Proceedings of the British Cardiac Society

THE 63RD ANNUAL GENERAL MEETING of the British Cardiac Society was held at the University of Leicester on Wednesday and Thursday, 11 and 12 April 1984. The President, M F OLIVER, took the Chair during private business.

The following were elected to the British Cardiac Society.

New Ordinary Members: J G Bennett (London); M Boyd (Surrey); R M Boyle (York); W C Brownlee (Manchester); R S Bexton (Newcastle upon Tyne); I C Crawford (London); K M Daly (London); C Davidson (Littleborough); D Davies (Gwent); E T L Davies (Cheshire); J V de Giovanni (Birmingham); D F Dickinson (W Yorks); D S Dymond (London); E Ewem (Newcastle upon Tyne); W H Fennell (Ireland); W R Fitzgerald (Cambridge); R A Foale (London); J C Forfar (Oxford); I M Graham (Ireland); G J Green (Clwyd); R A Greenbaum (Middlesex); G J Grotte (Cheshire); A J Handley (Essex); G Hart (Leeds); R Hayward (London); W G Hendry (London); N M Hudson (Leicester); K P Jennings (Aberdeen); E K Jepson (London); R C Joshi (Staffs); A Mackay (Edinburgh); J Marcomichelakis (Surrey); R McKay (Liverpool); J H McKillop (Glasgow); M W Millar-Craig (Glasgow); J R Milne (Herts); A J Mourant (Cornwall); N Naqvi (Wigan); A W Nathan (Middlesex); G D Oakley (Sheffield); D B O'Keefte (Ireland); D O'Neill (Glasgow); I Ostman-Smith (Oxford); J R Parratt (Gloucester); D W Pitcher (Avon); J C S Pollock (Glasgow); J M Rawles (Aberdeen); P G Rees (Middlesex); N P Silverton (Leeds); D P Southall (W Sussex); R de L Stanbridge (Middlesex); I R Starkey (Oxford); C A Sykes (Cumbria); K M Taylor (London); G Terry (Durham); D S Thompson (London); P R Walker (Bristol); S Westaby (Middlesex); G F P Wharton (Kent); P R Wilkinson (Middlesex).

New Corresponding Members: A A A Yacoub (Sudan); L Pelides (Cyprus); C Fessas (Cyprus).

New Overseas Members: K A A Fox (USA); S A Qureshi (Pakistan).

New Extraordinary Members: R M Marquis, F G M Ross.

Resignations: M W McNicol, J B Partridge, E F McKeown.


Elections: M F Oliver re-elected President for the following year; a President-elect to be elected by ballot; D J Coltart elected Assistant Secretary; D J Rowlands elected to Council.

Abstracts of papers

Acute coronary thrombosis with a single intracoronary injection of BRL 26921

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BRL 26921 is a “protected” streptokinase derivative which selectively binds to thrombus. It was given as a single intracoronary injection to 20 patients presenting with chest pain of less than four hours’ duration, ST segment elevation on the electrocardiogram, and angiographically confirmed coronary occlusion not responding to oral or intracoronary nitrates. The mean time between onset of pain and administration of BRL 26921 was 3.2±1.3 hours. Reperfusion was assessed by repeat coronary arteriography between three and 20 (mean 10) hours later. Reperfusion occurred in nine out of nine patients with right coronary artery occlusion, six out of nine patients with left anterior descending coronary occlusion, and two out of two patients with left circumflex occlusion. Transient reperfusion arrhythmias occurred in 10 patients with ventricular fibrillation (successfully treated) in one. There were two late deaths, one at eight days in a patient with persisting left anterior descending coronary occlusion and one at 10 days following papillary muscle rupture. Despite successful reperfusion 19 out of 20 patients had electrocardiographic and plasma enzyme evidence of myocardial infarction. Seventeen patients showed some evidence of systemic fibrinolysis, but there were no serious bleeding complications. The efficacy of reperfusion correlated with the extent of fibrinolytic activation.

Intracoronary thrombosis with a single injection of BRL 26921 is practicable and may have advantages over prolonged streptokinase infusion.
Early beta blockade in acute myocardial infarction: radionuclide study of infarct size and left ventricular function

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Twenty patients presenting within four hours of the onset of their first uncomplicated myocardial infarction were randomised on a double blind basis to receive timolol maleate or an indistinguishable placebo. Planar thallium-201 scans in the anteroposterior, 45° left anterior oblique, and left lateral planes, rotating slant hole tomography, and technetium-99m gated blood pool scintigraphy were performed before treatment; scintigraphy was repeated hourly for six hours and daily for six days and planar thallium scans and tomography one week after myocardial infarction.

No significant reduction in infarct size in beta blocked patients was seen by quantifying planar thallium scans or reconstructed tomograms. There were three known reinfarctions in the timolol treated group. The most notable finding was a transient early deterioration in left ventricular function in the beta blocked patients, which was detected better by regional wall motion score (p<0.05) and phase analysis (p<0.01) than by global left ventricular ejection fraction (NS). This trend was reversed towards ultimate greater improvement in seven of 10 beta blocked patients compared with placebo at one week.

Early beta blockade after acute myocardial infarction may, therefore, temporarily depress left ventricular function. Subsequent improvement in these patients is not associated with a significant reduction in either thallium planar or rotating slant hole tomographic measurements of infarct size.

Infarct size and mortality in diabetic patients

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Four hundred and seventeen diabetic patients admitted with acute myocardial infarction between 1967 and 1983 had a hospital mortality of 33%, far exceeding the death rate of non-diabetic patients (17·5% in 3602 patients; p<0.001). This study was designed to determine whether this excessive mortality is caused by greater myocardial necrosis in diabetics or by an undue vulnerability of the diabetic myocardium to the effects of ischaemia.

A 16 year retrospective comparison of diabetic and non-diabetic mortality rates according to maximum values of aspartate aminotransferase activity was performed. In both groups, mortality rose with increasing enzyme activity, but for any specific value diabetic mortality significantly exceeded that of non-diabetic patients. One hundred and ten diabetic patients were then prospectively matched by age and sex with 110 non-diabetic infarct patients, and although the diabetics had a greater mortality (17% v 6%; p<0.05) and increased haemodynamic complication rate (45% v 25%; p<0.01), maximum values were not significantly different (388 IU/l v 349 IU/l). In order to measure infarct size more precisely creatine kinase MB enzyme release was studied in 19 diabetics and 19 matched controls. There was no significant difference in peak creatine kinase activity (227 IU/l diabetic v 315 IU/l non-diabetic), total creatine kinase enzyme release (384 IU/l v 529 IU/l), or peak aspartate aminotransferase activity (497 IU/l v 503 IU/l).

It is concluded that diabetic patients do not have larger infarcts than non-diabetic patients and that the excessive mortality in diabetic patients is due to an abnormal sensitivity of the diabetic myocardium to ischaemic insult.

Are the clinical benefits of prenalterol in ischaemic heart failure due to beta blockade?

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The clinical effects of the oral beta, agonist prenalterol were investigated in 37 patients (29 male, eight female, mean age 57±7 years (±SD)) with chronic ischaemic left ventricular failure (ejection fraction 0·26±0·10) using a placebo controlled randomised double blind protocol over six months. All patients were limited by dyspnoea (New York Heart Association class III) despite taking digoxin and diuretics. Plasma sampling confirmed drug compliance in all patients. Twenty eight patients completed the protocol. Clinical improvement (symptoms and signs) was seen in 15 of 19 patients taking prenalterol and in nine of 18 patients taking a placebo. Clinical deterioration was not seen in the prenalterol group but was
observed in seven patients taking a placebo (p<0.05). Bicycle exercise capacity increased in the prenalterol group (307±178 to 432±248 watt min; p<0.01) and was unchanged in the placebo group (288±158 to 338±160 watt min; NS). Maximum heart rate was reduced in the prenalterol group (136±19 to 120±22 beats/min; p<0.01) and unchanged in the placebo group (136±22 to 140±21 beats/min; NS). Rest and exercise radionuclide ejection fraction and cardiothoracic ratio were unchanged in both groups. There was no evidence of increased angina or ventricular arrhythmias in the prenalterol group.

Prenalterol appeared to produce clinical benefit by reducing exercise heart rate without improving left ventricular performance, perhaps mediated by a partial beta, antagonist effect.

Effects of nitrates on nutrient myocardial blood flow

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The distribution of myocardial blood flow and the effects of 0.4 mg sublingual nitroglycerin were evaluated using xenon-133 in 26 patients undergoing coronary angiography. Eight had normal vessels and five had high grade obstructions in a single major vessel, nine in two major vessels, and four in three major vessels. Xenon-133 400 MBq (10–8 mCi) was injected intracoronary under direct vision and images acquired by a gammacamera in the 40° left anterior oblique projection for five minutes, with curves fitted to the first 30 seconds for washout. Electrocardiogram, heart rate, and intra-arterial pressure were monitored continuously. Nitrate produced an increase in heart rate of a mean (±SD) of 2 beats/minute from 63±2 to 65±3 and mean blood pressure fell by 7 mm Hg from 87±3 to 80±3 mm Hg. Flow in normal right coronary artery arteries increased from a mean (±SD) of 30±4±5 (p<0-01) to 37±±6±8 ml/100 g, in the left anterior descending from 41±5±9±7 to 44±5±9±2 ml/100 g, and in the left circumflex from 56±8±7±7 to 61±7±13±9 ml/100 g after trinitrin administration. In areas supplied by coronary arteries with a high grade obstruction flow in the right coronary artery fell by 17% (p<0-01), in the left anterior descending by 19% (p<0-01), and in the circumflex distribution by 7% after nitrates. Similarly, in ischaemic areas supplied by collaterals, flow diminished by 27% (p<0-05) after nitrates. These results suggest that nitrates do not increase nutrient flow in ischaemic areas of the myocardium in patients with coronary heart disease.

Ischaemia and reperfusion induced arrhythmias in the in vivo rat: a possible role for free radicals?

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Xanthine oxidase activity is a major source of superoxide radical production during ischaemia and particularly during reperfusion. Since free radicals play a role in the development of injury the ability of allopurinol, the specific inhibitor of xanthine oxidase, to modify arrhythmias caused by ischaemia and reperfusion was assessed. Rats were pretreated with allopurinol (20 mg/kg orally 24 h before study and 20 mg/kg intravenously 15 min before study). Arrhythmias were quantitated in an anaesthetised open chest preparation with (a) coronary artery occlusion for 30 min and (b) coronary occlusion for 5 min followed by 10 min reperfusion (n=18 in each group). Allopurinol treatment reduced the incidence of ischaemia induced ventricular tachycardia from 89% to 50% (p<0-02) and the number of ventricular extrasystoles from 471±120 to 116±46 (p<0-02) but had no effect on the incidence or duration of ventricular fibrillation, duration of ventricular tachycardia, or mortality. In contrast, during reperfusion dramatic protection was observed, such that ventricular fibrillation was reduced from 67% to 11% (p<0-001), duration of ventricular fibrillation and tachycardia were reduced from 230±70 to 14±1 s and from 93±26 to 38±8 s (p<0-05) respectively, and mortality was reduced by half (56% to 22%; p<0-05).

In conclusion, allopurinol pretreatment affords some protection against ischaemia induced arrhythmias and a high degree of protection against reperfusion induced arrhythmias. It is proposed that superoxide production may be an important new factor to consider in relation to tissue vulnerability to ischaemia and reperfusion induced arrhythmias.

Use of amiodarone in children

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Little is known about the efficacy of amiodarone in childhood. Twenty four patients aged from 1 week to 14 (mean 6-7) years with life threatening arrhythmias were treated for from two weeks to 4-6 years (mean 1-5 years). Indications were supraventricular tachycardia (8), Wolff-Parkinson-White syndrome (7), ventricular tachycardia (5), atrial flutter (3), and His tachycardia (1). Five patients had associated structural lesions and one cardiomyopathy. Twenty three had received on average 2-4 antiarrhythmic agents before starting treatment with amiodarone. Four received initial intravenous treatment. The arrhythmia was controlled in 22 of the patients at drug dosages of 2-7-3-4 mg/kg/day (mean 10-6) associated with trough blood concentrations of 0-4-2-3 mg/l (mean 1-02) for amiodarone and 0-2-2-6 mg/l (mean 0-88) for desmethyl amiodarone. Treatment was ineffective in two in whom amiodarone concentrations were 1-0 and 1-1 mg/l. Amiodarone was used in combination with digoxin in five and verapamil in one. Side effects were photosensitivity (11), grey pigmentation (2), sleep disturbance (2), deranged liver or thyroid function tests (2 each), complete heart block (1), sinus arrest (1), skin rash (1) and gritty eyes (1). Corneal deposits occurred in seven of 11 patients examined by slit lamp. Side effects necessitated cessation of treatment in three patients. It is concluded that amiodarone is an effective drug in childhood, but in contrast to previous reports side effects in this study were common and sometimes serious.

Natural history of perimembranous ventricular septal defects: a prospective echocardiographic haemodynamic correler study

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Fifty eight consecutive infants in whom a large isolated perimembranous ventricular septal defect was identified by cross sectional echocardiography were followed for a mean period of 1-9 years. Nineteen outlet, 25 inlet, and 14 confluent perimembranous defects were studied. No defect closed spontaneously. Eight have so far required surgical closure (six outlet and two confluent types). In the remaining patients, 31 showed early clinical improvement suggesting a reduction in defect size. In two patients improvement was associated with developing infundibular pulmonary stenosis. Clinical improvement in the remaining 29 was associated with adherence of tricuspid tissue to the margins of the defect to form a "pseudoaneurysm." This was consistently visualised by echocardiography. In three patients a pseudoaneurysm was identified at birth. In the remaining 26 there was evidence of pseudoaneurysm formation by 9 months. Pseudoaneurysm formation occurred only where the tricuspid valve was related to part of the defect margin. Correlative catheter data were available in all 58 patients (sequential studies in 23). In 28 of 29 patients pseudoaneurysm formation was associated with a right ventricular peak systolic pressure of less than half the systemic value; a large intracardiac shunt persisted in nine of these. In the remaining patient the pulmonary vascular resistance remained raised from birth.

It is concluded that the major determinant in the natural history of a perimembranous ventricular septal defect is the relation of tricuspid tissue to the defect margins which allows the potential for pseudoaneurysm formation which in turn reduces defect size.

Fallot's tetralogy: a comparative study of correction in infancy and later

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Controversy still exists regarding primary correction versus palliation with later repair for infants with tetralogy of Fallot requiring operation. During the past nine years 78 consecutive children underwent correction with an overall early mortality of 3-8%. These have been analysed as two groups; the first comprising 39 infants (two early deaths) and the second 39 children aged 1 to 5 years (one early death) (p<0.5). In contrast with other series, only five infants (12%) had initial palliation resulting in one early death and four subsequent successful corrections.

Deep hypothermia with total circulatory arrest was used in 38 infants and eight older children. Transannular patching was required in 82% of infants compared with 67% of older patients (p<0.25). The postoperative right ventricular to systemic pressure ratio exceeded 0-5 in 15% of the infants and 31% of the older patients (p<0.1). Postoperative inotropic support was required in 44% of infants and 28% of the older group (p<0.25). The infant group have been followed for a mean of 3-8 years and the older group for a mean of 5-2 years. Complications have included two complete heart block (both early deaths) and one residual infundibular obstruction (requiring reoperation). There are no significant residual ventricular septal defects.

It is concluded that with appropriate case selection
primary correction of tetralogy of Fallot in infancy can be achieved with no significant difference in early mortality or morbidity when compared with late correction and offers definite advantages over a two stage procedure.

Local abnormalities of right ventricular depolarisation after repair of tetralogy of Fallot: a basis for ventricular arrhythmia during daily life

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Ventricular arrhythmia is common after repair of tetralogy of Fallot and may be responsible for late sudden death. An electrophysiological study was performed in 22 patients (21 with right bundle branch block), from three to 22 (mean 13) years after repair, to determine factors which might predispose to ventricular arrhythmia. The HV interval and right ventricular apical activation times were measured: local electrograms were recorded from multiple sites in the right ventricle and from the left ventricle (10 patients). Findings were related to the results of 48 hour ambulatory electrocardiographic monitoring, which revealed frequent (>30/hour) or complex ventricular arrhythmias or both in 11/22 (50%) patients. Local right ventricular electrograms were normal in 10 patients. In the other 12, electrograms were split or delayed at one or more right ventricular sites, reflecting abnormal local depolarisation. Left ventricular recordings were normal in all. Ventricular arrhythmias were significantly more common (9/12 v 2/10; p<0.03) and more severe (ventricular tachycardia in 9/12 v 0/10; p<0.01) in patients with abnormal compared with normal electrograms. In contrast, there was no association between ventricular arrhythmia and left axis deviation (eight patients), HV prolongation (two patients), or central right bundle branch block (seven patients).

While abnormalities were found throughout the conducting system, ventricular arrhythmias during daily life were related to local inhomogeneity of myocardial activation. Re-entry associated with right ventricular depolarisation abnormality is likely to be the mechanism for ventricular tachycardia in these patients.

Does successful coronary angioplasty cause myocardial necrosis?

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Coronary angioplasty is now an accepted treatment for patients with single vessel coronary artery disease. Some patients with multiple vessel disease have only one artery which would be amenable to bypass grafting and which may also be suitable for angioplasty. Changes in plasma enzyme activity (total creatine kinase and its MB isoenzyme (CK-MB)) were used to estimate the degree of myocardial necrosis and were compared with the results after the dilatation of one vessel in patients with single and with multiple vessel disease. Eighteen consecutive patients with angina pectoris (11 men, seven women; mean age 47 years) had enzyme activities measured before and after successful angioplasty. Ten of these patients had single vessel disease and eight multiple vessel disease. In addition, measurements were made in 11 other patients (eight men, three women; mean age 49 years) undergoing routine coronary angiography and in five patients with full thickness acute myocardial infarction. In the 10 patients with single vessel disease angioplasty caused no increase in enzyme activities. There was, however, a significant increase in the activity of CK-MB in the eight patients with multiple vessel disease (p<0.05, paired t test). This increase was very small when compared with the changes seen in the patients with acute infarction.

No difference in technical factors could be found between the two groups of patients having angioplasty to explain the rise in enzyme activity. The mechanism of the myocardial necrosis is at present unknown.

Simultaneous conventional 12 lead electrocardiographic changes during coronary angioplasty procedures

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Transient occlusion of a coronary artery during balloon angioplasty mimics spontaneous reversible vessel occlusion. Forty one angioplasty procedures (33 left anterior descending, five right, and three circumflex coronary arteries) were monitored by continuous simultaneous conventional 12 lead electrocardiograms. Two patients had two and one had three vessel disease. One had a previous infarction. Left anterior descending coronary artery occlusion produced anterior ST elevation in 31 patients, the other two with good collaterals and distal pressure during occlusion having only transient T wave changes. Right coronary angioplasty produced ST elevation in the inferior leads in all patients with changes extending to V4-6 in two patients with very dominant right coronary arteries. All circumflex artery occlusions produced inferior ST elevation and anterior ST depres-
Coronary angioplasty may cause localised intimal damage, and smooth muscle proliferation may occur in the vessel wall. The incidence of coronary spasm after successful angioplasty was, therefore, assessed in nine consecutive patients by provocative testing with hyperventilation and intravenous ergonovine during follow up coronary angiography performed at a mean of 16 weeks after angioplasty. Only those patients with a less than 30% residual stenosis at the site of the dilatation were subjected to provocation by two minutes forced hyperventilation followed by 400 μg of ergonovine intravenously. All vasoactive drugs had been discontinued 48 hours before the study. Coronary spasm was documented in two patients at the site of the original successful dilatation. In both cases pain was reproduced and the spasm relieved by intracoronary isosorbide dinitrate. Both of these patients had had rest pain before angioplasty and had had severe symptoms after angioplasty. None of the patients in whom spasm could not be provoked had rest pain before or after the angioplasty. Patients who have a history suggesting coronary spasm may not be rendered asymptomatic despite successful dilatation of a significant coronary stenosis.

Outcome of acute coronary occlusion during percutaneous transluminal coronary angioplasty

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In a total of 197 percutaneous transluminal coronary angioplasty procedures acute occlusion of the stenosed coronary vessel occurred in 19 (10%) patients. In nine cases coronary dissection was seen either on angiography (8) or at subsequent emergency coronary artery bypass grafting. Severe coronary artery spasm resistant to sublingual and intracoronary nitrate was thought to be responsible for vessel occlusion in four cases. Intracoronary thrombus was seen on angiography in two cases. In the remaining four cases the cause of occlusion was thought to be balloon malposition in two. Immediate repeat angioplasty was successfully performed in all four cases of coronary spasm. Similar attempts were made in the two cases of thrombotic occlusion and three cases of coronary dissection with only one successful outcome. Emergency bypass grafting was performed in the remaining 14 patients with two hospital deaths.

Emergency coronary artery bypass grafting is usually required for acute coronary occlusion during percutaneous transluminal coronary angioplasty unless antegrade flow can be re-established by immediate repeat angioplasty. Recannulisation with the angioplasty catheter is more likely to be successful when occlusion is due to spasm rather than to dissection or intravascular thrombosis.

Continuous wave Doppler ultrasound as an adjunct to cross sectional echocardiography in the diagnosis of critical left heart obstruction in neonates

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If cross sectional echocardiography in isolation is used to diagnose critical left ventricular outflow obstruction in neonates false positive and false negative diagnoses may result. In order to determine the important sites of obstruction we have, therefore, used continuous wave Doppler ultrasound to measure blood flow velocity in the ascending and descending thoracic aorta in six such patients (age <6 weeks) presenting with reduced or absent peripheral pulses. Examination of the pulses suggested aortic stenosis in three patients and coarctation in three, but cross sectional echocardiography showed aortic valve thickening in
all six and coarctation in two. Doppler ultrasound demonstrated abnormal high velocity blood flow jets (>3 times normal) in the ascending aorta in three patients suggesting aortic stenosis with normal descending aortic flow velocity. In the remaining three, velocity in the ascending aorta was normal but high in the descending aorta suggesting coarctation. The diagnosis was confirmed in all five patients requiring surgery. Two patients had residual high velocity jets after aortic valvotomy. Both had significant pressure gradients across the aortic valve at cardiac catheterisation with good agreement between actual gradients and those predicted by the Doppler technique (58 mm Hg v 60 mm Hg; 77 mm Hg v 80 mm Hg).

Thus a combined anatomical and physiological approach using cross sectional echocardiography and continuous wave Doppler ultrasound enables accurate non-invasive definition of the site of left ventricular outflow obstruction and may obviate the need for invasive investigation in these sick patients.

**Non-invasive assessment of severity of ventricular outlet obstruction in children using Doppler echocardiography**

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Continuous and pulsed wave Doppler echocardiography was used to study 19 infants and children (aged 3 months to 14 years) with ventricular outlet obstruction defined by cardiac catheterisation and angiocardiology. Fourteen had right ventricular outlet obstruction (pulmonary valve stenosis or pulmonary artery banding) and five left ventricular outlet obstruction (aortic valve, subvalvar or supravalvar stenosis). Peak to peak pressure gradients at catheterisation ranged from 5 to 100 mm Hg. Patients were studied before catheterisation or afterwards by an observer who did not know the severity of the obstruction. The gradient was calculated from Doppler echocardiography by measuring the maximum velocity of blood flow at the obstruction and applying the modified Bernoulli equation—that is, pressure drop (mm Hg)=4 × the square of the maximum velocity (m/s). Comparison of Doppler and catheterisation gradients yielded a correlation coefficient of 0.91. This confirms recent reports on the accuracy of Doppler echocardiography in determining the severity of ventricular outlet obstruction. The question now presenting itself is whether it may be possible to dispense with catheterisation in the selection for surgical treatment of some patients with semilunar valve stenosis.

**Congenital heart defects and twinning**

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Several authors have suggested that monozygotic twinning is associated with excess cardiac malformations, but no study has combined adequate proof of zygosity with unbiased ascertainment and precise cardiac diagnoses in a sufficiently large series to provide confirmation.

Over 400 twins with cardiovascular malformations have been identified in five British centres: Freeman Hospital, Newcastle; The Hospital for Sick Children, London; and the twin/malformation registries in Aberdeen, Liverpool, and Birmingham. Where possible, twin pairs were examined and zygosity confirmed by examining blood polymorphisms. Even after conjoined twins and persistent ductus arteriosus had been excluded, monozygotic twin individuals have twice the expected incidence of heart defects. It is likely that the twinning process itself affects heart development in one of the pair. Disturbance of laterality, or "mirror imaging," appears to be more important than twin to twin transfusion. The recurrence risk faced by the parents of a monozygotic twin with a heart defect is less than that for parents whose affected child was a singleton birth. Genetic studies using twins have in the past caused inappropriate emphasis to be placed on environmental insults as causes of cardiovascular malformation.

**One stage anatomic correction of simple complete transposition of the great arteries in neonates**

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Between May 1982 and December 1983, 11 neonates aged between 3 and 35 days with complete transposition of the great arteries and an intact interventricular septum underwent primary correction at the arterial level. Balloon septostomy was performed in 10 and deliberately not undertaken in the youngest. The peak systolic left ventricular pressure ratio varied from 0.58 to 0.9 (mean 0.82). The vectorcardiogram showed initial counterclockwise forces in the horizontal plane in 10 patients while one already showed a clockwise shift. Deep hypothermia with circulatory arrest was used in seven patients and hypothermic cardiopulmonary bypass with low flows in the remaining four. There was one early and no late deaths with a follow up of 1–17 (mean 7-1) months. Postoperative diuretic treatment was continued for periods varying from three to six weeks, and patients were discharged.
from hospital 14 to 22 days after operation. Left ventricular function assessed by M mode and cross sectional echocardiography was within normal limits in all. It is concluded that early results of primary anatomical correction of simple transposition of the great arteries in neonates are encouraging. Further experience is required to assess the value of this procedure in this age group.

"Mal-conducted atrial ectopic tachycardia" masquerading as sick sinus syndrome: electrophysiological assessment and its medical management

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Many patients with "brady-tachy" variant of sick sinus syndrome continue to have symptoms despite pacemaker implantation and require additional medical treatment. Seventy patients were investigated electrophysiologically before pacemaker implantation. Fourteen had no detectable dysfunction of sinus node, atrioventricular conduction, or carotid sinus sensitivity. Intracardiac atrial electrocardiogram documented atrial ectopic rhythms, which at times were non-conducted. A simultaneous surface electrocardiogram had the appearance of sinus arrest. In 12 out of 14 patients ectopic activity was controlled by amiodarone, and subsequent bradycardic pauses were abolished. Symptomatic improvement, with Holter monitoring confirmation, was maintained for four to 20 months.

Some patients with the brady-tachy syndrome have primary abnormality of increased atrial ectopic activity rather than sinus node dysfunction and can be differentiated electrophysiologically. These patients with "mal-conducted atrial tachycardia" can be effectively managed with medical treatment alone and should not be grouped with the sick sinus syndrome.

Effectiveness of a simplified invasive study in the investigation of cardiac arrhythmias

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In the investigation of suspected cardiac arrhythmias the use of the intracardiac programmed stimulation study is limited to a small proportion of patients by the beliefs (a) that the facilities required can be made available only at special centres and (b) that the procedure is traumatic and prolonged, involving the insertion of three to five pacing leads and the use of a complex protocol of tests. Sixteen patients with minimal protocols tailored to answer only those questions crucial to their management were studied. Using only one or two leads, standard three channel (or in three cases four channel) electrocardiographs and either an external pacemaker with a high rate switch or a simple portable programmed stimulator satisfactory results were obtained in all cases. Of 10 cases of suspected unidentified tachycardia, origins were identified in nine by induction of the arrhythmia and strongly suggested in one. Of four cases with electrocardiograms suggesting pre-excitation, an accessory pathway with a dangerously short refractory period was identified in one and excluded in three. In two cases, the sites of atrioventricular conduction defect were identified.

It is concluded that a simplified invasive study, possible outside a specialist centre, can yield the required answers and may be the appropriate test in a greater proportion of patients with suspected arrhythmias.

Interruption of anomalous atrioventricular conduction using a transvenous electrode catheter to deliver shocks in the coronary sinus

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Four patients with tachycardias associated with ventricular pre-excitation had not responded to antiarrhythmic drugs and were considered for transvenous electrode catheter ablation. Two patients had typical orthodromic tachycardias, and one had additional profound sinus bradycardia when taking antiarrhythmic treatment. Two patients had rapid atrial fibrillation at rates of up to 300 beats/min. Intracardiac studies located the anomalous pathway in the septal region in one patient, in the mid-posterosal region in one, and on the left lateral free wall in two. Coronary arteriograms showed a non-dominant circumflex artery remote from the coronary sinus in all patients. Venous phase films demonstrated the anatomy of the coronary sinus. In both patients with anomalous pathways in the septal or mid-coronary sinus region the sinus was of good size at the location of the pathway. In both patients with free wall pathways, the coronary sinus tapered distally, and for these reasons it was thought inappropriate to proceed to ablation. In the others, a new 7F electrode catheter was positioned at the site of the anomalous pathway, and four to six shocks of between 50 J and 100 J were delivered to one pole. The other output of the defibrillator was connected to a paddle placed on the anterior chest wall. In both patients, anterograde conduction
disappeared immediately after the first shock. One patient remains free of symptoms after three months. The other showed recurrence of pre-excitation after three weeks. A repeat ablation procedure was successfully undertaken. This method may provide an alternative to other non-pharmacological treatment in selected patients with pre-excitation.

Endocardial ablation as an antiarrhythmic technique: the background to its application to ventricular tachycardia

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Ablative techniques in arrhythmia management have been applied to the His bundle and bypass tracts. The in vitro effects of high energy electrical impulses on the conducting medium, guinea pig, and pig ventricles were investigated using unipolar, bipolar, and helix electrodes. A plastic tank, with side viewing port, was filled with Ringer's solution. Impulses of 10 J to 400 J were applied to the different catheters. The effects were recorded on video tape and high speed cine film. Pressure measurements were recorded. The unipolar electrode fractured on application of 100 J. The bipolar and helix electrodes withstood 400 J. Over the range of energies used, flash sizes of 5–20 mm with the bipolar electrode and 4–24 mm with the helix electrode were recorded. Peak pressure pulses of several atmospheres were observed approximately 10 cm from the electrode tips. Theoretical temperature rises of several hundred degrees Celsius were calculated. The application of 200 J to isolated guinea pig and pig myocardium produced macroscopic changes (haematoma). Microscopical changes occurred at lower energies, penetrating to various depths depending on the electrode and energy used.

Thus ventricular tachycardia foci might be ablated using high energy and an active fixation electrode if isolation techniques are sufficiently precise.

Modified cephalic vein approach with axillary pacemaker implant relatively free from myopotential inhibition

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The percutaneous subclavian direct puncture approach for the pectoral implantation of a pacemaker unit is time saving, but the creation of a pneumothorax or inadvertent puncture of the arterial and thoracic ducts is not rare. The safer cephalic vein dissection is time consuming and occasionally unrewarding. With a modified cephalic vein approach prior catheterisation by direct puncture of the external antecubital vein delineated the cephalic vein radiologically and physically and indicated suitability. Direct dissection through a small incision on to the catheter in the deltopectoral groove facilitated cannulation.

A pacemaker implanted over the pectoral region is unsightly and exposed to trauma and electromyopotential inhibition. Axillary implant of the unit through a high mid-axillary line incision with a dorsal pocket is comfortable and cosmetically acceptable. Stimulation of the muscles of the anterior and posterior axillary folds can be avoided by positioning the unit in the deep axillary fat. In 100 axillary implants myopotential inhibition on isometric exercise was less than 4%, which is significantly lower than the published figures for other implant sites.

This modification of the cephalic vein approach provides rapid and safe access to alternative venous pathways for atrial or ventricular electrodes. An axillary pacemaker implant is not exposed to superficial injury and is cosmetic and relatively free from muscle stimulation or myopotential inhibition.

“Concertina” pacing for tachycardia reversion

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A new automatic multiple beat (one to seven) scanning pacemaker for tachycardia reversion has been developed and implanted. The first coupling interval and subsequent intervals are programmable, and all may decrement in 6 ms steps. To evaluate its efficacy an external version was used for atrial or ventricular pacing in 19 patients; 18 had junctional and one ventricular tachycardia. One stimulus was used initially, and its coupling interval decremented until tachycardia was terminated or refractoriness reached. This was repeated using two to seven stimuli. When more than one beat was used the initial coupling interval and all subsequent pacing intervals were always equal and all decremented in 6 ms steps (“concertina” pacing). Termination was achieved by one stimulus in five patients, by two in 17 patients, and by more than two in all patients. There was a relation between the number of beats used and the maximum terminating cycle length: one stimulus, 253 ms (68% of tachycardia cycle length); two stimuli, 232 ms (71%); three stimuli, 254 ms (77%); four stimuli, 267 ms (81%); five stimuli, 274 ms (83%); six stimuli, 283 ms (85%);
and seven stimuli, 287 ms (86%). In three cases, one or two closely coupled stimuli provoked atrial arrhythmias, but more than two were never proarrhythmic. This pacemaker was implanted in five patients with junctional tachycardias. Pacings from the right atrium with seven stimuli was used in three patients and with four stimuli in one. Double scanning ventricular stimuli were used in one patient. Tachycardia was rapidly terminated in all five patients, none of whom required additional antiarrhythmic drugs.

Concertina pacing using multiple stimuli of long cycle length is a simple, safe, and effective anti-tachycardia pacing mode.

Early and late results of surgical management of patients with Marfan's syndrome

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Forty nine patients with the skeletal manifestations of Marfan’s syndrome were operated on between September 1970 and December 1983. Seven patients, all female, had floppy mitral valves with or without aneurysm of the ascending aorta. Two patients had aneurysm of the descending aorta and 40 aneurysm of the ascending aorta with or without dissection. This latter group comprised 28% of all aneurysms of the root of the aorta operated on during this period. The age at operation varied between 7 and 58 (mean 30-8) years compared with a mean age of 56-4 years for the other patients with aneurysms of the aortic root. Fifteen (30%) patients underwent emergency operation. Twenty five patients required valve replacement, while in the remaining 18 valve conserving operations were performed. There were three early deaths (6% mortality), all in the emergency group: one patient with acute dissection of the descending aorta and two in low output state with chronic aortic regurgitation. With a follow up of one to 148 (mean 66) months, there were 10 (20%) late deaths, eight occurring in patients with chronic dissection or aneurysm and two in the mitral group, giving an actuarial survival in the whole group of 65% at six years. Thirteen patients developed subsequent aneurysms, of whom 10 were resected with one death; five patients died of rupture of subsequent or undiagnosed aneurysms. It is concluded that surgical treatment of Marfan’s syndrome gives good early results and that careful follow up is essential to detect and correct any further lesions.

Long term follow up of the Shiley made pericardial xenograft

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The pericardial xenograft valve has been used at Leeds General Infirmary since 1971. Since 1976 the pericardial valve has been manufactured by a specialised laboratory (Shiley). This paper reviews the experience with 788 Shiley made pericardial xenografts implanted in 601 patients between 1976 and 1983. Single valve replacement was undertaken in 438 patients (205 aortic, 230 mitral, and three tricuspid). Multiple valve replacement was done in 163 patients (double 139 patients, triple 24 patients). Follow up ranged from three to 92 (mean 40-2) months with a total follow up of 1790 patient years. Actuarial analysis showed the survival rate at eight years to be 86-8±7-2% (aortic), 89-6±3-9% (mitral), and 77-4±9-4% (multiple replacement). Long term anticoagulants were not used. Warfarin (1976-82) or persantin (from 1 July 1982) was given for the first six postoperative weeks only to patients with mitral or multiple valve replacement. Embolisation occurred in seven patients (five early and two late). The actuarial freedom from embolisation at eight years was 98-8±0-8%, 96-8±2-9%, and 99-2±0-8% for patients with aortic, mitral, and multiple valve replacement respectively. Valve thrombosis was not encountered. Valve dysfunction occurred in seven patients (0-39% a year), calcification in three, and mechanical abrasion in four. The actuarial freedom from valve failure was 94-5±3-8% at eight years of follow up.

This analysis shows a good survival record and a low incidence of valve failure and embolisation in the absence of long term anticoagulants in patients with Shiley made pericardial xenograft valves.

Digital subtraction aortography for evaluation of coronary bypass graft patency: potential for outpatient use

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Aortography performed with digital subtraction techniques may permit the angiographic evaluation of coronary bypass graft patency with a small calibre, non-selective catheter. To evaluate the accuracy of this method conventional selective graft cineangiography was compared with digital subtraction aorto-
the purpose of the study was to examine the usefulness of digital subtraction angiography in the evaluation of left ventricular function. Left ventricular function was examined in 24 patients by three methods: (a) conventional venous catheterization using an intravenous injection of 40 ml of contrast medium, (b) small volume (10-15 ml) left ventriculography, and (c) intravenous injection of 30 ml contrast medium. Images were recorded with a conventional image intensifier-television chain on to video tape and later analysed using a nuclear medicine computer with a digital interface. There was excellent correlation of ejection fraction and wall motion between conventional ventriculography and small volume left ventriculography (r=0.92 and r=0.71 respectively) and good correlation between conventional and intravenous methods (r=0.88 and r=0.67 respectively). Minimal contrast induced ventricular extrasystoles were observed in either the small volume or intravenous methods compared with approximately 60% in the conventional method. Exclusion of studies containing ectopic cardiac cycles considerably improved the correlation between conventional and small volume methods (r=0.97) and between conventional and intravenous methods (r=0.95). Digital subtraction angiography techniques can be successfully applied to the evaluation of left ventricular function and wall motion with a lower incidence of ventricular extrasystoles, less risk of toxicity, and less radiation exposure to patient and operator.

**Mortality from infective endocarditis**

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Factors influencing mortality were studied in 92 consecutive patients with infective endocarditis admitted to two district general hospitals between January 1975 and April 1982. The estimated disease incidence in the locality was 16/100000/year. Overall mortality was 35% including 13 patients who died before diagnosis. Nineteen of the remaining 79 (24%) patients died despite aggressive antimicrobial therapy. Bactericidal antibiotic concentrations were monitored in 39 cases, but these did not appear to influence mortality. There were no cases of relapsing infection. Mortality was lowest for *Streptococcus viridans* infections (15%) but rose to 50% for infections with *Streptococcus faecalis* and other less common organisms. Most deaths were in patients over 50 years old. Cardiac failure on admission was a poor predictor of mortality, although this was the principal cause of death during treatment (14 cases). Other causes of death were cerebral embolus (three cases) and pneumonia (two cases). Eight patients had emergency valve replacement and three died postoperatively. When the diagnosis was missed during life (13 cases) arterial embolus was a common presenting feature (46%). Classical signs of endocarditis, other than pyrexia, were absent. A cardiac murmur (always mitral incompetence) was noted in only six of these patients and considered to be insignificant. The continuing high mortality from infective endocarditis, despite advances in antimicrobial therapy, suggests that a reappraisal of management is required, co-ordinating medical and surgical treatment.

**Association between sudden death in squash players and cardiovascular disease**

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Squash has enjoyed an increase in popularity in recent years. Unfortunately, an increasing number of sudden deaths have been reported in association with the sport. The principal causes of such deaths have not been defined. A series of 30 sudden deaths (29 men, one woman) associated with squash is reported. The mean age (±SD) was 46±7±9-58 years; the age range 22-66 years. Necropsy results were available in 27 subjects. Significant coronary heart disease was found in 23, valvular heart disease in three, hypertrophic obstructive cardiomyopathy in one, and cardiac...
Evidence that cation transport in vivo is inhibited by short term but not long term digoxin therapy

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Cation transport in man can be studied in vivo by measuring the changes in plasma and red cell rubidium concentrations after an oral load of rubidium chloride. Using this method in normal volunteers a loading dose of digoxin produced changes that are consistent with reduced sodium, potassium, and adenosine triphosphatase activity in vivo. The results in patients receiving digoxin for less than one week (short term digoxin, n=8) or more than three months (long term digoxin, n=12) are now reported and compared with those in well matched control subjects. After an oral load of rubidium chloride patients taking short term digoxin had a significantly greater increase in plasma rubidium concentrations and a significantly smaller increase in red cell rubidium concentrations compared with control subjects, but the results in patients taking long term digoxin did not differ from those in control subjects. The rate of net red cell rubidium accumulation, corrected for the plasma rubidium concentration, was significantly (p<0.05) reduced in patients taking short term digoxin (median 0.17, range 0.0-0.32/h) compared with control subjects (0.28, 0.15-0.45/h) but was not altered in patients taking long term digoxin (0.33, 0.23-0.75/h) compared with control subjects (0.30, 0.19-0.46/h).

These data support previous in vitro findings, which suggest that the inhibitory effect of digoxin on cation transport does not persist during long term therapy.

Non-invasive assessment of cardiac output at rest and exercise using Doppler ultrasound

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Cardiac output can be obtained from a knowledge of the mean ascending aortic blood velocity and aortic root cross sectional area. Ascending aortic blood velocity was obtained non-invasively from the suprasternal notch using a Bach-Simpson 2.2 MHz directional blood velocity meter and integrated to give mean velocity. Aortic root area was determined by conventional M mode echocardiography.

Simultaneous measurements of Doppler and thermodilution cardiac output were made on 36 occasions in 17 patients at rest. A further 24 observations of cardiac output were made in four normal subjects at rest and at two levels of bicycle ergometer exercise (50 and 100 W) simultaneously with a nitrous oxide (N₂O) rebreathing technique. Values of cardiac output for both groups ranged from 0.9 to 9.9 l/min. Linear regression analysis of the data gave r=0.98 for Doppler versus thermodilution output (Doppler=0.04+0.99 Therm), and r=0.97 Doppler versus N₂O (Doppler=0.36+0.91 N₂O). Doppler mean velocity, the only changing variable in the cardiac output equation—cardiac output (l/min)=mean velocity x aortic root area x 60—correlated well with thermodilution in those patients who had an aortic root area within the normal range (4.9-11.3 cm²). In those 12% of patients with an abnormally large aortic root area, mean velocity alone could not be used as an index of cardiac output, although serial changes in cardiac output within any one patient can still be accurately monitored.

Cardiac output can thus be accurately measured over a wide range in both patients at rest and normal subjects at rest and exercise.

Relation of electrical and mechanical events in left ventricular hypertrophy

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The presence of an electrocardiographic “strain” pattern is a time honoured feature of left ventricular hypertrophy, and while its clinical significance is well known its aetiology is unclear. To study the relation of electrical and mechanical events digitised M mode echocardiograms and 12 lead electrocardiograms were recorded in 99 patients with left ventricular hypertrophy (pressure overload and hypertrophic car-
diomyopathy) and compared with those of 14 athletes and 20 normals. Left ventricular mass was increased (p<0.01) and fractional shortening and peak velocity of circumferential fibre shortening reduced (p<0.05) in patients with strain in comparison to those without. In addition, strain was associated with significantly reduced peak rate of dimension increase and posterior wall thinning (p<0.01) and delayed mitral opening (p<0.01). Despite abnormal repolarisation, the normal timing of the QT interval and electromechanical systole was maintained with the end of the T wave preceding minimum left ventricular cavity dimension by 79±45 ms in normals and 100±61 ms in patients with left ventricular hypertrophy. Athletes, who exhibited an equivalent degree of left ventricular hypertrophy to patients, had normal systolic and diastolic function, but electromechanical systole was shortened from normal (p<0.01) and the end of T wave and minimum dimension were synchronous. Therefore, there appears to be a close relation between an electrocardiographic strain pattern and diastolic abnormalities of function in left ventricular hypertrophy.

Left ventricular hypertrophy: relations of regional echo amplitude to left ventricular function and the electrocardiogram

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In order to determine the relation between three manifestations of left ventricular hypertrophy, ST-T wave changes on an electrocardiogram, diastolic disturbances, and increased myocardial echo intensity, digitised M mode and cross sectional echocardiograms were recorded in 12 normals, 15 athletes, 16 patients with hypertrophic cardiomyopathy, and 42 with secondary left ventricular hypertrophy. In patients with hypertrophy regional echo amplitude was significantly increased in mid and basal septum and posterior left ventricular wall. Patients with increased echo amplitude in any region showed a higher incidence of ST-T wave abnormalities than those without (p<0.01) and of diastolic abnormalities, including prolongation of isovolumic relaxation, delayed mitral opening, and reduced peak rate of posterior wall thinning and dimension increase (p<0.01). There was a significant correlation between median pixel count and these diastolic abnormalities. By contrast, electrocardiogram, diastolic function, and pixel count were uniformly normal in athletes, although the increase in left ventricular mass was similar to that in the patients. Therefore, increased left ventricular mass alone is not responsible for repolarisation or wall motion abnormalities occurring in pathological left ventricular hypertrophy. These latter changes are, however, strongly associated with the change in myocardial properties detected as an increase in echo intensity and may be due to increased interstitial fibrosis.

Inotropic support with milrinone in congestive heart failure

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Milrinone is a new orally active positive inotropic agent. Its potential value in severe heart failure was examined in 10 patients who underwent acute and chronic haemodynamic studies. Acutely milrinone 5 mg significantly increased cardiac index (2.5±0.2 to 3.0±0.2 l/min/m²) despite a useful reduction in left ventricular end diastolic pressure (24±4 to 13±4 mm Hg) (p<0.001). Blood pressure did not change but heart rate increased from 85±11 to 95±11 beats/min (p<0.001). The improvement in left ventricular function was due largely to positive inotropism as reflected by a leftward shift in the end systolic pressure/dimension relation and increments in both left ventricular dP/dt max (1432±191 to 1646±246 mm Hg/s; p<0.05) and left ventricular dP/dt/P (21±3 to 36±5; p<0.001). Milrinone did not affect coronary blood flow or myocardial oxygen consumption. During chronic treatment milrinone 20 mg daily increased treadmill exercise tolerance from 7.8±1.1 to 9.5±1.2 minutes (p<0.001) after 48 hours. Measurements at submaximal exercise showed that milrinone increased stroke index (30±1 to 37±1 ml/beat/m²) and reduced arteriovenous oxygen difference (14±3±1 to 10.8±2 vols%; p<0.01). Changes in pulmonary wedge pressure (22±3 to 23±4 mm Hg) were not, however, significant. Haemodynamic indices and exercise tolerance were measured again after four weeks of treatment: there was no evidence of tachyphylaxis. These observations indicate that the inotropic properties of milrinone provide sustained improvement in left ventricular function and symptomatic status both at rest and during exercise in patients with congestive heart failure.
Factors associated with variable plasma renin responses in heart failure

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Plasma renin concentration is high in some patients with heart failure but normal in others, and the factors associated with these responses are not well described. Thirty oedema-free patients with chronic heart failure in whom digoxin and diuretic doses had been unchanged for more than one month were studied. Plasma active renin concentration was measured in supine patients after an overnight fast and was high (>50 µU/ml) in 18 patients (mean (±SEM) 279±80 µU/ml) and normal (<50 µU/ml) in 12 (mean 28±5 µU/ml). Total body electrolytes are expressed as the ratio of measured to predicted, based on studies in healthy subjects and corrected for height, weight, and age. Functional class (NYHA), frusemide dose, and age were similar in both groups (2.8±0.2 v 2.9±0.2, 158±27 v 177±22 mg/day, and 63±2 v 57±2 years respectively). Total body sodium (in vivo activation analysis) and potassium (counting of endogenous 40K) were higher in patients with normal renin (111±4% v 103±2% of predicted, p<0.05; and 106±2% v 87±3%, p<0.001 respectively) as were serum sodium (142±1 v 137±1 mmol/l; p<0.01), serum potassium (3.8±0.1 v 3.4±0.1 mmol/l; p<0.005), and mean blood pressure (107±5 v 87±4 mm Hg; p<0.005). Similar trends for total body and serum chloride were not significant (112±5% v 106±6%, NS; and 100±1 v 96±2 mmol/l, NS).

Thus in patients with heart failure, if body sodium remains raised despite the clearance of oedema by diuretic treatment blood pressure is maintained and plasma renin does not rise; reduced body potassium in heart failure is associated with a high plasma renin concentration.

Does the maximal ST segment/heart rate slope predict the extent of coronary artery disease?

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The regression of ST segment depression on heart rate (ST/HR slope) during bicycle exercise was studied in 32 patients the day before coronary arteriography (27 in taking beta blockers and six nifedipine). A 12 lead electrocardiogram with CM5 substituted for aVR was recorded at workloads which increased heart rate by 10 beats at each stage. In 12 patients no ST/HR slope was obtained in any lead. Eleven of these patients, however, had significant proximal coronary disease (75% luminal diameter reduction). Twenty patients did yield ST/HR slopes: five with single vessel disease ranged from 24–95 mm. beats⁻¹. min. 10⁻³; nine with double vessel disease from 27–123 mm. beats⁻¹. min. 10⁻³; and six with triple vessel disease from 75–143 mm. beats⁻¹. min. 10⁻³. We were, therefore, unable to confirm the ST/HR slope as an accurate predictor of the extent of coronary artery disease. Furthermore, the test was not always reproducible when examined at intervals ranging from hours to four weeks in patients with stable angina.

Inability of the ST segment depression/heart rate slope to predict the severity of coronary artery disease, and the superior results of the Bruce treadmill exercise test

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The rate of depression of the ST segment with increasing heart rate (ST/HR slope) obtained during exercise has been claimed to accurately predict the extent of coronary artery disease seen at angiography. This ST/HR rate slope was calculated in 84 patients who also underwent coronary arteriography; in 81 modified Bruce exercise tests were also performed. In 22 (26%) patients the exercise tests could not be interpreted because they did not fulfil the electrocardiographic criteria laid down by Elamin et al. In the remaining 62 patients the presence of zero, one, two, and three vessel disease was predicted in four of the 16 (25%), seven of 19 (37%), eight of 16 (50%), and six of 11 (54%) patients respectively. The sensitivity and specificity of the ST/heart rate slope in predicting significant coronary disease (>75% narrowing) was 64% and 23% respectively. The corresponding values for the modified Bruce test were 81% and 64% respectively. Thus the maximum ST/heart rate slope predicted the severity of coronary disease in only 40% of patients in whom a slope could be obtained. The modified Bruce test was superior in predicting the presence of coronary disease.
Assessment of dermal nitrate preparations for patients with angina using treadmill exercise

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Dermal nitrate preparations are claimed to be useful in the treatment of angina as their delayed absorption leads to a sustained action. Ten patients with severe angina had their antianginal treatment withdrawn while hospital inpatients. Exercise on a treadmill (Sheffield protocol) was used with severe angina as the endpoint. The tests were performed on four control days and then on three days at one, three, and six hours after the application of a dermal preparation. The preparations given on a double blind basis were 16-4 mg (2.5 cm) of glyceryl trinitrate, 100 mg of isosorbide dinitrate, and placebo. The mean duration of exercise (in seconds) was: 523,*** 492,* and 472 for glyceryl trinitrate; 454,* 483,** and 455 for isosorbide; and 377, 365, and 375 for placebo at one, three, and six hours respectively. Exercise duration was significantly increased at one and three hours (p<0-01**) but not at six hours. The calculated work performed was significantly increased at one and three hours (p<0-01) for both preparations and also by isosorbide at six hours (p<0-05). These results confirm a sustained action of dermal nitrates whose clinical value was discussed.

Mechanisms of rest angina evaluated during sleep

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Exertional angina is due to increasing myocardial oxygen demand, whereas rest and nocturnal angina is considered to be secondary to spasm. Nine patients with frequent day time and nocturnal angina, seven with transient ST depression, significant coronary artery disease, and positive exercise tests at low workload, and two with ST depression and elevation, insignificant coronary disease, negative exercise tests, and spasm at angiography were studied. Patients were studied for 6–16 hours of nocturnal sleep when the electroencephalogram, electromyogram, electrooculogram, chest wall movements, nasal airflow, and oxygen saturation were recorded continuously. A mean of 2-9 episodes per patient of ST depression were recorded (55% painful). Two patients had a mean of 3-5 episodes of ST elevation (2-5 painful). In the seven patients with obstructive coronary disease all but one episode of ST depression were preceded by arousal and lightening of sleep pattern on the electroencephalogram, bodily movement, and sudden increases in heart rate. One episode of ST depression was preceded by apnoea and a fall in oxygen saturation (96 to 80%). In the two patients with coronary spasm episodes of ST depression and elevation were not preceded by arousal, apnoea, or increases in heart rate. Thus nocturnal ischaemia in the presence of coronary artery disease is likely to be precipitated by increased myocardial oxygen demand produced by arousal in sleep and sudden increases in heart rate.

Comparative effect of amiodarone and propranolol in combination with digoxin for the control of the fast ventricular response in atrial fibrillation

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Patients in atrial fibrillation not uncommonly continue to be symptomatic, despite full digitalisation, owing to inadequate control of ventricular rate on effort. Twenty such patients with valvular and ischaemic heart disease were studied. The exercise response of the ventricular rate was assessed on treadmill exercise testing by the Sheffield protocol. Patients were randomly divided into two equal groups and received additional oral amiodarone (average maintenance dose 200 mg daily) or propranolol (average 80 mg three times a day). Digoxin dosage was readjusted according to blood concentrations. In the amiodarone group four out of 10 patients showed subjective improvement with objective increase in exercise capacity and control of ventricular rate. Symptomatic improvement occurred in three further cases. Two patients showed a reduction in exercise capacity, and one was withdrawn because of side effects. The beta blocker group consistently showed reduction in ventricular rate at rest and on exercise. Exercise performance was increased in two out of 10; three additional patients had subjective improvement only. Four deteriorated and two had to be withdrawn from the study.

Propranolol in combination with digoxin has earned an accepted place in the control of fast ventricular response in atrial fibrillation. This series suggests that amiodarone has an improved efficacy in this respect but requires careful monitoring of side effects.
Diurnal variation of the QT interval: influence of the autonomic nervous system

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Twenty four hour electrocardiographic monitoring was performed in six pacemaker dependent patients with normally innervated hearts, in six cardiac transplant patients with anatomically denervated hearts (but which respond to circulating catecholamines), and in nine diabetic patients with proven autonomic neuropathy. There was little change in spontaneous heart rate throughout the 24 hours in the transplant and diabetic patients. QT intervals from hourly intervals were measured blind by two observers and those during sinus rhythm corrected using Bazett's formula. QT intervals were normalised (QTn) by dividing by the mean QT for the 24 hours in each patient and expressed as a percentage.

Diurnal variation of normalised QT was pronounced in the innervated patients with longer QTn during sleep than waking hours (6:00 v 18:00 h: 102.5% v 97.8%, p<0.01), present but blunted in the transplant patients (101.3% v 98.1%, NS), and absent in the diabetic patients (100.0% v 100.3%, NS). In the innervated patients the most pronounced changes occurred at the time of waking (6:00 h v 9:00 h: 102.5% v 95.4%, p<0.001). No change in normalised QT occurred in the transplant and diabetic patients at this time. There was no significant difference between normalised QT for the three groups during sleep but was shorter in innervated patients during waking hours (10.00 h: innervated, 96.5%; transplant, 100.7%; diabetic, 100-7%, p<0.01).

Diurnal changes of the QT interval may be pronounced and are dependent on both autonomic tone and circulating catecholamines.

Revelation of latent cases of long QT syndrome by rapid autonomic tone modulation

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Valsalva manoeuvres at 20–30 mm Hg for 15–20 s were performed in 18 control subjects and 18 members of four families with the long QT syndrome. In controls the measured QT intervals significantly decreased (356±40 to 331±32 ms; p<0.001) during phase 2 (sympathetic predominant) and increased (367±32 ms; p=0.05) during phase 4 (parasympathetic predominant). After intravenous propranolol (0.2 mg/kg) there were no significant changes in the measured QT intervals during phase 2 (390±46 to 378±34 ms), but the significant increase during phase 4 (406±39 ms; p<0.01) persisted. Corrected QT intervals (control, 398±32: phase 2, 437±35, p<0.001; phase 4: 373±36 ms, p<0.005) clearly followed the pattern of changes in the RR intervals. In the patients with the long QT syndrome the measured QT increased during phase 2 (467±18 to 500±20 ms). There was a similar increase in the measured QT (403±37 to 412±44 ms) during phase 2 in some relatives of the familial long QT syndrome patients despite normal QT intervals at rest but not in the six family members of the patient with idiopathic long QT syndrome. These changes were normalised by beta blockade.

Thus the trend of changes in the measured (but not corrected) QT during Valsalva manoeuvres is extremely useful in the diagnosis and follow up of patients with the long QT syndrome. It is also helpful in detecting the latent cases among patients' relatives.

Sinus pauses and syncope

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In patients with chronic sinus node disease the principal indication for a pacemaker is the presence of major symptoms. There is, however, controversy concerning the management of those who have sinus pauses but few complaints. The aim of this study was to assess the likelihood of such patients developing syncopal attacks. Cases were recruited from the Devon Bradycardia Survey, a prospective study started in 1968. One hundred and forty five patients with pauses ≥1.8 s were found. Pauses antedated syncpe in 40 patients, and these were divided into two groups: those with pauses ≤2.2 s (group 1) and those with longer pauses (group 2). None of the 25 patients in group 1 had syncpe or required pacing during the first two and a half years of follow up, whereas four of the 15 patients in group 2 had syncopal attacks and two more required pacing for lesser disturbances of consciousness within this period (p<0.01). At five years there were still 17 patients being followed up in group 1 with only one syncopal attack (at 58 months).

It is concluded that in the patients in this study the risk of syncope is small in those with pauses ≤2.2 s.