Proceedings of the British Cardiac Society

The 64th Annual General Meeting of the British Cardiac Society was held at the University of Birmingham on Wednesday and Thursday, 17 and 18 April 1985. The President, M F Oliver, took the Chair during private business.

The following were elected to the British Cardiac Society.

New Ordinary Members: F Akhras (London); L D Allan (Kent); S H Armistead (Glamorgan); M Been (Edinburgh); N A Boon (Oxford); H Brown (Newcastle); C Bull (London); J E Burns (Edinburgh); J C Catford (Hampshire); S Chierchia (London); C M Dancy (London); M K Davies (Birmingham); J E Deanfield (London); N G Dewhurst (Edinburgh); S J Edmondson (London); B E Griffiths (Cardiff); D J Gwilt (Buckinghamshire); J D S Higginson (Co Down); J D Hill (Derbyshire); C J Hilton (Newcastle); D W Holt (London); P M Holt (Hertfordshire); E Jackson (Lincoln); M P G Jameson (Glasgow); O D H Jones (London); H Larkin (Harrogate); P Magee (London); M A Martin (Cheshire); J McComb (Belfast); W J McKenna (London); C A Morley (Leeds); A Murray (Newcastle); J B O’Riordan (London); C Pumphrey (London); I J Reece (Glasgow); R H Robinson (Carlisle); F P Shabbo (London); L M Shapiro (London); D F Shore (Southampton); H Singh (Cardiff); R H Smith (Cleveland); A D Timmis (London); B D Vallance (Glasgow); J Weir (Kincardineshire); C Wilson (Co Antrim); N Wilson (Leeds).

New Corresponding Members: A C Arntzenius (Netherlands); P Avogaro (Italy); R Conti (USA); L Ceremuzynski (Poland); T Killip (USA); B Pitt (USA); T W Smith (USA); A Waldenstrom (Sweden); J V Warren (USA).

New Extraordinary Members: D H Makinson, J Norman, G B Shaw, D S Short, R E Steiner.

Resignations: J R Belcher, J M Bishop, J Dark, M B Matthews, A D McInnes, D Verel.

Death: D C Muir.

Elections
D G Julian elected President; J H S Horgan and M Petch elected to Council.

Abstracts of papers

Natural history of patients following intravenous thrombolytic therapy for acute myocardial infarction

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Intravenous thrombolytic therapy (BRL 26921) was administered to 48 patients (31 male, 17 female; mean age 61 years) within six hours from the onset of symptoms. The group was comprised of 23 anterior and 25 inferior infarctions. Reperfusion of the infarct related vessel was confirmed angiographically in 42 (87%) patients, and of these, nine (21%) subsequently reoccluded. Reocclusions occurred between 2 and 11 days postmyocardial infarction and most commonly occurred in patients with severe residual narrowing of the reperfused vessel with poor antegrade flow or in patients where anticoagulant control was suboptimal. There was no correlation between reocclusion and the age or sex of the patient or the time to administration of thrombolytic treatment or the number of diseased vessels present.

All patients underwent follow up for at least six months and up to 12 months. Nine deaths occurred, all within 17 days of myocardial infarction, and these include six patients who showed no evidence of reperfusion or subsequently reoccluded. The other three deaths were among the 33 patients in whom coronary artery reperfusion was demonstrated and vessel patency was maintained. During the follow up period eight (17%) patients subsequently developed angina associated with a positive exercise test, and four of these were treated successfully with surgery. One perioperative death occurred.

Therefore, intravenous thrombolytic therapy with BRL 26921 resulted in a high reperfusion rate, but failure to achieve reperfusion or subsequent reocclusion was associated with an approximately fourfold increase in short term mortality. Residual coronary artery stenoses may result in further ischaemic episodes for which coronary angioplasty or surgery may be indicated.

Reocclusion following coronary reperfusion: incidence, time course and consequences

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A severe residual stenosis is common following acute coronary thrombolysis, and there is concern regarding the further "natural history" of these lesions. In a series of 50 patients with a first myocardial infarction and successful coronary thrombolysis with acylated streptokinase, further episodes of pain occurred in 18. Reocclusion was suggested in nine patients by a second rise in cardiac enzymes and demonstrated at angiography in one without creatine kinase elevation. The standard postreperfusion regimen was heparin for five days followed by warfarin for 3–6 months except when contraindicated. Forty four were maintained on anticoagulation and reocclusion occurred in seven (16%) of these compared with three of six patients in whom anticoagulation was not maintained (50%). Reocclusion occurred at a median time of nine days after initial reperfusion.

Radionuclide ejection fraction was measured routinely at 10 days and again after reocclusion if this occurred later than 10 days. In the group with both measurements the left ventricular ejection fraction fell by 10% (mean) following reocclusion. Intervention coronary artery bypass graft (CABG) or percutaneous transluminal coronary angioplasty (PTCA) was performed in 11 at a median time of eight weeks (range two weeks to 11 months) in patients thought to be at risk of reocclusion causing extensive infarction.

Our results suggest that anticoagulation is important in maintaining reperfusion. Reocclusion occurs most commonly within the first two weeks following reperfusion with acylated streptokinase and may be maintained without major additional interventions. The place of CABG and PTCA following coronary reperfusion requires further study.

Factors influencing early results of percutaneous transluminal coronary angioplasty

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The results of 306 consecutive coronary angioplasty procedures have been analysed in order to evaluate the factors predictive of angiographic success. Ability to cross the stenosis was the principal determinant of success. Multiple regression analysis of all baseline variables identified six additional factors associated with success. These were the number of dilatations performed, preoperative stenosis, age, male sex, the experience of the operator, and the severity of preoperative angina. Univariate predictors of success by $\chi^2$ testing were the ability to cross the stenosis ($p<0.001$) and performing more than five dilatations per stenosis ($p<0.05$). Other more weakly predictive variables were preoperative stenosis <90%, age <50 years and male sex ($0.05<p<0.1$). Of interest were the factors unrelated to success which included elective versus emergency procedures, brachial versus femoral approach, single versus multivessel disease, and single versus multivessel angioplasty. These data illustrate the interaction of both procedural and patient variables in determining the success of coronary angioplasty. Because crossing the stenosis is the principal predictor of success, advances in catheter technology are likely to improve further the early results of the procedure.
Stenosis recurrence following coronary angioplasty: changes in stenosis length

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Stenosis recurrence is the major long term problem following successful percutaneous transluminal coronary angioplasty, and its causes are unknown. Little attention has been given to measurements of stenosis length after recurrence. We have studied the coronary angiograms from 35 of the 41 patients who had a successful outcome from angioplasty when it was undertaken in 50 consecutive subjects. Twenty nine men and six women with a mean age of 50 years were evaluated immediately before and then several months after (5–12, mean 7) successful angioplasty. In every case angioplasty was carried out using balloons with a length of 2.0 cm and a notional diameter of 3.0 mm on inflation. The vessels treated were the left anterior descending artery (29 cases) and the right coronary artery (six cases). Stenosis severity and length were measured directly from tracings of single frames of the coronary angiogram, and the measurements were made (where possible) in three standard radiological projections. Twelve (34%) patients were found to have restenosis; in two of the 12 the treated vessel was totally occluded at the site of dilatation. In the remaining 10 patients with recurrence, the calculated length of the restenosis was greater in seven, similar in one, and less in two patients than the length of the original stenosis. Considering the projection in which the stenosis length was greatest the mean length before angioplasty was 8.8 mm (range 5.8–16.3), whereas several months later the mean restenosis was 10.4 mm (range 8.7–15.3) long, although this did not reach statistical significance.

These results confirm the high frequency of restenosis after successful percutaneous transluminal coronary angioplasty and suggest that coronary angioplasty may induce a longer stenosis.

Absence of late relapse following percutaneous transluminal coronary angioplasty

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Initial analysis of patients who have relapsed following successful percutaneous transluminal coronary angioplasty showed that this had always occurred within the first year. We therefore analysed all relapses occurring in patients who have been followed for more than one year after successful angioplasty. Twenty two of 137 (16%) eligible patients had relapsed after a mean time of 22 (range 1–52) weeks. Six of the 22 (27%) relapses occurred between six and 12 months. The relapse rate in patients followed for more than two years was 9/58 (16%) also. Only one of 11 patients followed for more than three years has relapsed (9%).

Presentation was by recurrence of angina in 75% and by an abnormal exercise test in the remainder. Reangiography was performed in all those who relapsed. No patient was found to have relapsed solely as a result of routine follow up angiography. Early relapse was associated with inadequate dilatation of the original lesion.

In 14% of those relapsing the site of the original angioplasty was still wide open but a new lesion had developed. A further 9% had restenosed at the original site and also developed a new lesion elsewhere. Treatment following relapse was medical in one third, by further angioplasty in another third, and by referral for surgery in the remainder. The longest follow up after reangioplasty was in a patient with recurrence of left anterior descending artery stenosis who is still symptom free on maximal treadmill exercise 3½ years after redilatation.

As one in four of patients who will relapse have not done so at the six months point the calculated relapse rate will be artificially low if patients with short follow ups are included. In this series the relapse rate did not rise during the second or third year of follow up.

Beneficial effect of high dose propranolol treatment in infants with symptomatic hypertrophic cardiomyopathy

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Hypertrophic cardiomyopathy presenting with congestive heart failure in infancy carries a grave prognosis, with a mortality of virtually 100%. A high dose (7–10 mg/kg/day) oral propranolol treatment was used in five infants presenting with symptomatic hypertrophic cardiomyopathy confirmed by cardiac catheterisation. The age of presentation ranged from neonatal period to 18 months, and the symptoms included uncontrollable congestive heart failure, failure to thrive, and syncopal episodes. Propranolol treatment caused improvement in all infants; in one
infant propranolol treatment was discontinued and he died shortly afterwards from heart failure. The other four are alive and asymptomatic after two to four years follow up. The start of propranolol therapy was associated with disappearance of congestive heart failure, return to normal weight gain, and a gradual improvement in electrocardiographic evidence of hypertrophy with a resolution of abnormal ST and T wave changes. M mode and cross sectional echocardiography has shown regression of abnormal hypertrophy, with in one case virtual return to normal appearances.

It is concluded that propranolol can cause not only symptomatic relief but also partial regression of pathological changes in infants with hypertrophic cardiomyopathy but that a high dose is essential in order to achieve the latter effect.

Use of pulsed Doppler echocardiography to assess shunts and gradients in congenital heart disease

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This study compares Doppler measured haemodynamic variables with those found by conventional methods at cardiac catheterisation. The comparison was made in 162 cases. Fifty nine children with obstructive lesions and 41 with pressure gradients across ventricular septal defects were studied using high pulse repetition frequency Doppler. Peak jet velocities were obtained by placing the Doppler sample volume in the jet stream and the pressure gradient calculated using the modified Bernoulli equation (ΔP=4V², where V is the peak jet velocity). Right ventricular pressure was predicted by subtracting the ventricular septal defect gradient from the systemic blood pressure.

Flow ratios (QP:QS) were measured by Doppler in 62 patients with intracardiac shunts. Systemic flow (QS) was measured from the suprasternal notch by placing the sample volume in the ascending aorta and obtaining a mean flow velocity (V). The cross sectional area (CSA) was derived from the aortic diameter; QS=V×CSA. Pulmonary flow (QP) was similarly measured from the main pulmonary artery. The Doppler derived QP:QS was compared with that obtained at catheterisation (Fick).

There was good correlation between the two methods for measuring pressure gradients (r=0.94, n=100) and flow ratios (r=0.92, n=62). Predicted right ventricular pressure in patients with ventricular septal defect also correlated well with catheterisation values (r=0.93, n=41).
Percutaneous balloon valvotomy for pulmonary valve stenosis

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Significant pulmonary valve stenosis has usually been managed by surgical valvotomy. We have attempted relief of pulmonary valve stenosis at cardiac catheterisation on 21 occasions in 20 patients between April and December 1984. There were 12 males, eight females (age range 8 days to 12 years, median 31 months, two aged less than 2 weeks). Two patients had Noonan's syndrome, one had an associated right coronary artery to right ventricle fistula, and two had undergone previous surgical valvotomy. The remaining 15 patients had isolated pulmonary valve stenosis. Pulmonary valve annulus diameter was estimated by cross sectional echocardiography to assist in choice of balloon size. Predilatation right ventricular systolic pressures ranged from 41 to 190 (median 92) mm Hg, being suprasystemic on nine occasions. Right ventricle to systemic systolic pressure ratios and pulmonary systolic pressure gradients (mm Hg) were 1.01(0.43) (mean (SD)) and 76.3(41.6) respectively prior to dilatation compared with 0.69(0.29) (p<0.001) and 34.3(29.1) (p<0.001) immediately following balloon dilatation. Six patients so far have been reinvestigated six months and one patient one week after dilatation. Five had maintained the immediate haemodynamic improvement previously demonstrated. Two patients who had little immediate change in right ventricle to systemic systolic pressure ratio or pulmonary systolic pressure gradient had major reductions in both of these at one week and six months respectively. There were no complications. Percutaneous balloon pulmonary valvotomy appears to provide good short and medium term relief of pulmonary valve stenosis and may obviate the need for surgery in many cases.

Outcome of children with double inlet ventricle presenting in the first year of life

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Definitive repair is now possible for selected older patients with double inlet ventricles. However, the overall outcome of children presenting in infancy with this condition has not been investigated. We therefore studied 107 consecutive patients presenting at less than 1 year of age between 1973 and 1984. Eighty one (76%) had double inlet left ventricle, 18 double inlet right ventricle, and eight double inlet indeterminate ventricle. Sixty two (63%) had two atrioventricular valves and 45 (47%) had a common atrioventricular orifice. Presentation was determined by one or more severe associated lesions (pulmonary stenosis 35, pulmonary atresia 23, aortic coarctation or interruption 25, extracardiac anomalous pulmonary venous connection 15). Fifty one (46%) underwent palliative surgery, but the operative mortality was high (30%): 3/17 systemic-pulmonary shunts, 2/15 pulmonary artery banding, 3/7 atrial septectomies, 8/12 repair of associated lesions. The remaining 56 were initially treated medically either because they had very complex anatomy (29, 25 dead), were unfit for surgery (nine, nine dead), or had balanced physiology (18, four late deaths). Five of the balanced group subsequently required palliative surgery. Among those palliated, five died late (four sudden, one pneumonia), two required a second shunt, and two developed subaortic obstruction after pulmonary artery banding. Of 19/39 survivors for 2 years who were reinvestigated, five were unsuitable for definitive repair (because of subaortic obstruction in two, common atrioventricular orifice regurgitation in one, pulmonary vascular disease in one, distorted pulmonary arteries in one). Only two modified Fontans (one death) and one septation have so far been performed. Thus, even with palliative surgery, only a minority of patients born with double inlet ventricle survive and are suitable for eventual definitive repair.

Patient status 10 or more years after primary total correction of tetralogy of Fallot under the age of 2 years

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Twenty two children who underwent primary total correction of tetralogy of Fallot (irrespective of their anatomy), under the age of 2 years, have been followed up for more than 10 (mean 11.3) years. Their ages at operation were between 3-5 to 24 (mean 13.7) months. Nine (41%) children had additional reconstruction of the right ventricular outflow tract with an
aortic homograft monocusp. With a follow up of 10 to 13-25 (mean 11-3) years, there have been no late deaths. The first child in the series required reoperation at 28 months for relief of residual right ventricular outflow tract gradient. (He did not have an outflow tract reconstruction at the first operation.) All children are asymptomatic and have a normal exercise tolerance. Four (44%) children with homograft reconstruction and three (23%) without developed soft pulmonary diastolic murmurs 2-4 years after operation. This murmur has not become louder and the cardiothoracic ratio (mean 0-54) on chest radiograph has not increased with time, neither has the right ventricular/left ventricular dimension obtained from routine M mode echocardiography, at the level of the tip of the mitral valve. Ventricular ectopies have not been noted on either the standard electrocardiogram or 24 hour monitoring. Sixteen children have an axis of 0° to 30°. All patients have been routinely reinvestigated by cardiac catheterisation and angiography two weeks to 12 years (mean 27 months) after operation.

In 20 (91%) patients the peak systolic right ventricular to left ventricular ratio was between 0-2 to 0-4 and the right ventricular outflow tract gradient less than 15 mm Hg. There was no increase in ratio or gradient with time in those patients who obtained adequate relief of their right ventricular outflow tract obstruction at operation.

It is concluded that primary total correction of tetralogy of Fallot, under 2 years of age, continues to give good clinical and haemodynamic results more than 10 years after operation.

**Automatic detection of cardiac arrhythmias by analysis of electrogram morphology**

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Pacemaker recognition of pathological tachycardia currently relies on heart rate analysis. Sinus tachycardia on exercise or after arrhythmia termination are thereby commonly mistaken for pathological tachycardia. To overcome this, we have developed a potentially implantable computerised method of automatic arrhythmia recognition. This operates independently of changes in heart rate by analysing the changes that occur in the intracardiac sequence of gradients during arrhythmias.

In 12 patients bipolar electrograms were obtained from conventional endocardial pacing sites in the atrium (six patients), ventricle (three), and both (three) during sinus rhythm (three pre-excited) at rest and exercise and during a total of 14 abnormal rhythms: orthodromic atrioventricular re-entry tachycardia (AVRT) with or without left bundle branch block (four), antidromic AVRT (one), atrioventricular nodal tachycardia (AVNRT) in five, and ventricular tachycardia (VT) in four. Patient posture and respiration were varied during all rhythms. The electrograms were recorded at a band pass of 0-16-1 kHz and digitised at a frequency of 2*
Hz before analysis by electrogram gradient pattern detection. Gradient pattern of atrial electrograms during sinus and abnormal rhythms distinguished AVRT and AVNRT from sinus rhythm in all patients. Gradient pattern detection of ventricular electrograms differentiated sinus rhythm from VT in all patients, orthodromic AVRT from pre-excited sinus rhythm in both patients, sinus rhythm from antidromic AVRT in one patient (partial vs complete pre-excitation), and intermittent left bundle branch block during AVRT in one patient. Although alterations in amplitudes of atrial electrograms occurred with respiratory and postural variation in four patients, the electrogram morphologies and hence gradient pattern detection were unaffected. It is concluded that gradient pattern detection reliably detects arrhythmias at atrial and ventricular level and overcomes a major problem of present day antiarrhythmia pacemakers.

Reliability of the QT interval in determining the pacing rate in patients with the TX pacemaker

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The TX pacemaker uses a conventional electrode to sense T waves of paced ventricular complexes, and it adapts the pacing rate to varying physiological demands by responding to changes in the QT, or more correctly stimulus artefact-to-T wave apex interval. This pacing system was assessed in 13 patients. Relation of heart rate to stimulus to T interval and effect of programming on rate changes during exercise were studied on several occasions in each patient. Exercise performance during TX and asynchronous ventricular demand (VVI, 70 beats/min) pacing modes were compared.

T wave sensing was successful in 12 patients. Chronic deterioration in T wave sensing, however, occurred in most patients. The relation of heart rate to stimulus to T interval was found to be described by the following linear regression equation: stimulus to T interval = 590 - 1.58 × paced heart rate, r = -0.62. This relation, however, was subject to wide interpatient and intrapatient variation. Consequently, given identical programmed variables and exercise protocol, the quality of rate response varied widely from patient to patient and in the same patient from one occasion to another. Treadmill exercise tolerance, however, was significantly better in the TX mode: total distance (yd) walked on treadmill (mean (1 SD) for TX mode

Pace mapping: a valuable alternative technique for localisation of the accessory atrioventricular pathway at surgery

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Localisation of the accessory atrioventricular pathway for surgical ablation may be impossible by activation mapping if anterograde and retrograde conduction via the atrioventricular pathway is temporarily lost during the procedure. The technique of pace mapping was used in five patients undergoing such surgery. A 12 lead electrocardiogram was recorded with a clear delta wave, during sinus rhythm or atrial pacing both before surgery and if possible after exposure of the heart. Pacing pulses were applied to sites around the atrioventricular ring first epicardially and then endocardially until the pattern of the initial deflection of the QRS complex matched that of the previously recorded delta wave in all 12 leads. This site was cut and cauterised. In two patients activation and pace mapping were performed and the sites identified by the two techniques coincided. In the other three patients accessory atrioventricular pathway conduction was lost and successful division was achieved by pace mapping alone.

It is concluded that pace mapping is a valuable additional technique in surgery for Wolff-Parkinson-White syndrome.

A randomised trial of heart valve prostheses

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Between December 1975 and August 1979, 540 patients undergoing valve replacement were entered into a randomised trial and received either a mechanical (Björk-Shiley, 274 patients) prosthesis or a porcine heterograft valve (initially Hancock, 106 patients, and latterly Carpentier-Edwards, 160 patients). Analysis of multiple variables showed the treatment groups to be well randomised. For mitral valve replacement (268 patients) there was an unexplained excess hospital mortality of 16-4% associated with the Carpentier-Edwards valve compared with 7-6% overall. There was no significant difference in hospital mortality for the different prostheses for aortic valve replacement (210 patients), 8-5% overall, nor for the combined valve replacement (62 patients), 14-5% overall.

Mean follow up was 5-6 (range 2-8-8.3) years. The actuarial survival curves for both aortic valve replacement, mitral valve replacement, and the combined valve replacement for the three prostheses remained similar for 7-5 years. Actuarial survival at 3-3, 5, and 7-5 years following mitral valve replacement was 70-6%, 67-2%, and 51-8%; for aortic valve replacement, 83-6%, 80-1%, and 67-7%; for the combined valve replacement 74-7%, 72-9% and 62-5% respectively. Thirty four patients underwent valve rereplacement: 13 Björk-Shiley, 10 Hancock, and 11 Carpentier-Edwards prostheses (p=NS); 12 died at reoperation (operative mortality 35-3%).

There was no significant difference in the incidence of thromboembolism for the different prostheses up to seven years after surgery though approximately 50% of patients with heterograft valves were not anticoagulated. Complications of anticoagulation were rare and occurred in only 16 patients over the course of the study.

It is concluded that up to 7-5 years there is no significant difference in the outcome of valve replacement with the three prostheses studied, but further follow up is necessary as important differences may still emerge.

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Recent experience with acute ventricular septal defect: the case for immediate surgery with restricted use of balloon pumping

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From 1980 to 1984, 29 patients with an acquired ventricular septal defect have been treated by a policy of increasingly early surgery after immediate investigations on admission to our hospital. Twenty five patients had defects associated with an anterior myocardial infarction and four with an inferior myocardial infarction. The mean age was 66 (range 48-77) years and the mean time interval from onset of murmur to operation was 10-3 (range 1-60) days, a reflection of delayed referral. Twelve patients were in cardiogenic shock (blood pressure <80 mm Hg, poor peripheral perfusion, and urine <300 ml in 24 hours). Coronary angiography in 28 patients (one arrest, no study) showed one vessel disease in 38%, two in 19%, and three in 38%. Only five patients early in the experience had preoperative balloon pumping. Double patch closure of the ventricular septal defect with infarctectomy in eight patients and saphenous vein grafting in 14 was undertaken. Two patients had cardiac massage to bypass and two required immediate postbypass balloon pumping. Overall hospital mortality at 30 days was 33% reducing to four of 19 (22%) in the last two years. Mortality in the presence of cardiogenic shock was 58% and renal failure (>20 mmol/l) was 40% and infarctectomy 0%. Two recurrent ventricular septal defects occurred, one requiring reoperation. Death resulted from myocardial failure in three patients, multiorgan failure in three, and cerebrovascular disease in one, and there were two sudden deaths five days and three weeks after an initial satisfactory postoperative course. The policy of early closure of ventricular septal defect with ressection of large infarctions and simultaneous bypass grafting seems appropriate. Referral to a surgical centre prior to the onset of cardiogenic shock or renal failure should achieve better results. Preoperative intra-aortic balloon pumping has a very limited role in current management.

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Left ventricular contractile state and reserve capacity in humans after cardiac transplantation

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Limited data are available concerning left ventricular contractility and contractile reserve in the denervated human heart. The slope value of the relation of left ventricular end systolic pressure to dimension is a
load independent sensitive index of contractility which can be determined using echo and calibrated carotid pulse tracings. This index was studied in 10 transplant patients (aged 48(4) years; interval between operation and study 1.2(0-8) years). None of the patients had evidence of rejection by biopsy. Results were compared with data from 10 normal control subjects (aged 25(4) years) matched for donor heart (aged 25(6) years). Baseline left ventricular contractility was assessed over a wide range of afterload generated by methoxamine infusion. Contractile reserve was measured during infusion of methoxamine plus 5 mg/kg/min of dobutamine.

Baseline heart rate and values after drug infusion for controls were 88(21) and 97(20) beats/min respectively (p<0.01); the corresponding values for transplant patients were 92(6) and 117(8) beats/min (p<0.01). The difference between baseline values for controls and transplant patients was not significant; that between values after drug infusion for the two groups was significant (p<0.01). Control baseline values and those after drug infusion for the slope value of the relation of end systolic pressure to dimension were 104(13) and 129(15) respectively; the corresponding figures for transplant patients were 99(9) and 126(12) respectively. The differences between both groups for baseline values and those after drug infusion were not significant.

It is concluded that the transplanted human heart had normal baseline and reserve contractile capacity while demonstrating an augmented chronotropic response. Chronic denervation does not appear to alter left ventricular contractility in humans.

Annual study of transplant function included right and left heart catheterisation and right ventricular biopsy. Response of preload and afterload pressures, cardiac output, and pulmonary and systemic vascular resistance to maximal exercise testing was investigated. The grouped data show that (a) cardiac function of the transplanted heart provides for normal output response to exercise; (b) normal functional responses are maintained without significant decline for one to five years; (c) the normal neurally mediated physiological rate response is absent but is compensated by stroke volume response; (d) abnormally high preoperative pulmonary vascular resistance returns to normal and shows a wide range of change in response to exercise; (e) patients receiving cyclosporin A have an abnormal systemic pressure and resistance response; (f) there is no evidence of motor reinnervation of the transplanted heart; and (g) good function is maintained in the presence of significant coronary stenoses and occlusions.

**Symptoms plus exercise test: a reliable basis for managing angina?**

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The practice of basing the diagnosis and management of patients with suspected coronary disease on the history and exercise test alone is generally considered inadequate. The diagnostic and prognostic value of a simple method of patient classification based on symptoms and exercise testing was tested in 300 patients with suspected angina, reviewing their progress after 36-48 months. Patients with typical pain and positive exercise testing (ST depression or elevation) were classified as having coronary artery disease (group 1); those with atypical pain and a negative exercise test (at target heart rate) as not having coronary artery disease (group 2); and those whose type of pain conflicted with their exercise test, or who failed to reach target heart rate, as having possible coronary artery disease (group 3). In group 1 (n=186), 122 underwent coronary arteriography, and 121 had significant coronary artery disease (99% specificity). Nineteen coronary deaths occurred. In group 2 (n=41), none had arteriography and no coronary events occurred. In group 3 (n=73), 22 underwent arteriography; 13 were normal. Two coronary deaths occurred, both in patients with severe angina who

**Function of the transplanted heart in long term survivors**

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Thirty eight heart transplant recipients were studied in detail after five years (one patient), four years (four patients), three years (six patients), two years (11 patients), and one year (16 patients). Six of these patients subsequently died; two of lung cancer and four of coronary artery disease, of whom two had no angiographically detectable lesions. One patient has been retransplanted for coronary artery disease, and another six have angiographically demonstrated lesions from one to five years after transplantation.
were studied angiographically. In group 1 patients, an exercise test duration of six minutes or less appeared to identify a subgroup (n=71) who required urgent surgery (coronary artery bypass grafting): seven of the 26 (27%) who did not undergo grafting died or suffered an ultimately fatal myocardial infarction within four months of their exercise test. This contrasted with a 3% annual mortality among 45 patients in this subgroup who underwent grafting and with a 1.3% annual mortality among 82 non-surgically treated group 1 patients who exercised for longer than six minutes. It is concluded that the combined use of symptoms and exercise testing can be relied on to identify patients in whom arteriography is superfluous and those requiring urgent grafts.

What is the need for coronary artery bypass procedures?

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During the six year period 1979–84, 518 patients were referred by a district general hospital for invasive investigation and cardiopulmonary bypass procedures. The resident catchment population was 202 000. There was a sevenfold increase in the number of patients undergoing coronary artery bypass graft procedures during this period while the requirement for valve surgery showed little growth. The need for grafting plateaued in 1982–4, and based on the figures for 1982–3 (the data for 1984 as yet incomplete) there was a requirement for 330 procedures/million population/year after correction for cross boundary inflow. The requirement for valve surgery during this period was 61 procedures/million population/year. Analysis of the clinical and angiographic data indicates that if grafting had been offered only for angina (≥NYHA grade II in patients receiving maximal drug therapy) the requirement would have fallen to 204 procedures/million population/year, although this would have increased to 215 procedures/million population/year if surgery was also offered for significant left main stem disease. Two hundred and eighty one and 305 procedures/million population/year would have been required respectively if patients with significant three vessel and two vessel with significant left anterior descending stenosis were also included. The health district concerned (North West Surrey) has a standardised mortality ratio of 0.78 for cardiovascular diseases, and these figures therefore probably underestimate the need for coronary artery bypass grafting nationally.

By extrapolation, however, the national need for surgery for symptoms alone appears to be at least twice the present provision, three or four times the present provision being required if surgery is also offered to improve prognosis.

Non-invasive testing and coronary arteriography in patients with unstable angina pectoris

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In patients with unstable angina the diagnostic accuracy of thallium scintigraphy combined with maximal exercise stress testing related to coronary arteriography is unknown. During 124 consecutive acute admissions with spontaneous chest pain at rest in the absence of acute myocardial infarction, 110 patients had a maximal exercise stress test with thallium scintigraphy. In 66 this was followed by coronary arteriography. Fifty four patients had a positive angiogram (stenoses ≥ 50%) in the disease distribution: single vessel 15 (28%), double vessel 17 (31%), triple vessel 20 (37%), and main stem two (4%). Of these, 28 had a positive exercise electrocardiogram (≥2 mm ST segment depression), two a negative electrocardiogram, and 24 an inconclusive electrocardiogram (no electrocardiographic changes but inadequate heart rate). Fifty of 54 with coronary artery disease had a positive thallium scan (reperfusion, fixed defect or both). When the exercise electrocardiograms and thallium scan were combined and a positive result from either or both obtained then non-invasive testing predicted coronary artery disease in 52 of 54 patients. The two cases missed had single vessel disease. Of the 12 patients without angiographic coronary artery disease, eight were normal and four had other cardiac diagnoses (two mitral valve prolapse, one hypertrophic cardiomyopathy, and one left ventricular hypertrophy). Of the eight normals, one had a negative exercise electrocardiogram, two a positive one, and in five it was inconclusive. Four had positive thallium images and four negative.

It is concluded that maximal exercise testing early after the identification of patients with unstable angina is safe but that the exercise electrocardiogram on its own is poorly predictive and should not be used to exclude ischaemic heart disease (28/54, 52%). Thallium scintigraphy combined with the exercise electrocardiogram greatly improved diagnostic accuracy (52/54, 96%).
Risk stratification following myocardial infarction: a comparison of the Norris index and exercise testing

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Recent controversy surrounds the ability of predischarge exercise test to predict subsequent cardiac events in survivors of acute myocardial infarction. In contrast, the Norris prognostic index remains a recognized discriminant of high risk. To determine the relative value of these potential risk markers the results of predischarge exercise testing and the Norris index were compared with the clinical outcome in 350 survivors of acute myocardial infarction followed for a mean of 12 months. Exercise testing was performed at a mean of nine days and defined as positive by ST segment depression >0.1 mV in any of the 12 leads recorded or exertional hypotension or both. On clinical grounds, 50 of the 350 patients were considered unable to perform predischarge exercise. These 50 patients had a higher Norris index (7.0 vs 4.43; p<0.01), higher mortality (18% vs 5%; p<0.01), higher frequency of heart failure (52% vs 12%; p<0.01), and recurrent infarction (20% vs 8%; p<0.05) than the 300 patients able to exercise. In the 300 exercise patients, however, the Norris index in 170 patients with positive tests (4.38(1.7)) was similar to the index in 13 patients with negative tests (4.49(1.7)). In contrast, mortality (7% vs 2%), recurrent infarction (13% vs 2%; p<0.001), heart failure (22% vs 2%; p<0.001), angina (58% vs 9%; p<0.001), and cardiac surgery (22% vs 2%; p<0.001) were significantly more common in those with positive tests compared to those with negative tests.

These data support the clinical value of the Norris index as a marker of high risk following acute myocardial infarction. In terms of both mortality and morbidity, however, predischarge exercise testing provided a more sensitive risk stratification in infarct survivors.

First dose hypotension with angiotensin converting enzyme inhibitors in heart failure

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In patients with heart failure first dose hypotension with captopril is thought to be uncommon, occurring only in subjects with markedly increased plasma renin; it has been suggested that enalapril does not cause this owing to its delayed onset of action. In a series of 100 such administrations (75 captopril and 25 enalapril) in 68 patients, seven cases of vasomotor syncope occurred (hypotension accompanied by bradycardia and sweating). With enalapril (three cases) the onset of hypotension was later (>2.5 h vs <90 min), more sustained, and accompanied by evidence of organ damage (myocardial necrosis or renal dysfunction). In those monitored invasively profound falls in pulmonary artery diastolic pressure accompanied or preceded syncope suggesting that a fall in venous return rather than a loss of peripheral arteriolar tone was involved. Large increases in plasma adrenaline but not noradrenaline during syncope suggested a dissociation of adrenal and sympathetic neuronal responses. Two recovered spontaneously, two responded to head down tilt and intravenous atropine, and three required intravenous angiotensin II. Two showed a poor response to this until given intravenous saline.

Neither clinical state, aetiology of heart failure, pre-treatment mean blood pressure (60–100 vs 56–119 mm Hg), serum sodium (127–141 vs 125–150 mmol/l), plasma active renin (41–2234 vs 5–6687 uU/ml), nor angiotensin II concentrations (25–284 vs 0.5–292 pmol/l) reliably predicted syncope. (Figures are ranges for hypotensive and non-hypotensive groups respectively.) Thus first dose hypotension is difficult to predict. Patients should be observed for some hours after dosing with converting enzyme inhibitors and angiotensin II, and saline infusions should be readily available.

Prolonged clinical benefit of enalapril in treatment of congestive cardiac failure

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Angiotensin converting enzyme inhibition is a valuable form of vasodilator treatment of congestive cardiac failure. Enalapril is a new angiotensin converting enzyme inhibitor with a long (12 hours) duration of action. Fifty five patients with chronic congestive cardiac failure receiving diuretics and digoxin had
enalapril (10 mg per day) or placebo added to their treatment and were assessed over six months on a random double blind basis. Mean exercise times on a treadmill to the Naughton protocol at baseline, after one month, and after six months were for placebo 513, 549, and 562 s respectively and for enalapril 596, 683, and 737 s respectively. The difference in values after one month and after six months between placebo and enalapril were significant (p<0.001). There were no significant changes in ejection fraction, heart rate, blood pressure, weight, and haematological or biochemical values with either enalapril or placebo. Of 27 placebo patients, two died and two were withdrawn with worsening cardiac failure. With 28 enalapril patients one died and three were withdrawn with hypotensive symptoms.

This study, the longest yet of an angiotensin converting enzyme inhibitor for congestive cardiac failure, has shown sustained clinical improvement over six months for patients receiving enalapril.

Can the pumping capability of a failing heart improve with inotropic stimulation?

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The beneficial effects of the inotropic agents used in the treatment of severe cardiac failure are often coupled to their vasodilatory effects. When these agents are used in patients with minimal pumping reserve, the vasodilatory effects would predominate. A means of separating the direct effects of the inotropic agents on the cardiac pumping capacity from their vasodilatory effects is required. A new technique was devised to fulfil this aim, and it was tested by infusing dobutamine at graded incremental doses to 12 ischaemic cardiac failure patients in NYHA classes III and IV. The haemodynamic data were obtained using a thermodilution Swan-Ganz catheter. At each infusion rate of dobutamine the left ventricular power output (W = cardiac output × mean arterial pressure) was calculated, and the range of power output values resulting from the concomitant change in the peripheral resistance was also determined. A power output value that was found to be above the range defined by the latter signified a direct increase in the cardiac pumping capacity resulting from the inotropic challenge. Five patients (group A) could demonstrate definite augmented pumping capacity to dobutamine challenge; three patients (group B) could increase the left ventricular power output secondary to the vasodilation; and four patients (group C) had maximum power output which did not exceed 1-2 W at any rate of dobutamine infusion. The prognosis of group C patients was grave in that three of them died within one month of the study and the remaining patient required transplantation.

It is concluded that direct effects of dobutamine on cardiac pumping can now be separated from its vasodilatory effects and that the pumping capability of the heart evaluated thereby reflects the amount of viable myocardium present in the left ventricle. Such information would be of therapeutic and prognostic significance.

A radionuclide model of acute myocardial infarction

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To construct a model of the relation of infarct size to left ventricular function in acute myocardial infarction, 65 patients were imaged in the acute phase to acquire thallium 201 tomograms and a technetium-99m gated blood pool study using a rotating slant hole collimator and mobile gammacamera. Percentage of normal left ventricular function measured by left ventricular ejection fraction, regional wall motion score, and phase analysis was plotted for each patient against percentage volume defect from reconstructed thallium tomograms, previously shown to correlate \((r=0.82)\) with pathological infarct size.

A non-linear relation was seen between deterioration in left ventricular function and thallium defect size, better visualised by regional indices of wall motion score and phase analysis than by global left ventricular ejection fraction. A greater than 40% volume defect in thallium tomograms was associated with accelerated deterioration in left ventricular function. A 45% volume defect showed the widest spectrum of associated left ventricular function. Anterior infarcts were associated with the largest left ventricular perfusion defects and deterioration in left ventricular function, although extensive inferior infarcts showed comparable results.

Thus there may be a critical infarct size above which left ventricular function may deteriorate rapidly and approaching which value attempts to limit infarct size may be most important. The variable left ventricular function shown at this critical defect size probably reflects the ability of non-infarcted cardiac muscle to compensate for the infarct.

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**Myocardial perfusion: an assessment by parametric digital subtraction angiography**

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There is a need for the objective assessment of myocardial perfusion, which may supplement the anatomical information obtained by selective coronary arteriography. Digital subtraction angiography with parametric analysis was used to study six patients. Following conventional angiography a timed sequence of images was acquired in arrested respiration, during and after selective left coronary injection of electrocardiogram; three images were stored per cardiac cycle for up to 20 cycles. This allowed subsequent optimisation of the image sequence, minimising movement artefact. The images were all stored as 512 × 512 pixel matrices, offering 0.3 mm of spatial resolution. Subsequent computer analysis defined a time density curve for each pixel. The time of peak arrival of contrast (T-MAX) and the time of ½ peak arrival of contrast (T-½MAX) were colour coded into two parametric images, with normalisation to a heart rate of 70 beats/min. The colour coding permitted easy appreciation of overall myocardial perfusion (T-½MAX) and allowed objective measurement of coronary artery to coronary sinus transit time (T-MAX). Two of the six patients had normal coronary arteries; in these cases the transit time from coronary artery to the myocardium was 7 s and the transit time from the coronary artery to the coronary sinus was 10 s. The remaining four patients had varying degrees of disease severity. The amount of delay in both transit times reflected the amount of left coronary artery disease. Following administration of sublingual vasodilators the abnormal delays were reduced and the transit times fell. In one case with severe left coronary artery disease the artery to sinus and artery to myocardium transit times were 13 and 9 s respectively. These times fell to 11 and 8 s respectively following vasodilatation.

This method may permit objective assessment of myocardial perfusion and supplement anatomical information.

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**Clinical measurement of ventricular dimensions and stroke volume using magnetic resonance**

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Magnetic resonance provides a unique non-invasive means of delineating cardiac function and structure. Measurements taken from magnetic resonance sagittal, coronal, and transverse sections were compared with corresponding measurements from anteroposterior and lateral angiograms in 20 male patients. A GEC/Picker superconductor machine at 0.24 Tesla with an electrocardiogram R-wave gate was used and magnetic resonance end systolic image data were acquired between 36 and 12 ms prior to A2. Diastolic image data was taken 34 and 10 ms before the minimum RR interval. A coronal section was taken at the level of the centre of the aortic valve, a sagittal section at the greatest vertical diameter of the left ventricle and a transverse section at the greatest hori-
Proceedings of the British Cardiac Society

Horizontal diameter of the left ventricle. Four angiographic slices were made as follows: (a) vertical diameter in anteroposterior projection, (b) vertical diameter from centre of aortic valve to inferior wall on lateral projection, (c) transverse diameter on anteroposterior projection, and (d) anteroposterior diameter on lateral projection. Significant correlations were obtained from both measurements taken from the anteroposterior angiographic projection \((r=0.50-0.78)\) but no significant correlation was found from those in the lateral views. The ability of the magnetic resonance to measure ventricular volumes accurately was further tested in 14 normal subjects by comparing the left and right ventricular stroke volumes using a multislice technique. The right ventricular stroke volume was 74(6) ml (mean (SEM)) and left ventricular stroke volume 72(4) ml \((p>0.05)\).

These findings indicate that magnetic resonance provides a non-invasive means of measuring ventricular dimensions and stroke volumes.

**Non-invasive assessment of right ventricular function at rest and on exercise in obstructive airways disease**

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Non-invasive assessment of right ventricular function is of clinical interest in the patient with obstructive airways disease. Gated xenon-133 scanning allows right ventricular function to be evaluated in isolation from the left ventricle, and with rapid clearance from the lungs scans may be repeated within 5 minutes. Four hundred millibecquerels of xenon-133 were injected intravenously over 20 s and images were obtained gated to the electrocardiogram, using a mobile gammacamera in the 10° left anterior oblique projection with 6° caudal tilt for optimal separation of atrium from lung. Acquisition was initiated when xenon activity reached the right ventricle and was terminated as activity left the ventricle. Maximal symptom limited exercise was performed on a supine bicycle ergometer. The normal range for right ventricular ejection fraction was obtained from 10 volunteers (40–55% at rest rising by 5–15% during exercise). In 10 patients with acute obstructive airways disease, all had reduced values (21(3)%). In chronic obstructive airways disease, if resting values were greater than 30%, ejection fraction increased on exercise. If resting ejection fraction was abnormal then values were reduced or unchanged on exercise (mean 15(9)%), and this was associated with dilatation of both the right ventricle and atrium. In 20 patients in whom simultaneous haemodynamic measurements were made, increased calculated pulmonary vascular resistance at rest tended to be associated with reduced right ventricular ejection fraction. On exercise, however, there was no definite correlation between the haemodynamic variables and the exercise right ventricular ejection fraction response.

In conclusion, gated xenon-133 offers a simple method of assessing right ventricular function at rest and on exercise in patients with obstructive airways disease.

**Survival from ventricular fibrillation**

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Many factors are involved in predicting survival following ventricular fibrillation. This study identified the most significant factors present at the initial and last arrests which predicted survival to leave hospital. During 1983 125 patients (79 male, 46 female aged 16–91 (mean 64) years) were managed with 173 episodes of ventricular fibrillation: 106 had a single episode, forty six had ventricular fibrillation outside hospital, and 53 survived to leave hospital. At the initial arrest, 86 patients had primary ventricular fibrillation (absence of heart failure or cardiogenic shock). Using single factor analysis of the initial arrest, the place of arrest, aetiology of ventricular fibrillation, coarse ventricular fibrillation—that is, \(>0.5 \text{ mV}\) before the first shock—or prior treatment with beta blocking drugs, diuretics, or digoxin were not related to survival to leave hospital. Nevertheless, those who had ventricular fibrillation \(<24\) hours from the onset of symptoms \((p<0.02)\), received the first DC shock \(<1\) min after ventricular fibrillation developed \((p<0.01)\), or who required \(\leq5\) shocks to terminate the ventricular fibrillation \((p<0.01)\) had a significantly improved long term survival. The average number of shocks required at the first arrest in those who survived to leave hospital was three and for those who did not survive, four. After correction of ventricular fibrillation, if the rhythm was idioventricular, complete heart block, or asystole this was associated with a worse prognosis \((p<0.01)\). A discriminant function analysis of the initial arrest showed that if \(\leq5\) shocks
were necessary to correct ventricular fibrillation the time from onset of ventricular fibrillation to the first shock (<1 min), type of ventricular fibrillation (primary), and absence of antiarrhythmic therapy were of greatest significance in predicting survival. At the last arrest factors of most significance were <5 shocks to correct ventricular fibrillation, primary ventricular fibrillation, absence of antiarrhythmic therapy, and absence of a previous cardiac arrest. For the initial arrest the sensitivity and specificity of predicted survival were 59% and 89% and for the last arrest 78% and 75% respectively.

Prognostic significance of ventricular arrhythmia after repair of tetralogy of Fallot: a prospective study

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Ventricular arrhythmia is common after repair of tetralogy of Fallot, but the prognostic significance and the indications for therapy are unknown. A prospective study of 86 patients (59 male, 27 female) who had undergone repair between 1959 and 1978 (at age 3–45 (mean 13-6) years) was performed. All underwent 48 hour electrocardiographic monitoring 4–22 (mean 14-6) years after surgery: 77 (89%) had postoperative haemodynamic data and 38 (44%) radionuclide angiography. Thirty nine (45%) patients had significant ventricular arrhythmia consisting of frequent (>30/hour) uniform extrasystoles (two patients), complex extrasystoles (30 patients), or ventricular tachycardia (seven patients). Only 15 patients were symptomatic (11 palpitation, four syncope). Of these, eight had ventricular arrhythmia, four supraventricular tachycardia, and 10 were started on antiarrhythmic medication. There were no significant clinical or haemodynamic differences between asymptomatic and symptomatic patients. All 86 patients were then followed for a further 44–78 (mean 63) months with no drug treatment given to asymptomatic patients. During this time one patient died suddenly (eight extrasystoles on previous 48 hour monitoring) and only one showed increased symptoms requiring treatment. All high risk patients with complex ventricular arrhythmia or ventricular tachycardia and either high (>60 mm Hg) right ventricular pressures (seven patients) or reduced right ventricular ejection fraction (six patients) remained alive and well. Thus ventricular arrhythmia did not affect the excellent outlook of patients after repair of tetralogy of Fallot, regardless of residual haemodynamic disturbances or impaired ventricular function. There does not appear to be any advantage in potentially dangerous long term prophylactic antiarrhythmic therapy for asymptomatic postoperative patients.

Ablation of atrioventricular nodal conduction using 50 J and an active fixation electrode

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Endocardial ablation of the His bundle has been attempted using high energies and standard pacing electrodes. In this study a reduction in energy requirements was attempted using an active fixation electrode.

Ten patients (five men, five women) aged 34–69 years were studied. Six had paroxysmal atrial fibrillation, three tachycardias due to dual atrioventricular nodal pathways, and one a concealed left accessory atrioventricular pathway. A temporary pacing electrode was inserted into the right ventricle, and a Vitatron Helix electrode positioned via the right femoral vein to obtain the maximal His bundle deflection. Four shocks of 50 J each were delivered via the latter electrode at one minute intervals. The anodal output of the defibrillator was connected to a paddle placed on the posterior chest wall. Blood for cardiac enzyme estimation was obtained. All patients developed complete heart block immediately post-ablation. This persisted in seven patients, while two had first degree atrioventricular block and right bundle branch block (follow up 2–5 months). These nine patients were all asymptomatic on no drug therapy; eight required permanent pacemakers. Atrioventricular conduction returned in only one of 10. There were no complications. The A:H ratio and creatine phosphokinase values were unrelated to the outcome.

Catheter ablation of normal and abnormal atrioventricular pathways: long term follow up

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In a single centre, 28 patients have been followed for 2 to 37 (mean 16) months after catheter ablation of either normal or abnormal atrioventricular conduc-
tion pathways. One had persistent sinus tachycardia, three chronic atrial tachycardia, four paroxysmal atrial flutter, 11 atrial fibrillation, and nine paroxysmal junctional tachycardias. The pathways treated were the normal atrioventricular node His bundle in 20 patients, dual atrioventricular nodal pathways in one, and atrioventricular accessory pathways in six (posteroseptal, 4; anteroseptal, one; left freewall, one), and both a posteroseptal accessory pathway and the atrioventricular node in one. In the patients in whom atrioventricular nodal ablation was attempted, between 1 and eight (mean 3-5) shocks (320 to 350 J) were given. Seventeen (80%) patients have persistent complete heart block, two (10%) have much slower atrioventricular conduction, and two (10%) have had unsuccessful procedures. All but the latter two have received pacemakers and are asymptomatic. In those in whom accessory pathway ablation was attempted from the coronary sinus, between five to 46 shocks of up to 125 J per pole were given. In two there was complete ablation, in two significant modification of conduction, and in two no effect. In the patient with dual atrioventricular nodal pathways five shocks were used, and in the patient with an anteroseptal accessory pathway one shock was used, and both were cured.

All patients are alive. Cardiac enzymes were raised in 23 of the patients (mean serum aspartate aminotransferase 99 IU/l (normal <40; mean hydroxybutyrate dehydrogenase 183 IU/l (normal <125)) but no patient suffered clinical infarction or had signs of cardiac decompensation. Complications consisted of early ventricular tachycardia in three, pneumonia in one, and deep vein thrombosis in one. Long term results from atrioventricular catheter ablation are excellent, and the procedure is relatively safe with minimal complications.

Responsiveness of pulsed Doppler cardiac output measurements to changes in left ventricular function

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Clinical validation of non-invasive measures of cardiac output requires not only that they should correlate closely with measures obtained by established techniques but also that they should be rapidly responsive to changing left ventricular function. In the present study simultaneous bedside measurements of cardiac output by thermodilution and by the pulsed Doppler technique were made in 10 patients during incremental atrial pacing, inotropic stimulation (dobutamine 250 to 1000 μg/min IV) and vasodilatation (nitroglycerin 10 to 90 μg/min IV). Fixed rate atrial pacing controlled for changes in heart rate during the drug interventions. A total of 110 cardiac output measurements (ranging from 2-1 to 15-0 l/min) made by both techniques showed a close linear correlation (r=0.90) described by the regression equation Y=0.15+1.04X (p<0.001). Thermodilution cardiac output was not significantly affected by atrial pacing but increased during dobutamine infusion from 5.8(3-2) to 6.9(2-8) l/min (p<0.05). Nitroglycerin on the other hand lowered thermodilution cardiac output from 6.7(1-9) to 5.6(1-7) l/min (p<0.05) owing to a reduction in pulmonary capillary wedge pressure from 21.1(4-8) to 12.9(4-4) mm Hg (p<0.05). Directional changes in Doppler cardiac output measurements in response to the interventions were identical and mean values were always within 0-6 l/min of thermodilution values. The inotropic response to dobutamine was reflected in a sharp rise in peak aortic blood velocity from 70(29) to 89(31) cm/s, but this variable was unaffected by nitroglycerin.

Thus the pulsed Doppler technique provides a reliable non-invasive means of measuring cardiac output at the bedside. Importantly, measurements obtained by this technique are rapidly sensitive to changes in output induced by inotropic stimulation or preload reduction.

Cross sectional and pulsed Doppler echocardiographic study of aortic root in idiopathic infantile hypercalcaemia (Williams-Beuren syndrome)

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Idiopathic hypercalcaemia is often associated with supravalve aortic stenosis. In the present study the aortic root anatomy was studied by cross sectional and pulsed Doppler echocardiography. Forty-nine successive patients with idiopathic hypercalcaemia (mean age 10-0 years) were studied without regard to the previous documentation of cardiac murmurs or defects. Aortic root was studied by cross sectional echocardiography in the parasternal long axis view and pulsed Doppler echocardiography was used to detect disturbances in the normal flow pattern. The results were compared with normal age matched controls with a mean age of 9-8 years in whom the same
procedures were carried out. The internal diameter of the aortic root and ascending aorta were measured in end diastole at (a) aortic annulus (D1), (b) sinuses of Valsalva (D2), (c) sinotubular junction—junction of the aortic root with the ascending aorta—(D3), and (d) distal ascending aorta (D4). In the control group the diameter at D3 was greater than D1 (p<0.005) whereas in all the study patients D3 was less than D1 (p<0.001). Three categories of aortic root abnormality were recognised. (a) hourglass constriction at D3 (42/49), (b) tubular hypoplasia involving D3 and D4 (5/49), and (c) membranous supravalvar diaphragm at D3 (2/49). Pulsed Doppler echocardiography showed dispersion of laminar flow in 42/49 patients and in none of the controls. Such flow patterns were maximal in those with sinotubular narrowing (D3) and with tubular hypoplasia (D3 and D4). Correlation with clinical findings demonstrated that those with absent murmurs had the least sinotubular narrowing and normal Doppler flow pattern.

It is concluded that abnormal sinotubular junction is an inherent feature of idiopathic hypercalcaemia and that its demonstration by cross sectional echocardiography is of diagnostic value. Additionally, serial cross sectional echocardiography and pulsed Doppler echocardiography examinations may be useful in determining the progress and management.

Intravenous adenosine in the treatment of supraventricular tachycardia

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Intravenous adenosine is an effective treatment for atrioventricular re-entrant tachycardia induced in the electrophysiology laboratory. Initial experience using intravenous adenosine in the acute treatment of spontaneous narrow complex, regular tachycardia is presented. Ten episodes of tachycardia were treated in six patients (four male) aged 22–73 years. Adenosine was given in a series of bolus doses, starting at 40 μg/kg, increasing in steps of 40 μg/kg, to the maximum of 200 μg/kg, if required, except for one patient who received an initial dose of 10 μg/kg. Adenosine restored sinus rhythm in seven episodes in three patients, about 10–30 s after the effective dose was injected. Those patients who did not revert to sinus rhythm were shown to have atrial flutter. Two patients were also receiving dipyridamole therapy. In one of these, 40 μg/kg adenosine produced asystole lasting 15 s. In the second patient a dose of 10 μg/kg restored sinus rhythm. This dose contrasts with an effective dose of 120–200 μg/kg in the other patients. Dipyridamole potentiates the effects of adenosine by limiting red cell uptake and degradation. Side effects were usually transient consisting of dyspnoea and facial flushing. Our results suggest that in the treatment of supraventricular tachycardia (a) adenosine may restore sinus rhythm in some patients with supraventricular tachycardia, although not in patients with atrial flutter; (b) dipyridamole potentiates the cardiac effects of adenosine (dose reduction is advisable if alarming bradycardias are to be avoided); and (c) side effects are slight if an appropriate dose of adenosine is given.

Further studies are required to establish efficacy and safety in larger patient groups and to compare adenosine with standard treatment.

Defibrillator waveform and cardiac injury

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Are there differences in the efficacy and safety of different defibrillator waveforms? To study this greyhounds (27.2±0.7 kg) were anaesthetised with pentobarbitone (30 mg/kg IV) and randomised to receive either no shocks (control group), or to one of five groups receiving five synchronised transthoracic shocks at intervals of 30 s: group 1, Lown waveform (undamped sine wave); group 2, Edmark waveform (critically damped sine wave); group 3, Belfast waveform (overdamped sine wave); group 4, trapezoid (5 ms duration); group 5, trapezoid (20 ms duration). Groups 1 to 3 received 400 J stored energy: in groups four and five, 1100 V were stored on the capacitor. Average first shock delivered energies and peak currents were respectively 286, 277, 267, 130, and 418 J and 55, 68, 58, 27, and 28 A. Three days following the shocks the hearts of six survivors in each group were excised and the weight of damaged tissue was determined after incubation in 1% triphenyltetrazolium chloride. ST segment elevation at one hour after the shocks was significantly greater (p<0.05) in group 1 (9.1±1(SEM 1.7) mV), group 2 (11.7±2.4 mV), and group 3 (14.5±2.5 mV) than in either the control (1.1±0.2) mV or group 4 (1.8±0.4 mV). Ventricular ectopic activity at 24 hours was significantly greater (p<0.02) in group 2 (202(12) per min) and group 3
Autonomic tone modulation of atrioventricular accessory pathway conduction

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During sinus rhythm and fixed rate atrial pacing sustained deep inspiration provoked pre-excited QRS complexes in two patients with type B Wolff-Parkinson-White syndrome (aged 26 and 54 years). The anterograde refractory periods of the accessory pathways could not be determined during normal breathing but were 540 and 280 ms lying and 300 and 280 ms standing respectively during sustained deep inspiration. Isoprenaline (3 μg/min) but not atropine (0.04 mg/kg) provoked pre-excitation in sinus rhythm during normal breathing. Atropine as well as propranolol (0.2 mg/kg) decreased the provocation of pre-excitation by sustained deep inspiration. Pre-excitation was provoked only during the first three minutes of exercise but reappeared immediately after exercise. The vacuum neck collar (pure parasympathetic effect) prolonged the RR interval but did not provoke pre-excitation. The Valsalva manoeuvre at 35 mm Hg for 15 s during sinus rhythm provoked pre-excitation during phase 4 (parasympathetic predominant) in the two patients but not during phase 2 (sympathetic predominant). The effect of the Valsalva manoeuvre was studied in 17 other patients with Wolff-Parkinson-White syndrome. In nine (53%) patients the pre-excitation decreased or disappeared in phase 2 but increased in the early stages of phase 4 (71%). These effects were not due to changes in the atrioventricular conduction time (AH interval). These observations suggested that pre-excitation was usually provoked when parasympathetic stimulation occurred against a background of high sympathetic tone (as in sustained deep inspiration, Valsalva manoeuvre, isoprenaline infusion, and postexercise). This demonstrates (a) the mutual agonistic effect between the sympathetic and parasympathetic tone and (b) the importance of sympathetic-parasympathetic balance on the regulation of accessory pathway conduction.

Pouyria associated with supraventricular tachycardias

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Supraventricular tachycardias may be associated with distressing polyuria. The mechanisms of this...
phenomenon were investigated in six patients in whom tachycardia was initiated by programmed stimulation. Four patients had atrioventricular re-entrant tachycardia and two atrioventricular nodal re-entrant tachycardia. Their ages ranged from 23–72 (mean 46) years. Two patients complained of polyuria. Changes in blood pressure, urinary sodium and free water excretion, and plasma antidiuretic hormone, noradrenaline, and dopamine were assessed during sinus rhythm and tachycardia, urine was obtained by voluntary micturition at frequent intervals, and each patient was water loaded to achieve a constant baseline urine flow. When this was achieved the arrhythmia was initiated by either rapid atrial pacing or atrial extrastimuli and this was performed at a similar time of day in each patient. The mean tachycardia rate during the study was 184 beats/min and the mean tachycardia duration was 28 minutes. Immediately following the arrhythmia there was an increase in free water excretion from a mean of 3.8 ml/min to a mean of 7.8 ml/min in five cases. Sodium excretion increased from a mean of 1.2 mmol/ml to a mean of 1.7 mmol/ml in four cases and was unchanged in two. In these two cases the arrhythmia was atrioventricular re-entrant tachycardia. There was no correlation between sodium excretion and mean blood pressure during tachycardia. There was no relation between dopamine and noradrenaline concentrations and sodium and free water excretion. Plasma antidiuretic hormone concentrations were consistently low during the study confirming the efficacy of the water loading.

In conclusion this study demonstrates that the diuresis accompanying supraventricular tachycardias is in some cases due to an increase in both free water and sodium excretion but may also be due to an increase in free water excretion alone.

Analysis of pacing policy and outcome in a single district pacing service with high implant rate: over enthusiasm or practical practice?

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Audit of indications for permanent pacemaker implantation for a single district pacing service was occasioned by discovery of a pacing rate well above the estimated national average (197.9 vs 114.5 implants/million population/year for 1981). Over a 5-8 year period 177 patients (97 male and 80 female, mean age 68.9 (range 30-97) years) underwent first implantation of a permanent pacemaker (mean implant rate 179.5/million population/year). Indications for implantation were classified according to guidelines set out by the Joint American College of Cardiology/American Heart Association Task Force on Assessment of Cardiovascular Procedures, published in August 1984. In 144 (81.4%) patients sinoatrial (62.5%) or atrioventricular conduction abnormalities were documented; 104 (72.2%) of these were class I indications (generally agreed indications) and the remainder class II (frequently accepted indications). In 11 (6.2%) patients, although a slow pulse was found during acute episodes, electrocardiographic documentation was never achieved. All but one of these patients were rendered symptom free by pacing. In 22 (12.4%) patients neither a slow pulse nor electrocardiographic documentation was recorded, and pacemaker implantation was prompted by a history thought to be typical of Stokes-Adams attacks. On follow up over periods ranging from 6–42 months, 12 (54.5%) of these were rendered symptom free; eight (36.4%) had symptomatic episodes that seemed different from the ones that had prompted pacemaker implantation and two (9.1%) had no change in symptoms.

It is concluded that this policy of pacing symptomatic patients with sinoatrial abnormalities and carefully selected patients with a history strongly suggestive of Stokes-Adams attacks is an effective approach and results in an acceptably low risk of inappropriate pacemaker implantation.

Initial clinical experience with a new software based tachycardia reversion pacemaker

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Current generation antitachycardia pacemakers suffer from limitations concerning detection and distinction of pathological tachycardia and also from the termination modes available. To overcome many of these limitations, a new device (Intermedics Intertach 262–12) has been developed and has now been tested as an external unit in eight patients and implanted in three. It is small (49 g) and is bipolar with an inline connector. Tachycardia recognition may be achieved manually or automatically using high rate, sudden onset, rate stability, or sustained high rate, alone or in combination. Termination may be effected using 1–250 stimuli, which may be fixed rate or rate related. Extrastimuli or bursts may be scanned with the S1 and S2 to Sn intervals being independently programmed. Scanning may start from either preset or from rate
related coupling intervals, and there is also a programmable memory function, optionally dependent on interval similarity. Autodecremental bursts (± rate related) are also available. The number and size of scanning (or autodecremental) steps can be programmed, as can the minimum cycle length. Two termination modes, 1st and 2nd, may be selected. There is telemetry with full diagnostic functions, and non-invasive electrophysiological studies can be performed. The pacemaker was implanted in three patients, all with atrioventricular nodal re-entrant tachycardia (cycle lengths 260, 300, and 330 ms). They had frequent tachycardias (one, two, and 12 per month) and had all failed drug therapy. Right atrial pacing was used, with seven stimuli in rate related scanning modes. All three devices terminate tachycardias almost immediately without additional drug therapy, and sinus tachycardias have not triggered pacing. This pacemaker represents a considerable advance over previous devices and offers improvements in patient management because of its flexibility.

### Ventricular tachycardia masquerading as supraventricular tachycardia: management of His bundle tachycardia

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Until recently, the natural history of children surviving with narrow QRS (His bundle) ventricular tachycardia was unknown. Most reports indicated a poor prognosis and did not provide guidelines for effective treatment. Five children (three girls, two boys aged 5 weeks to 18 months) have presented with His bundle tachycardia at rates of 250–290 beats/min since 1978. Since this ventricular tachycardia resembles supraventricular tachycardia, four had been treated inappropriately with digoxin or verapamil, causing ventricular tachycardia in three and acceleration of His bundle tachycardia in one. Careful analysis revealed ventriculoatrial dissociation on the electrocardiogram in four during His bundle tachycardia. His bundle tachycardia occurred following a viral myocarditis in one; no child had congenital heart disease. Until the age of 3 years, 24 hour electrocardiographic recording was performed three monthly then annually in older children. His bundle tachycardia was suppressed and sinus rhythm in four of the five children (follow up 1-3-6-3 (mean 3-1) years) by disopyramide alone in two, disopyramide and mexilitine in one, and by mexilitine and amiodarone in the other. Disopyramide and mexilitine were used together to control the His bundle tachycardia rate at 100–130 beats/min in the fifth child; attempts to further suppress the His bundle tachycardia resulted in sinus node depression and cardiotoxicity. All treatment has been withdrawn in one child who has been free of His bundle tachycardia for three years. There has been no recurrence thus far three months off all drugs. There has been no apparent adverse effects of long term high dose antiarrhythmic therapy on their physical or academic development. Although intravenous verapamil is usually the most appropriate antiarrhythmic agent for the emergency treatment of narrow QRS tachycardia, the response to this nodal drug must be monitored carefully. If no slowing occurs after two thirds of the recommended dose or if ventriculoatrial dissociation is seen on the electrocardiogram, then His bundle tachycardia should be suspected and treatment replaced with a class I drug—for example, disopyramide.

### Prevention of leg wound complications associated with saphenous vein harvesting for bypass grafting using the Mayo vein stripper

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Conventional techniques of vein harvesting are time consuming and may result in serious complications. In an attempt to expedite vein removal without compromising its integrity and prevent the early and late morbidity of open dissection, a prospective study was undertaken to evaluate a method of limited subcutaneous dissection using the Mayo vein stripper. The early and late clinical findings in 297 unselected consecutive patients are discussed. An appraisal of the operative technique illustrating its distinct advantages is presented. The harvesting technique is quick and easy to learn. Limited tissue dissection, reduction in harvesting time, and rapid wound closure expedite the entire surgical procedure. There was no instance of wound dehiscence or frank sepsis and no patient required re-exploration. Superficial wound inflammation occurred in 3% of patients, wound haematoma (mainly groin) in 1-6%, saphenous nerve damage in 1-3%, and persistent leg oedema in 0-3% of cases. Light and scanning electron microscope studies confirm lack of trauma to the main trunk, particularly the tributaries. Symptomatically the patients were notably more comfortable, as manifested by early and improved mobility and a dramatic reduction of early and late morbidity associated with leg incisions, particularly if the patient is overweight, diabetic, or suffered concomitant peripheral vascular ischaemia and neuropathy.
Intraoperative real time scanning during coronary and peripheral vascular surgery: morphological appearances and postanastomotic imaging

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The use of high resolution real time ultrasound was explored intraoperatively during coronary, carotid, and peripheral vascular reconstruction. A 12 MHz scanning probe was used and the findings in 30 patients undergoing myocardial revascularisation and 20 undergoing carotid and peripheral vascular reconstruction were analysed. Scanning was rapidly achieved without any complications. Scanning techniques are described with special reference to the value of postanastomotic and postendarterectomy imaging. The percentage decrease in diameter of 30 coronary angiographic lesions was correlated with the same measurement on the corresponding ultrasonic images. The mean difference was 2.5% (SD 9.8%) and a correlation coefficient of 0.87.

Real time operative ultrasound offers a safe, rapid, and readily available means of obtaining high resolution images in multidimensional views with sufficient detail to allow accurate estimates of luminal diameter and quantitative assessment of obstructive lesions. It is useful in identifying obscure coronary arteries and selecting suitable anastomotic sites thereby aiding decision making. Postanastomotic imaging defines technical errors, allows early correction of defects when indicated, and provides feedback on surgical techniques.

Valve surgery for active infective endocarditis: factors affecting mortality

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A retrospective study was conducted into the causes of mortality in patients undergoing valve surgery during active infective endocarditis (1975–84). All 48 patients included in the review continued to show signs of active infection at the time of operation. Resistant heart failure and inadequate response to antimicrobial treatments were major indications for surgery. Eighty five percent (n=41) had positive blood or valve cultures; 61% of these had streptococcal and 34% staphylococcal infections. Perioperative mortality (surgery 30 days) was 27% (n=13), most fatalities being during induction of anaesthesia or at surgery. There was a 75% mortality of *Staphylococcus albus* prosthetic endocarditis. The overall mortality of streptococcal and staphylococcal infections of native valve endocarditis was similar (15%). Only one patient died, however, out of 12 with *Streptococcus viridans* endocarditis. As expected patients with impaired renal function (judged by preoperative blood urea and creatinine) had a higher mortality. There was no difference in duration of antibiotic treatment prior to surgery between the fatal and non-fatal groups. Seven out of 35 developed postoperative paravalvar leaks, five requiring reoperation. Two developed fatal aneurysms of ascending aorta 18 to 28 months postoperatively at the site of the aortic vent.

The overall mortality reported in medically treated endocarditis is in the region of 25% with 60% mortality in patients with heart failure. Apart from the present cases with *Staph albus* infections of prosthetic valves that had a high mortality the perioperative mortality in these relatively sick patients with active infective endocarditis resistant to medical treatment was 17%. Thus valve surgery is positively indicated in this group.

Hypercholesterolaemia and endothelium dependent vasomotor responses

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Experimental hypercholesterolaemia has been reported to enhance vasoconstrictor responses. One explanation might be reduced activity of endothelium derived relaxant factor. This possibility was explored with isolated aortic ring preparations from 20 week old rabbits (male New Zealand white) after free feeding with standard diet or diet enriched with 2% cholesterol for 10 weeks. Endothelium was removed from half the rings by gentle abrasion. Preparations were mounted isometrically in oxygenated Holman’s solution at 37°C (n>23 for each experiment). In control preparations, the maximum response to 5-hydroxytryptamine (5HT) was greater with endothelium than without (1526(SEM 109) vs 1251(82) mg, p<0.05), shown previously to be due to basal endothelium derived relaxant factor activity. In hypercholesterolaemic preparations endothelium did not significantly affect the 5HT response. In neither control nor hypercholesterolaemic preparations did
endothelium significantly alter maximum response or EC₅₀ to ergometrine. Maximum responses to 5HT or ergometrine, with or without endothelium, did not differ between control and hypercholesterolaemic preparations, implying that smooth muscle constrictor responses were not altered by cholesterol feeding. Acetylcholine (≥10⁻⁹ mol/l) induced, endothelium dependent relaxation, in preparations preconstricted with 5HT, was significantly greater in control than hypercholesterolaemic preparations (for example, at 10⁻⁶ mol/l, 70(5) vs 10(5)%, p<0.005). This implies less endothelium derived relaxant factor activity in hypercholesterolaemic animals. Whether this reflects reduced reduction, release, activity, or penetration is unknown. Endothelium derived relaxant factor is unstable and increased diffusional distance could account for these observations. These observations are consistent with the possibility that atheroma may reduce endothelium derived relaxant factor activity and enhance constrictor responses in vivo.

A study of aspirin or sulphinpyrazone in unstable angina

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A randomised, double blind, placebo controlled trial of aspirin (acetyl salicylic acid) 325 mg four times daily or sulphinpyrazone 200 mg four times daily was carried out in 555 patients of either sex with unstable angina. Patients entered the trial within eight days of admission to the coronary care unit and were followed for up to two years (mean 19 months). Primary analysis of efficacy was based on cardiac death or non-fatal myocardial infarction in eligible patients who had not been off medication for 28 consecutive days preceding an outcome. There was no evidence of interaction between the two drugs; therefore outcomes were analysed separately for each drug. Aspirin reduced the number of cardiac deaths or non-fatal myocardial infarction by 55%, from 37 (13%) to 16 (6%) (p=0.004). Sulphinpyrazone produced no statistically significant effect with 27 events off the drug and 26 events on the drug. The total number of deaths was reduced by 70% by aspirin, from 22 (8%) to six (2%) (p=0.005). Sulphinpyrazone reduced total deaths from 15 (5%) to 13 (5%) (p=0.329). On the basis of an intention to treat analysis, aspirin reduced the number of cardiac deaths or non-fatal myocardial infarctions from 42 (15%) to 29 (11%), a risk reduction of 33% (p=0.053), and reduced all deaths from 28 (10%) to 16 (6%), a risk reduction of 43% (p=0.036). The observed benefits were similar for both sexes.

It is concluded that aspirin 325 mg four times daily results in a marked reduction of cardiac death or non-fatal myocardial infarction and of total mortality in patients hospitalised with unstable angina.

Practical aspects of ambulatory ST segment monitoring: comparison of frequency modulated and direct recording systems

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Ambulatory ST segment recording requires a low frequency range down to 0-05 Hz which has necessitated the use of frequency modulated systems (Oxford Medilog II, range 0-05-40 Hz at -3 dB). Recently a direct recording system (Reynolds Tracker TRIB, range 0-07-100 Hz at -3 dB) has been introduced and is widely used in clinical practice for arrhythmia monitoring. The purpose of this study is to determine whether the Reynolds system is reliable for ST segment monitoring in routine clinical practice. Twenty four hour ambulatory ST segment monitoring was performed concurrently on the Reynolds Tracker and Oxford Medilog II systems. Tapes were analysed at 60 times recorded speed and a trend of ST segments obtained with each system. Thirty episodes of transient ST depression (≥1-3 mm) were recorded and their onset, duration, and maximum magnitude noted. On visual analysis, the Reynolds system detected 90% of episodes with one false positive. Visually the mean duration of episodes and the maximum magnitude of ST depression were similar using both systems. The trend analysis the Reynolds system was more accurate (26 out of 30 episodes) than the Oxford system (19 out of 30). The Oxford trend was more prone to artefacts and particularly inaccurate for ST depression >3 mm. The mean duration of the episodes detected by both trend systems was identical. Thus for routine clinical practice the Reynolds Tracker system was capable of detecting the majority of episodes of ST segment depression both visually and using the trend analysis with few false positives.

The "normal" ST segment: a study of ST variability in 105 healthy volunteers by ambulatory monitoring and exercise testing

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There is at present no definite consensus on the pattern of ST segment variability in healthy man. One hundred and five normal volunteers (36 women, 69 men, between the ages of 20–67 years) selected at random from the general population were studied. All underwent a clinical examination, an electrocardiogram, and questioning regarding their personal and family history. They then underwent ambulatory electrocardiographic monitoring for 24–48 hours (CM5 and CC5) using an Oxford Medilog II recorder, followed by a symptom limited treadmill exercise test. Simultaneous electrocardiograms during exercise were made on a fresh Medilog II tape, the signal being picked up from the same electrodes as the exercise system. The peak exercise heart rate achieved varied from 88% to 96% of the age predicted maximum, and eight subjects showed a positive ischaemic response and were excluded from the final analysis. Orthostatic testing was performed in all subjects. The J point shift on standing varied from a fall of 0.5 mm to a rise of 0.4 mm in 96% cases. Only five had a higher shift, with falls up to 0.9 mm and rises up to 0.8 mm. Validation of ambulatory ST recording was achieved by comparing ST changes with the Medilog and a computerised exercise system. The standard deviation of differences in ST segment was 0.2 mm for lead CM5 and 0.3 mm for CC5. Of the tapes analysed, 25% revealed episodes of significant abnormal ST depression, over half in subjects under 40 years and three quarters in men. All episodes of ST depression were related to increased heart rate, secondary to some activity. Very few cases showed ST elevation. This study defines the ST segment behaviour during normal life in healthy man and affords a standard with which to compare studies in disease.

Exercise induced ST depression before and immediately after successful left anterior descending coronary angioplasty

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Twenty four patients with single vessel left anterior descending coronary artery disease (22 males, mean age 52 years) had maximal stress tests one day before and three days after successful left anterior descending coronary angioplasty to investigate the pattern of exercise induced ischaemia due to left anterior descending artery disease detected by a 12 lead electrocardiogram and the immediate effects of angioplasty on reversible myocardial ischaemia and exercise variables. Twenty patients had exercise induced ST depression before angioplasty. The number of patients with ST depression in each lead was: 19, V5; 14, V6; 11, V4; 5, V3; 5, II; 0, V1, the remaining leads each detecting ST depression in one patient. Exercise induced angina and ST depression occurred in 16 and 20 patients respectively before angioplasty and in five (p<0.01) and 10 (p<0.01) after the procedure. There was a significant increase in the mean maximal exercise duration after angioplasty (15.7(SD 7.5) min) compared with the value before angioplasty (12.0(3.7) min p<0.001), but there were no significant changes in mean maximal heart rate or in the maximal rate pressure product.

It is concluded that (a) reversible ischaemia due to left anterior descending coronary artery disease is best detected by leads V5 and V6 and not by the septal leads during stress testing, (b) features of reversible ischaemia and exercise duration are significantly improved immediately after successful angioplasty, and (c) ST depression on exercise may persist immediately after angioplasty defined as a primary success.

ST segment changes during left anterior descending coronary angioplasty: the significance of reciprocal changes

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There is debate about the significance of inferior ST segment changes in patients with anterior myocardial infarction. At angioplasty continuous six lead (I, II, III, V2, V5, and CM5) surface electrocardiograms were recorded during balloon inflation in the left anterior descending coronary artery. Nine patients with single left anterior descending coronary artery disease and eight patients with significant stenoses also in the circumflex or the right coronary arteries or both were studied. ST segment changes were measured with a magnifying lens to an accuracy of 0.1 mm. In patients with isolated left anterior descending artery disease, occlusion resulted in ST elevation in V2 in all nine patients (0.8–5.1 mm) and was first observed in this lead in six (mean duration 14(12) s). Reciprocal ST depression occurred in lead III in seven patients, and one patient each had ST elevation and
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no ST change. In patients with multivessel disease and left anterior descending artery occlusion, V2 showed ST depression in four and ST elevation in four, whereas lead III had ST depression only. In 15 of the 17 patients, occlusion of left anterior descending artery resulted in inferior ST segment depression. In seven patients with isolated left anterior descending artery disease, these changes are likely to be reciprocal. Thus, the presence or timing of inferior ST segment changes in the event of left anterior descending artery occlusion do not signify presence or absence of disease in other vessels.

Compared tomographic assessment of intracardiac thrombus

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Thirty eight patients with clinical conditions associated with intracardiac thrombus formation were studied by computed tomography and cross sectional echocardiography within a seven day period. Computed tomographic scans were performed during intravenous infusion of contrast medium at 1 cm intervals to image the appropriate cardiac chambers. Cross sectional echocardiography was performed in long and short axis and apical four chamber views. Echocardiography identified five cases of left ventricular and one right atrial thrombus. Computed tomography also demonstrated these cases, and in addition identified a further eight left ventricular and eight left atrial filling defects having the same appearances as in those cases in which echocardiography had identified a thrombus. Coincidental left ventricular angiography confirmed the presence of left ventricular filling defect in three of the eight cases identified by computed tomography alone. Measurement of thrombus density at computed tomography showed a significant difference in density (p<0.02) between those cases suspected of having new thrombus (for example, myocardial infarct) and those with organised thrombus.

These results suggest that computed tomography is an accurate method for identifying intracardiac thrombus and for differentiating new from organised thrombus. In addition, it may be a useful technique in those cases in which echocardiography is unhelpful.

The heart in middle aged first time marathon runners

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Marathon running continues to increase in popularity, though in older untrained subjects there is concern about its effect on the cardiovascular system. Forty one previously unfit middle aged men (mean age 43(2) range 35–50 years) who underwent a structured training programme involving 3-5 hours running by 15 weeks training rising to 8 hours per week after 30 weeks were recruited. Cardiac function was assessed by first pass radionuclide ventriculography at rest and at maximum exercise in 15 subjects using the short lived isotope gold-195m. Left ventricular ejection fraction rose from 59(3)% to 66(7)% (p<0.01) before and from 61(7)% to 70(6)% (p<0.005) and 59(8)% to 70(8)% (p<0.005) after 15 and 30 weeks training. Exercise ejection fraction was significantly higher after training (p<0.05). Resting end diastolic volume did not change (150(32), 156(26), and 160(31) EDV units). In 10 subjects cardiac function was assessed by gated radionuclide ventriculography. A mobile gammacamera positioned at the finish enabled a postmarathon scan to be performed within 30 minutes of finishing. Left ventricular ejection fraction was 54(6)% before, 61(9)% and 62(9)% after training, and was maintained postmarathon at 63(11)%; regional wall motion analysis was normal, and moreover no significant electrocardiographic change occurred in any of study group (n=30). Thus training for the marathon increased left ventricular ejection fraction response to exercise at an early stage in training, and no adverse effect on cardiac function was evident immediately after the race.

Stress induced right ventricular dysfunction: an indication of reversible right ventricular ischaemia

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Stress induced changes in left ventricular ejection fraction are widely used in the detection and assessment of coronary artery disease. This study demonstrates that right ventricular ischaemia may also occur and assesses its significance in terms of coronary
artery anatomy. Fourteen normal subjects and 26 with coronary artery disease were studied by equilibrium radionuclide ventriculography at rest and during maximal dynamic exercise. Right ventricular ejection fraction was calculated from count changes within a right ventricular region of interest after functional background subtraction. Mean normal resting right ventricular ejection fraction was 0.42 (SD 0.13) and all normal subjects increased right ventricular ejection fraction with stress (mean difference +0.13 (SD 0.10)). Mean difference in right ventricular ejection fraction in the subjects with coronary artery disease was significantly lower at 0.00 (SD 0.08), but there was overlap between the two groups. The largest falls in right ventricular ejection fraction were, however, seen if there was severe disease of both right coronary and left anterior descending coronary arteries or if there was right coronary artery occlusion without retrograde filling. In this subgroup with the most severely compromised right ventricular perfusion (11 subjects) right ventricular ejection fraction always fell with stress, and mean difference in right ventricular ejection fraction was −0.07 (SD 0.05). There was no significant correlation between the mean differences in left ventricular and right ventricular ejection fractions, implying that the right ventricular dysfunction was due to right ventricular ischaemia rather than secondary to left ventricular dysfunction. Stress induced right ventricular ischaemia can therefore be detected readily by radionuclide ventriculography.

**Withering Commemoration Symposium**

The following are abstracts of papers that were presented on Thursday 18 April 1985, at the joint meeting of the Association of Physicians and British Cardiac Society, to commemorate the bicentenary of the publication of William Withering's "An Account of the Foxglove." Other papers on digitalis will appear in a later issue.

**Pharmacology of digoxin**

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Among the interesting facets of the pharmacology of the cardiac glycosides are the origins of the distinctly different clinical practices in the use of digoxin extant in the United Kingdom and the United States. These can be traced in large part to the patterns established by Sir James Mackenzie and Henry Christian in the early twentieth century. Current areas of active research interest considered include the basic mechanism(s) of digitalis action at the cellular level, which were discussed in this lecture chiefly in terms of sarcolemmal sodium pump inhibition and its consequences. Pharmacokinetics and bioavailability were touched on briefly, with comments on the clinical use of serum digoxin concentrations. Finally, an update was provided on the reversal of advanced life threatening digitalis toxicity with purified digoxin specific Fab fragments. Sixty three patients have been treated, of whom 33 ingested digoxin accidentally or with suicidal intent. Digoxin specific Fab doses were calculated to be equimolar to the body burden of cardiac glycoside. The onset of reversal of toxicity was within 30 minutes in most cases; free serum digoxin concentrations were undetectable within minutes of Fab administration. Digoxin induced hyperkalaemia was reversed in all 29 patients presenting with this abnormality. Among 56 patients meeting criteria for advanced digitalis toxicity who were not yet agonal when treated, 53 responded positively and 52 had full resolution of toxicity. No obvious adverse reactions to treatment were observed.

**Modern views on myocardial contractility**

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The structures of the contractile and regulatory systems of cardiac muscle are very similar to those of skeletal muscle but are composed of proteins, the synthesis of which are controlled by genes that are uniquely expressed in the heart. The general metabolic processes involved in adenosine triphosphate production in cardiac muscle are fairly well understood and knowledge of them is used in clinical practice. Important advances have been made in the development of nuclear magnetic resonance techniques for non-invasively determining metabolic levels in the intact working heart and hence monitoring its function. Energy transduction in the heart is almost certainly very similar to that of other muscles, but the precise mechanism still remains uncertain despite intensive research. The regulation of contractile activity is of special significance to the myocardium, and recent investigations have detected aspects that are unique to cardiac muscle.
Digitalis and membranes

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The cardiotonic steroids are specific inhibitors of the membrane sodium-potassium activated adenosine triphosphatase responsible for the electrogenic exchange of sodium for potassium ions. One of the first actions of digitalis therefore is to perturb the surface membrane current. These current changes and their correlation with tension changes have been well characterised in recent work. Above $10^{-7}$ mol/l, strophanthidin reduces outward membrane current and increases the force of contraction. At lower concentrations, however, the drug can increase the pump current and this may be associated either with a reduction in force or with an increase in force.

Membrane current changes also occur as a secondary consequence of changes in pump activity either as a result of changes in electrochemical gradients or in the form of the "transient inward" current that may underlie glycoside induced arrhythmia. It has now become possible to reconstruct these and other glycoside induced changes using a computer model of electrical activity and calcium sequestration.

Digitalis for arrhythmias

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Excellent anecdotal evidence suggests that some of the original patients given digitalis by Withering and his contemporaries responded in exactly the same fashion as was later shown to be the case when, more than a century later, atrial fibrillation was recognised and the value of digitalis in controlling the ventricular rate by influencing atrioventricular nodal conduction demonstrated. Subsequently, it was shown to help block atrioventricular nodal conduction in atrial flutter but on some occasions to cause the return of sinus rhythm, often through a transient phase of atrial fibrillation. More than 50 years ago, digitalis preparations given intravenously were shown sometimes to terminate supraventricular arrhythmias, and it became widely used for this purpose. Its relative success rate is, however, low in comparison with more recently developed agents, especially some calcium antagonists, but it is potentially valuable, either alone or in combination with other agents, in the prophylaxis of re-entry atrioventricular tachycardias. Its greatest value is when given orally in atrial fibrillation in order to slow conduction through the atrioventricular node, where it has not been usurped by other agents; it is, however, contraindicated when atrial fibrillation complicates pre-excitation.

Digitalis toxicity

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Clinical manifestations of digitalis toxicity were clearly described by Withering. One hundred years later certain digitalis induced arrhythmias were inscribed on the smoked drum, the polygraph, and shortly thereafter, with the introduction of the electrocardiograph, manifestations of digitalis toxicity as recognised today were recorded in animal and man.

With popularisation of the direct writing electrocardiograph in the late 'forties and the introduction of digoxin in recommended doses that in retrospect appear inappropriately high, the documented prevalence of digitalis toxicity rose rapidly. With increased understanding of the interaction of electrolytes and digitalis and perhaps, but more importantly, the widespread use of digoxin in doses derived largely from its inotropic action and thus inappropriately low for the management of many of arrhythmias, the prevalence of toxicity began to decline. In addition, the advent of serum concentrations and the widespread acceptance of the concept of "therapeutic" concentrations, which frequently fall short of the desired clinical endpoint, served to preclude digitalis toxicity.

With the decline in digitalis toxicity as a result of the above factors, some of the digitalis related arrhythmias that once were common are now rarely observed. This discussion focused on arrhythmias which are highly specific for digitalis toxicity and are less commonly encountered. The discussion and classification of the arrhythmias are based on their most probable electrophysiological mechanism.

Unfortunately, Dr Fisch was unable to present his paper on account of ill health.