarditis, and one suddenly and no definite cause was found at necropsy, though there was evidence of mitral
valve disease, coronary artery disease, and left ventricular hypertrophy.

In 3 cases there was great deterioration as shown by heart failure or great increase in heart size. In one the cause was bacterial endocarditis, in the second, chordae of a floppy ballooning mitral valve had ruptured and the valve had to be replaced, and in the third, aged 74 years, the mitral regurgitation had increased in severity with the onset of atrial fibrillation.

In 10 cases there was electrocardiographic or radiological evidence of deterioration over a period of time averaging 10-8 years but they were all free of symptoms and free of heart failure. In 2 of the 10 cases there was obvious Marfan’s syndrome.

In the remaining 42 cases there was no change.

Cardiac lesions of Reiter’s syndrome and ankylosing spondylitis

J. A. Cash, D. W. Barritt, and M. I. V. Jayson (introduced)

Cardiac complications of Reiter’s syndrome and ankylosing spondylitis have been documented, but in practice are rarely seen. We, therefore, wish to report our experiences of these in a combined rheumatological and cardiological centre.

Two patients with Reiter’s syndrome developed severe aortic incompetence, necessitating aortic valve replacement. The operation presented particular difficulties in one because of a dilated aorta and very narrow coronary ostia. The histology of the cusps was shown. This patient is in left ventricular failure two years after operation with a normally functioning prosthesis. Left ventricular failure is thought to be due either to the poor coronary blood flow as a result of ostial narrowing or to ischaemic damage at operation. The second patient has an excellent result at four years. Another patient with Reiter’s syndrome showed temporary partial heart block coinciding with activity of the Reiter’s disease.

A survey of 47 patients with ankylosing spondylitis revealed only one with aortic incompetence. Four other cases of ankylosing spondylitis with severe aortic incompetence were found separately. One died and the pathology of the aortic valve was shown. Unexplained heart failure occurred in a further patient with ankylosing spondylitis. In other patients without aortic incompetence conduction defects were also present.

The cardiac lesions of Reiter’s syndrome and ankylosing spondylitis are remarkably similar, if not identical. The similarities and differences between the degrees of spinal involvement in the two conditions were presented and discussed. Reiter’s disease can easily be overlooked as a cause for severe aortic incompetence.

Localization of lesions in endomyocardial fibrosis

A. G. Shaper and B. J. Bellhouse (introduced)

The lesions in tropical endemic endomyocardial fibrosis have a characteristic localization at the ventricular apex and on the mural endocardium behind the posterior cusps of the mitral valve. There is often a conspicuous ridge on the septal wall of the left ventricle. In general, lesions are more conspicuous and thrombi are more frequent in the left ventricle.

The use of a model left ventricle provides a possible explanation for the localization and character of the lesions in endomyocardial fibrosis (Bellhouse, 1972). A study of ventricular diastolic flow patterns shows that the incoming jet strikes the apex of the left ventricle and spreads around the sides of the ventricle to produce a strong asymmetrical ring-vortex. The main vortex strength and highest wall shear stress is in the outflow tract and behind the anterior cusp. The region behind the posterior cusp is almost stagnant during diastole and wall shear stress is very low. In systole, wall shear-stress is high only in the outflow tract. The distribution of endomyocardial fibrosis appears to be confined initially to regions of low wall shear-stress. The predominance of lesions on the left side may possibly be explained in terms of differential pressure fluctuations and muscle compliance.

Reference


Quantification of pulmonary blood flow by new radioisotope technique

Eric D. Silove, Elizabeth Jones, A. R. Chrispin (all introduced), and Gerald R. Graham

A new technique has been designed to measure pulmonary arterial blood flow in the presence of large shunts in congenital heart defects. The method embodies established concepts of indicator dilution and consists of injecting $^{99m}$Tc human serum albumin (10 μCi/kg) into the main pulmonary artery and recording the isotope dilution curve by external counting over the lung.

Validation of the method has been performed in dogs. Forty simultaneous dye and isotope dilution curves were obtained. The cardiac output was deliberately changed by drugs to obtain a range of values and, in some experiments, dogs with surgical aortopulmonary shunts were used. Because the downslopes of the isotope dilution curves were interrupted by recirculation relatively later than the dye dilution curves, exponential extrapolation to the baseline was easier, particularly in the dogs with left-to-right shunts.

A significant correlation was found between the values for pulmonary blood flow obtained by the two methods (r = 0.96), there was no systematic discrepancy between them, and both were reproducible. It is suggested that the isotope dilution method may simplify pulmonary blood flow measurements in infants and children since it is relatively undisturbing, less invasive than other methods, and involves an acceptably low radiation dose.
Surgical management of pulmonary atresia with intact ventricular septum in first month of life

G. A. H. Miller, M. Paneth, and S. C. Lennox

Patients with intact septum pulmonary atresia have been classified into type I, with small right ventricle (RV) and no tricuspid incompetence, and type II, with large RV and tricuspid incompetence. Pulmonary valvotomy has been advocated for type II with an ‘adequate’ RV. In our experience a clear division based on RV size and tricuspid incompetence is an oversimplification and pulmonary valvotomy uniformly unsuccessful (in striking contrast to neonates with critical pulmonary stenosis in whom it is the operation of choice). Of 17 neonates with intact septum pulmonary atresia operations performed were: (1) closed pulmonary valvotomy, 3 (one with Waterston shunt): 2 hospital deaths, 1 late death; (2) open hypothermic valvotomy, 4: 4 hospital deaths; (3) Waterston shunt alone, 6: 3 hospital deaths, 2 late deaths, 1 good result (17%). (4) Waterston shunt plus atrial septectomy; 4: 1 late death, 3 good results (75%). Thus the only good results were obtained with a shunt and the best with a combination of shunt and septectomy. Only 2 patients had a large RV; both died after hypothermic valvotomy.

Subsequent complete correction demands development of the RV and tricuspid valve and this may be an indication for combining pulmonary valvotomy with a shunt and septectomy.

Aortic-left ventricular tunnel: presentation and management

Jane Somerville, Donald Ross, and Terence English (introduced)

Serious lone congenital aortic regurgitation is an uncommon problem. Four patients aged 6 years to 16 years presented at the National Heart Hospital with signs of severe aortic regurgitation which had been recognized before the age of 5 years in all. Anatomical proof was obtained and in each revealed an endothelialized aortic-left ventricular tunnel opening into the right coronary sinus.

There were clinical and radiological features which differentiated this condition from simple aortic valvar regurgitation. At operation in all the tunnel was closed from the aortic side. One patient, the eldest aged 16 years at operation, died at a third operation for persistent aortic regurgitation.

The diagnosis of this anomaly should be considered in all children presenting with serious aortic regurgitation that is possibly congenital, as it is unlikely to be due to a primary valve abnormality. The haemodynamic lesion can be ‘cured’ by surgical closure of the tunnel providing this is done early before the aortic valve and root are stretched, as this may leave a problem of true valve regurgitation. From this experience, it is suggested that all children presenting with important congenital aortic regurgitation should have angiocardiographic inv-}

vestigation early to differentiate those with a tunnel which can be dealt with easily, from patients with primary valvar regurgitation possibly requiring valve replacement which has an unknown long-term future.

Study of specialized conducting tissue in cases of single ventricle

R. S. Jones, R. H. Anderson, R. Arnold, M. Thapar (last three introduced), and D. Hamilton

A study of the published reports reveals that, though described under different names, most cases of single or common ventricle conform to the type in which both AV valves and one arterial trunk connect with a main ventricular chamber, while the other great vessel arises from a smaller ventricular chamber. We have studied 13 cases of this type, and we find the conducting tissue uniformly arranged in an unusual fashion. A posterior AV node in the interatrial septum makes no contact with ventricular myocardium. Atrioventricular continuity is effected through an anterior node-like structure situated parietally in the right atrium at its junction with the pulmonary ring. An AV bundle arises from this structure, pierces the fibrous ring, and runs down the right border of the foramen between the two ventricular chambers to bifurcate on the septum between the chambers. These results indicate the importance of diagnosing this type of single ventricle before possible corrective procedures, since the only previous report indicated that conducting tissue in single ventricle was posterior. The findings also suggest that the septum is true interventricular septum, while the finding of valvar tension apparatus in the smaller chamber suggests that this is a hypoplastic right ventricle.

Biological availability of digoxin

T. R. D. Shaw (introduced by John Hamer)

The recent alteration in the production process for Lanoxin tablets has revealed the extent of incomplete absorption of digoxin from many of the tablets currently available. Our previous studies had shown that similar plasma levels of digoxin measured by radio-immunoassay were obtained in most patients with a number of different brands of tablet, including the Lanoxin tablet in use before the change in the production process. However, there is considerable variation in digoxin absorption from one patient to another, and in a few patients a striking variation in biological availability from different preparations was noticed.

Studies with the new version of Lanoxin show a conspicuous improvement in biological availability compared to other preparations. Cross-over studies in a group of patients have shown an overall plasma level of 1.5 ng/ml after a dose of 0.5 mg a day, compared to 0.9 ng/ml for the preparation available previously. The absorption of digoxin from the new Lanoxin tablet approaches that found with digoxin powder in cachets.
Although the change in tablet formulation has given rise to many difficulties of patient management, the new preparation has the advantage of a more satisfactory biological availability in patients with critical limitation of digoxin absorption.

Variable dose comparative trial of propranolol and sotalol in angina pectoris

Margaret E. Horn and B. N. C. Prichard (both introduced by A. Hollman)

It is important that the dosage of drugs used in a comparative trial should be adjusted to optimum for the individual patient. This approach has shown that propranolol is more effective than practolol in angina (Prichard, Lionel, and Richardson, 1971). This study was similarly designed, each patient receiving randomized for two weeks, sotalol, propranolol, 1/8 propranolol. This cycle of randomization was repeated 4 times, 24 weeks for the trial. Placebo was not included as a significant difference was found between 1/8 and full dose propranolol (Prichard and Gillam, 1971). Propranolol was found superior to sotalol, sotalol superior to 1/8 propranolol. The difference between sotalol and the other treatments in terms of number of anginal attacks was not quite significant. If two patients who showed no difference between 1/8 and full dose propranolol are excluded, the difference in the number of attacks is significant; 41 (SE 13) propranolol, 67 (SE 25) sotalol. (P < 0.05, n = 12). These findings differ from our results with practolol which was found similar to 1/8 propranolol (Prichard et al., 1971).

References


Accelerated atrioventricular conduction induced by smoking in ischaemic heart disease

E. Fletcher, P. Morton, C. Murtagh, and S. Bekheit (last two introduced)

The effects of smoking on myocardial conduction were measured in 12 volunteer subjects with ischaemic heart disease, aged 49 to 67 years, 8 of whom had a recent myocardial infarction within a three-month period. Increments of conduction, atrial, AV nodal, and His-Purkinje system were made from simultaneously recorded His bundle electrograms and scalar leads. When basic records were taken, the conducting tissues were stressed by atrial pacing at selected rates between 90 and 150 a minute before and during smoking of one or two cigarettes. All observations were performed within 10 minutes. The technique of smoking was measured in puffs/minute. No complications occurred. Three subjects ‘oversmoked’ (2 cigarettes at 3 puffs/minute) resulting in nicotine intoxication with pallor and nausea. The following results were obtained.

1) AV nodal conduction was significantly accelerated by smoking (P < 0.005 < 0.001).

2) The normal Wenckebach block due to decremental AV nodal conduction during stress of the conducting system by incremental atrial pacing was abolished at specific rates by smoking.

3) Atrial conduction and His-Purkinje system conduction were not altered by smoking.

The specific acceleration of AV nodal conduction may result from adrenergic stimulation of nicotine inhaled in the main stream smoke. Ventricular ectopic beats induced by smoking appear to depend on increased automaticity (phase 4 depolarization) rather than slowed His-Purkinje conduction in ischaemic heart disease.

Results of aortic fascia lata and pericardium valve replacement

Marian I. Ionescu, Brojesh C. Pakrashi, Michael P. Holden, David A. Mary (last three introduced), William Whitaker, and Geoffrey H. Wooler

One hundred patients had aortic valve replacement with a three-cusp, frame-mounted graft made of autologous or homologous fascia lata or of heterologous pericardium. The follow-up period extended over 42 months. The incidence in both hospital and late mortality was 8 per cent, with myocardial failure and infective endocarditis as main aetiological factors.

Considerable symptomatic improvement was obtained by all surviving patients. There was a statistically significant reduction in cardiothoracic ratio and in the voltage of the electrocardiogram.

Twelve patients developed aortic diastolic murmurs between one and eight months after operation. The murmurs have remained unchanged. By clinical and angiographic assessment the aortic regurgitation was graded trivial in 7 patients (due in 3 of them to perivalvular leak), mild in 2, and moderate in 3.

Thromboembolic complications and haemolysis have been absent. Anticoagulants were not used.

The performance of the grafts was evaluated by angiography, pressure recordings, and by ‘in vitro’ hydrodynamic studies.

Conclusions of investigations and experimental work were discussed.

There has been no difference in performance between the 3 types of grafts used.

In the aortic position, these grafts have shown good function with no emboli and no graft failure over a period of 34 years.

Aortic valve replacement using fresh unstented homografts

Magdi H. Yacoub, E. Knight (introduced), Malcolm Towers, and Walter Somerville

Between August 1969 and July 1972, 223 patients aged 7 to 76 years had their aortic valve replaced by fresh
aortic valve homografts. The valve was purely or dominantly stenotic in 132 patients, regurgitant in 41, and mixed in 50.

In 130 patients the aortic valve alone was replaced. Additional procedures were performed in 83, including mitral valve replacement by fresh unstenosed homografts in 64, open mitral valvotomy or repair in 18, replacement of the ascending aorta by a Dacron graft in 6, and aorto-coronary bypass graft in 1.

The operative mortality for elective valve replacement was 5 per cent (5% for single and 9% for double valve replacement) and that for emergency aortic valve replacement was 5 in 13 patients.

In all, 125 patients were followed up for 1 to 3 years, the remainder for less than 1 year. There were 12 late deaths (5.5%) of causes not related to valve function. Trivial to mild aortic regurgitation developed in 18 patients and moderate to severe in 2. Late valve failure due to rupture or calcification was not observed. Infective endocarditis was a late complication in 5 patients, requiring a further operation in 4. Except for these, all patients are symptom free or considerably improved. Anticoagulants were not used; no systemic emboli have occurred.

This experience has encouraged the continued exclusive use of fresh homografts for aortic valve replacement at Harefield Hospital.

Results of Starr-Edwards valve replacement in 184 patients: factors influencing mortality and morbidity

Marion Crouchman (introduced), O. S. Tubbs, and I. M. Hill

Since 1963, a total of 189 Starr-Edwards aortic valve replacements have been carried out at St. Bartholomew’s Hospital in 184 patients (36 female, 149 male) aged between 14 and 65 years. There have been 22 operative deaths (i.e., deaths occurring during or after surgery up until discharge from the ward), giving an overall mortality of 11.6 per cent. However, this represents a reduction in operative deaths from 20 per cent in 1964 to 10 per cent in 1971, and there have been no deaths among the 23 patients operated on in the first half of 1972. There has also been no operative mortality among the small group (8 patients) undergoing their second bypass.

We have looked at immediate and long-term survival in relation to age, sex, preoperative status (in particular, the presence of left ventricular failure or angina), bypass time, coronary perfusion, and valve size, and have attempted to define the cause of deaths in both groups.

We have also recorded the incidence and outcome of neurological and psychological sequelae, embolic episodes, major and minor complications attributable to the use of anticoagulants (there have been 2 fatal cerebrovascular accidents), major sepsis, and postoperative subacute bacterial endocarditis.

Results of 100 consecutive mitral valve replacement operations using Starr-Edwards prostheses in a general hospital

B. A. Ross, H. Hosseini, A. J. Clement, A. Ersoz (all introduced), and M. V. Brainbridge

One hundred unselected consecutive cases of prosthetic valve replacement in the mitral position are reported. These have been treated between 1965 and 1971 at St. Thomas’ Hospital. Follow-up extends over a period of 9 to 79 months (mean 21 months). Preoperative symptoms placed the majority in group 2b with regard to exertional dyspnoea. One-third of the patients had a previous closed mitral valvotomy.

Important details of operative technique are emphasized, these points being supported by the low incidence of paravalvar leak and thrombembolic complications.

Operative mortality was 12 per cent and the late mortality during follow-up a further 11 per cent of the survivors, the causes of death being discussed. The operative mortality during 1970–71 was 3 per cent. Postoperative complications include subacute bacterial endocarditis in 5 cases; thromboembolism was seen in 3 cases, none of which were fatal. Mitral regurgitation necessitating reoperation for paravalvar leak occurred in one case, a pansystolic apical murmur suggestive of trivial mitral reflux in another. Neither haemolytic anaemia nor prosthetic valve dysfunction was seen in this series.

Of the 78 cases available for follow-up, 61 are well, improved on their preoperative status, and the majority are asymptomatic.

The authors feel that prosthetic mitral valve replacement can be performed with an acceptable mortality and a low incidence of postoperative complications.

Early experience with Björk-Shiley tilting disc prosthesis

W. H. Bain, M. A. Turner (introduced), and R. M. Thomson

The Björk-Shiley tilting disc prosthesis seems to offer several advantages as a heart valve replacement (Björk, 1969).

This paper presented clinical and laboratory results of its use to replace the mitral, aortic, and tricuspid valves in 54 patients (82 prostheses) followed for 4 months to 2 years.

Hospital and late mortality figures were as follows: Single valve replacement 2 out of 34; double valve replacement 3 out of 20.

There has been one early embolic episode associated with conversion of atrial fibrillation to sinus rhythm three weeks after operation. There have been no late emboli and no complications related to anticoagulant therapy.

In contrast to our experience with Starr-Edwards prostheses, there has been no incidence of traumatic
prosthetic anaemia, though the presence of a peri-prosthetic leak in 6 patients is associated with laboratory evidence of shortened red cell life.

Study of 3 prostheses at necropsy 6 months after implantation showed excellent incorporation of the sewing ring and no encroachment on the flow pathway, nor any evidence of wear.

Results in terms of exercise tolerance and ability to return to work are good and were detailed for each group.

Reference

Late results of valvoplastic for mitral regurgitation due to rupture of chordae tendineae of posterior cusp
B. A. Ross, A. Hedley Brown, C. Fox (all introduced), M. M. Webb-Peploe, and M. V. Brainbridge

Nine patients with severe mitral regurgitation due to ruptured chordae tendineae of the posterior cusp have been treated by a modified McGoon plication valvoplastic. The advantages of conservative procedures rather than prosthetic valve replacement when the annulus was normal were outlined. Relevant details of preoperative diagnosis, operative technique, and postoperative assessment were discussed.

Follow-up extends from 12 months to 6 years (mean 36 months). Assessment has been clinical but by an independent cardiologist. All 9 patients are greatly improved symptomatically. One patient shows an apical pansystolic murmur of moderate intensity (2/4), 7 patients have a murmur of slight intensity (1/4), and one patient has no murmur at all. All patients show a significant reduction of heart size on x-ray and resolution of pulmonary venous congestion, and this improvement has been maintained in all with no deterioration over the years.

The excellent clinical state of these patients makes further left heart catheter or angiographic assessment, though desirable, difficult to justify.

Haemodynamic studies 5 to 11 years after mitral anuloplasty
Brojesh C. Pekrashi, David A. Mary, Raymond J. Donnelly (all introduced), Marian I. Ionescu, and Geoffrey H. Wooler

From a total of 50 patients with mitral anuloplasty followed up to 15 years, 14 had preoperative haemodynamic studies performed at rest. All 14 were in class III (NYHA).

These patients were restudied, at rest and during exercise, five to eleven years after operation when 12 were found to be in class I, and 2 in class II (NYHA).

There was no significant difference in the oxygen uptake between these two investigations. The mean postoperative cardiac index was not significantly different (P > 0.05) from the preoperative mean value. The mean postoperative pulmonary wedge pressure and pulmonary artery pressure were significantly lower (P < 0.02 and P < 0.05, respectively) than the corresponding preoperative values.

Analysing the postoperative data only, the mean values at rest and during exercise were, for pulmonary wedge pressure 14 ± 6 and 33 ± 10 mmHg; for pulmonary artery pressure 24 ± 11 and 44 ± 15 mmHg and for left ventricular end-diastolic pressure 4 ± 6 and 8 ± 7 mmHg, respectively.

Ventriculography showed minimal or no mitral regurgitation in 10 patients, moderate in 3, and severe in one.

It is concluded that mitral annuloplasty results in satisfactory long-term haemodynamic improvement. The results were discussed in comparison with those obtained after mitral valve replacement.

Heart block in Devonshire
C. D. Eraut, R. C. Evans (both introduced), and D. B. Shaw

The necessity of a countrywide pacemaker service for patients with heart block is now accepted, but the data of incidence or prevalence of block are scant. The place of artificial pacemakers in patients with persistent Adams-Stokes attacks or gross bradycardia is well established, their use in subjects with less dramatic illness is controversial. Current assessments of the advantages of pacemaker therapy tend to come from metropolitan teaching hospitals. Inevitably, the patients upon whom these reports are based are highly selected and the size of population from which they are drawn is unknown. With these factors in mind, a survey was started to measure the prevalence, incidence, and mortality of patients with heart block living in the Devon clinical area, by making a direct approach to the general practitioners. This report gives the results of the first 4 years of the study.

The population in the study area is approximately 600,000 and is served by 290 general practitioners. 357 patients with conduction disturbances were seen, of whom 224 had complete heart block. The incidence of cases of complete block was close to the generally quoted figure of 63 per million population, but the prevalence of the condition was about double the expected figure. The overall mortality for patients with complete block was 25 per cent at one year and 33 per cent at two years.

Concealed bypasses of AV node, revealed by electrical stimulation techniques and intravenous verapamil
R. A. J. Spurrell (introduced), D. M. Krikler, D. C. Deuchar, and E. Sowton

A group of patients with paroxysmal supraventricular tachycardia has been studied using His bundle electro-
grams and programmed intracardiac electrical stimulation. None of the patients showed evidence of the Wolff-Parkinson-White or Lown-Ganong-Levine syndromes on their external electrocardiograms.

All patients were thought to have a reciprocating mechanism as the basis for their tachycardia.

In 4 patients ventricular pacing up to 180 beats a minute was carried out with no prolongation of retrograde conduction. This suggested a bypass of the atrioventricular node as normally retrograde conduction prolongs with increasing ventricular rates due to delay within the AV node. During termination of the tachycardia, after intravenous verapamil, it was found that antegrade conduction was progressively prolonged until it was blocked and the tachycardia terminated. However, verapamil had no effect on retrograde conduction which remained constant. It is known that the main effect of verapamil is on the AV node only and so the above finding suggested that retrograde conduction in these 4 patients was via an extra AV nodal bypass possibly of the James type as described in the Lown-Ganong-Levine syndrome.

A fifth patient was shown to use three intra AV nodal pathways during tachycardia but during termination of the tachycardia with verapamil an extra AV nodal bypass became manifest. This bypass was thought to be in the right atrioventricular groove as is found in the Wolff-Parkinson-White syndrome type B.

Electrophysiological and other effects on cardiac function of KÖ 1173

B. N. Singh (introduced) and E. M. Vaughan Williams

KÖ 1173, 1-(2',6'-dimethylphenoxy)-2-aminopropane, bears some chemical resemblance to lignocaine, but is completely and rapidly absorbed when taken by mouth. In its mode of action on the heart it resembles lignocaine in several respects. It depresses the maximum rate of depolarization without affecting the resting potential or increasing the duration of the action potential. It equals lignocaine in potency as a local anaesthetic on stripped frog nerve. In guinea-pigs anaesthetized with urethane, in which ventricular fibrillation had been produced by an intravenous infusion of ouabain, KÖ 1173 caused reversion to sinus rhythm in 10 out of 10 animals, the mean intravenous dose required being 3.3 mg (15.3 μmol)/kg. Pretreatment with KÖ 1173 before the start of the ouabain infusion did not prevent the occurrence of fibrillation, with the implication that the initial peak blood level of the drug fell rapidly. KÖ 1173 intravenous caused an initial bradycardia, but this did not last more than 5 minutes and was not affected before injection of atropine. KÖ 1173 had other effects typical of a class I antidysrhythmic drug; it reduced the maximum frequency at which rabbit atria would follow a stimulus, raised electrical threshold, slowed conduction velocity, and depressed contractions.

Effect of KÖ 1173, a new antiarrhythmic drug, on contractile state of diseased left ventricle and on frequency of 'stable' premature beats

T. R. D. Shaw and R. Royds (both introduced by John Hamer)

KÖ 1173 is a new antiarrhythmic agent which has a membrane stabilizing action like lignocaine but does not cause beta-blockade and is effectively absorbed after oral administration. It has been shown to have effective antiarrhythmic properties in dogs.

The effect on the contractile state of the abnormal left ventricle was assessed by measurement of the changes in aortic ball valve travel time after intravenous injections of the drug in patients with Starr-Edwards aortic prostheses. Ball valve travel time was prolonged after administration of KÖ 1173 indicating depression of left ventricular contractile state. The degree of prolongation increased with progressive increments in the total dose given.

The effect in these patients was similar to that produced by the same doses of lignocaine.

Propranolol, but not practolol, produced a greater degree of depression of contractility. Phenytoin had an effect similar to KÖ 1173 and lignocaine.

The effect of 100 mg intravenous bolus doses of KÖ 1173 on 'stable' premature beats was studied for a one-hour period after injection. Suppression of ectopic activity occurred very quickly in the majority of patients, and the effect persisted throughout the hour, though blood levels fell rapidly.

It was concluded that KÖ 1173 was an effective antiarrhythmic drug with effects on left ventricular contractile state comparable to those of lignocaine.

KÖ 1173 – an effective new antiarrhythmic drug

R. A. Clark, R. G. Talbot, J. Nimmo, L. F. Prescott (all introduced), and D. G. Julian

The effect of KÖ 1173, 1-(2',6'-dimethylphenoxy)-2-aminopropane, which has antiarrhythmic activity in animals, has been submitted to trial in 38 patients and in 6 healthy subjects.

In 6 patients with ventricular arrhythmias secondary to digoxin, intravenous doses of 30 to 250 mg proved effective. In 24 patients with acute ventricular arrhythmias (18 had resisted other therapy), 100 to 300 mg intravenously followed by infusions of 500 mg over 3 to 12 hours arrested or suppressed the arrhythmia. In 8 patients recurrent ventricular arrhythmias were prevented by a daily dose of 450 to 1050 mg.

Plasma concentrations of KÖ 1173 were measured by gas chromatography (30 patients). The minimum mean effective concentration (14 patients) was 1.42 μg/ml (range 0.66 to 2.90). Toxic effects were usual at concentrations of 2.5 to 5 μg/ml and were common when the drug was administered intravenously. The mean half life (11 patients) was 18½ hours (range 10 to 26 hours).
The drug disappeared quickly from the plasma after intravenous injection and rapid rates of infusion were required to maintain plasma levels. Plasma concentrations in 6 healthy volunteers measured 0.34 to 0.54 μg/ml 1 to 4 hours after oral doses of 3 mg/kg body weight. The mean half-life was 114 hours (range 8 to 14 hours). Ten per cent of the drug was excreted unchanged in the urine within 72 hours but the percentage varied with the pH of the urine.

KÖ 1173 is a useful oral drug in the long-term management of ventricular arrhythmias.

Effects of KÖ 1173 on ventricular arrhythmias

N. Campbell, J. Kelly, J. Strong (all introduced), R. G. Shanks, and J. F. Pantridge

Ousain and adrenaline/halothane induced ventricular tachycardia and ventricular dysrhythmias after coronary artery ligation were abolished in dogs by KÖ 1173. Its effects on oral and intravenous administration have been studied in 42 patients with ventricular dysrhythmias and the clinical results correlated with spectrofluorometrically measured plasma levels.

Intravenous administration of 50–200 mg KÖ 1173 abolished chronic ventricular ectopies. Similar bolus followed by intravenous infusion of 1–3 mg/min controlled lignocaine-resistant ventricular dysrhythmias in 9 of 12 patients. Intravenous KÖ 1173 has been used successfully as an alternative to intravenous lignocaine in the initial control of ventricular dysrhythmias complicating acute myocardial infarction. The therapeutic plasma level was 1–2 μg/ml.

Oral administration of KÖ 1173 in a dose of 0.6–1.2 g daily was also effective in the control of ventricular dysrhythmias complicating myocardial infarction.

Side effects seen usually with plasma levels >2.0 μg/ml included dizziness or drowsiness (9 patients), nausea (7 patients), neurological signs (15 patients). The majority of these side effects were mild and disappeared on reduction of the dosage. Bradyrhythmia and hypotension occurred in 9 patients and were immediately corrected by atropine in 8. The other patient responded to glucagon.

Synchronous AV pacing with a single percutaneous electrode

D. A. Chamberlain, D. J. Woollons, N. M. White, and M. J. English (last three introduced)

In the treatment of complete AV block, conventional pacing techniques result in the restoration of a satisfactory ventricular rate, but the loss of atrial synchrony. The unfavourable haemodynamic effects of asynchronous pacing may be of critical importance in some patients with severely impaired myocardial function. Pacing atria and ventricles sequentially restores co-ordinated action but pacemaker rate must exceed that of the sinus, and two electrodes are required. An external pacing system has been devised which uses only one percutaneous electrode both for sensing spontaneous atrial depolarization and also stimulating the ventricle after a preset delay. Intra-atrial signals as small as 0.3 mV will suffice to trigger the system; deflections resulting from ventricular depolarization are selectively gated out. Safe pacing rates are ensured by adjustable upper and lower limits for stimulus intervals, and the pacemaker functions in a demand (inhibited) mode to avoid competition with spontaneous beats. Preliminary experience has been gained in 12 patients, 6 with recent infarction. Reliable AV pacing was achieved in 5 instances (average 23 hours). In 4 other patients synchronous pacing was interrupted only by return of sinus rhythm or sinus bradycardia. The technique is simple and safe, and may be advantageous in low output states.

Measurement of instantaneous left ventricular volumes and filling rate in man by echocardiography

D. G. Gibson and D. Brown (introduced)

A method has been developed allowing measurement of instantaneous values of left ventricular dimensions and volumes together with their respective rates of change. Using an IBM 1800 computer, the positions of the echoes arising from the interventricular septum and posterior wall of the left ventricle were digitized and expressed as a series of 200 data points, from which the ventricular dimension was derived by subtraction. To illustrate its potential applications, a study was made of left ventricular filling in man. In normal subjects the peak early diastolic filling rate was 500–1200 ml/sec, while in patients with mitral regurgitation due to ruptured chordae it was significantly reduced (150–300 ml/sec). In a group of patients with mitral regurgitation due to ruptured chordae it was significantly increased to a mean value of 2300 ml/sec. It was also possible to define the relation between stroke volume and peak filling rate and to delineate abnormalities of ventricular filling associated with severe aortic regurgitation and mitral valve replacement by a Starr-Edwards prosthesis.

Assessment of left ventricular filling and compliance using an ultrasound technique

Clive Layton, Graham Gent, Ronald Priddle (all introduced), Alastair McDonald, and Wallace Brigden

Analysis of the diastolic closure rate of the structurally normal mitral valve has been performed in a group of patients undergoing diagnostic cardiac catheterization. All the patients had an abnormal ventricular diastolic pressure/volume relation as judged by the left ventricular ΔP/ΔV, indicating an increase in the resistance to ventricular filling. The linear relation which exists between the diastolic closure rate of the mitral valve and
the left ventricular filling pressure was found to be determined by the level of the resistance to filling, there being a further linear relation between the change in the closure rate per 1 mmHg change in filling pressure and the left ventricular ΔP/ΔV.

The analysis of the diastolic closure rate of the normal mitral valve in relation to the left ventricular filling pressures may therefore provide useful information on the level of the resistance to ventricular filling, a major determinant of which is the ventricular compliance. The method remains valid in the presence of mitral or aortic regurgitation and should therefore prove useful in clinical practice.

**Diastolic closure rate of mitral valve as determined by ultrasound**

G. Ziady, H. Madeira, R. Pridie, G. Callen (all introduced), and C. Oakley

The diastolic closure rate of the anterior leaflet of the mitral valve was recorded in 46 normal persons. It was found to range between 120–200 mm/sec.

It was also recorded in 14 patients with aortic regurgitation, in 12 patients with ventricular septal defect or persistent ductus arteriosus, in 22 patients with congestive cardiomyopathy and in 38 patients with hypertrophic obstructive cardiomyopathy.

The diastolic closure rate was outside the normal range in all the patients studied. In aortic regurgitation and left-to-right shunt it ranged between 245–425 mm/sec, being highest in those with the largest left ventricular stroke volumes. The rates fell to normal after surgical correction of the defect or aortic valve replacement.

In congestive cardiomyopathy, the diastolic closure rate ranged between 260–385 mm/sec, and showed a positive correlation with the height of the left atrial pressure.

The diastolic closure rate in hypertrophic obstructive cardiomyopathy ranged between 45–100 mm/sec. No relation was found between the diastolic closure rate and the presence or degree of mitral incompetence or with the height of the left atrial pressure.

Our conclusion is that the diastolic closure rate of the mitral valve has a relation to the height of the left atrial pressure and the left ventricular stroke volume. Reduced left ventricular compliance in hypertrophic obstructive cardiomyopathy, with a slow left ventricular filling rate, results in a retarded rate of diastolic closure of the mitral valve.

These observations give added insight into the mechanisms affecting diastolic closure of the mitral valve.

**Echocardiography of normal and diseased aortic valve**

Özgen Feisi (introduced), Cecil Symons, and Magdi Yacoub

Aortic valve echocardiography has been performed in 165 subjects, comprising 52 patients with isolated aortic valve disease, 60 with normal aortic valves but with other valvar disease, 43 with nonvalvar heart disease, and 10 healthy subjects. In each case, aortic cusp movement and thickness were assessed and aortic root diameter measured. In 92 patients, the findings were correlated with those obtained at operation, catheter angiography, or necropsy.

The normal aortic valve echocardiogram is described; evidence is given that the anteriorly visualized cusp is always the right coronary cusp, but the cusp which is posteriorly visualized may be the noncoronary or the left coronary cusp. The estimated size of the aortic root related accurately to that measured at operation or at necropsy.

Characteristic aortic valve ultrasound patterns for degenerative aortic valve disease, calcific aortic stenosis, aortic regurgitation, and mixed aortic valve disease were described. Echocardiograms after homograft replacement showed cusp movement indistinguishable from normal valves.

It is concluded that echocardiography of the aortic valve is valuable diagnostically, is easy to perform, and is contributory in the pre- and postoperative assessment of patients with aortic valve disease.

**Echocardiographic features of mitral Starr-Edwards paraprosthesis regurgitation**

H. C. Miller, J. Stephens (both introduced), and D. Gibson

Fourteen patients with persistent or recurrent symptoms after mitral valve replacement with Starr-Edwards prostheses were studied by echocardiography, right and left heart catheterization, and left ventricular cineangiography, and one additional patient was studied by echocardiography alone. Nine patients had moderate or severe regurgitation demonstrated on left ventricular cineangiography or at operation. Two patients had mild paraprosthetic regurgitation and 4 patients had no paraprosthetic leak, their symptoms being attributed to poor left ventricular function in 3 cases and an obstructed prosthesis in the fourth. A correct diagnosis was predicted by echocardiography in 14 cases before catheterization or operation, but clinical examination and analysis of systolic time intervals were unreliable. The normally functioning mitral prosthesis has associated paradoxical movement of the ventricular septum. When significant regurgitation is present the septum moves normally. Abnormalities of ventricular volumes and ventricular filling rates have allowed distinction between myocardial failure and obstruction at the mitral prosthesis. The value of echocardiography as a diagnostic method for assessment of patients after Starr-Edwards mitral valve replacement is discussed, together with an explanation of the echocardiographic changes.

**New method for production of isopotential surface maps from one cardiac cycle**

D. M. Monro, R. A. L. Guardo, J. Tinker, R. Freyer, and P. J. Bourdillon (all introduced by J. F. Goodwin)

Accurate delineation of an area of myocardial ischaemia
or infarction is of considerable clinical importance. Iso-
potential surface maps extend the capabilities for
achieving this, but because the methods used to obtain
and display them are cumbersome, the investigation
has not been widely employed. A new system is described
for deriving detailed maps from 24 chest electrodes with
the display in a dynamic mode on cine film.

By using three horizontal straps, each containing eight
equally spaced electrodes, the time for lead placement is
minimized. A simultaneous recording from all 24 ele-
ctrodes takes only a little longer to perform than does a
conventional electrocardiogram. A significant improve-
ment in the elimination of interference is obtained by
incorporating amplifiers into the electrodes. The signals
are converted into digital form and the mathematical
processing necessary to interpolate the potential values
at other points over the chest is carried out by a digital
computer.

A study of 12 normal subjects by this technique con-
firms that the thoracic potential distribution during the
QRS cycle is in part dipolar and in part multipolar, and
that significant information about the electrical activity
of the heart is to be found on the thoracic wall outside
the regions explored by the routine chest leads.

Positive inotropic action of ouabain

Winifred G. Nayler (introduced by Peter Harris)

The positive inotropic effect of ouabain is accompanied
by an increase in the amount of extracellular calcium
which can be used for contraction. The sensitivity of
the contractile proteins to calcium remains unchanged.
In heart muscle excitation-contraction coupling involves
an influx of calcium from the extra to the intracellular
phase. The inotropic activity of ouabain, therefore, may
reflect an activation of the 'carrier system' which trans-
ports calcium across the membrane. However, some of
the calcium which is displaced inwards during excitation
originates from superficially-located binding sites, prob-
ably from within the plasmalemma. The amount of
calcium stored at these sites can be determined by using
lanthanum to displace the calcium. The cell membrane
is impermeable to lanthanum which remains in the
extracellular space. Doses of ouabain which have a dose-
dependent positive inotropic effect on mammalian heart
muscle increase the amount of calcium stored at these
superficially located sites. According to the currently
held concepts of events involved in excitation-contraction
coupling, this effect of ouabain would result in an
increased availability of calcium for inwards displace-
ment during excitation.

Radiotelemetry of intra-arterial pressure in man

H. M. Brash, J. B. Irving (both introduced), Brian
J. Kirby, and K. W. Donald

We have developed a method for recording intra-arterial
pressure using radiotelemetry in order to study the fac-
tors influencing arterial pressure in normotensive and
hypertensive subjects. The system has three main
advantages: (1) it is unobtrusive, (2) observations can be
made during activity without the subject’s knowledge,
and (3) the arterial wave form can be accurately recorded.
Intra-arterial pressure is measured from a catheter in
the radial artery by a miniature pressure transducer
whose output is amplified and modulates a crystal con-
trolled transmitter. The signal is received up to 200
metres away and demodulated to produce the original
wave form. Recordings can be made continuously or
intermittently onto paper or electromagnetic tape.

We have recorded arterial pressure for 30-second
periods every 4 1/2 minutes for periods of 24 hours in 5
normal and 10 hypertensive subjects. Arterial pressure
varied widely in both groups throughout the day. We
found an obvious diurnal variation in both normal and
hypertensive subjects with a fall of approximately 40
mmHg in the diastolic pressure of both groups. Low arterial
pressures (e.g. systolic pressure < 80 mmHg) were often
observed in normal subjects during sleep. These findings
could account for the difficulties encountered in clinical
practice in the interpretation of casual blood pressure
recordings. The low pressures in normal subjects during
sleep suggest caution in the interpretation of data
acquired in intensive care situations.

Combined alpha and beta adrenergic blockade
in treatment of hypertension

P. A. Majid, B. Sharma, M. K. Meeran (all
introduced), and S. H. Taylor

The antihypertensive activity of the beta-blocking drugs
is associated with a reduction in cardiac output without
change in vascular resistance. The lowering of blood
pressure due to alpha-receptor antagonism is countered
by reflex increase in cardiac output. A combination of
the vasodilator alpha and beta receptor antagonists
should therefore have synergistic antihypertensive
effects.

Twelve patients with uncomplicated hypertension
were studied at rest and during submaximal bicycle
exercise. In 6 patients control studies were followed by
an infusion of phentolamine (1 mg min intravenously)
and the rest and exercise studies repeated. Oxprenolol
(0.2 mg/kg) was then given and the studies repeated for
the third time. In the remaining 6 patients, the order of
phentolamine and oxprenolol was reversed. In the first
group, phentolamine resulted in a reduction in sys-
temic arterial pressure, a reduction in left ventricular
end-diastolic pressure, and an increase in heart rate and
cardiac output. The addition of oxprenolol reduced the
heart rate and cardiac output and resulted in a further
lowering of the blood pressure both at rest and on exer-
cise. Reversing the order of the drug administration
had the same end result, namely a reduction in systemic
blood pressure to within normal limits, a normal cardiac
output, and a normal left ventricular end-dias-
tolic pressure.

These findings suggest that combined alpha and beta-
receptor antagonism has a conspicuous antihypertensive
effect in which the disadvantages of either therapy alone
are mutually counteracted.