Proceedings of the British Cardiac Society

THE 61ST ANNUAL GENERAL MEETING of the British Cardiac Society was held at the Medical School in the Queen's Medical Centre at Nottingham University on Wednesday and Thursday 14 and 15 April 1982. The President, M F OLIVER, took the Chair during private business. At the scientific sessions the Chair was taken by J R HAMPTON.

Abstracts of papers

Direct electrophysiological effects of disopyramide phosphate—evaluated in denervated human heart

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In order to evaluate the direct intrinsic effects of intravenous disopyramide phosphate (2 mg/kg), the drug was administered to eight orthotopic cardiac transplant recipients undergoing electrophysiological study.

The sinus cycle length of the denervated donor right atrium was significantly increased by disopyramide (626±53 ms to 716±60 ms, p<0.001) while that of the innervated recipient right atrium decreased (846±80 ms to 659±41 ms, p<0.02). The AH interval (55±5 ms to 78±5 ms, p<0.001), HV interval (38±3 ms to 58±5 ms, p<0.001), QRS duration (93±7 ms to 129±13 ms, p<0.001), QT interval (339±9 ms to 403±15 ms, p<0.001), and QTc (435±11 ms to 487±10 ms, p<0.01) measured during sinus rhythm were all very prolonged.

The sinus node recovery time (1128±252 ms to 1198±242 ms, p<0.05) and corrected sinus node recovery time (440±171 ms to 489±167 ms, p<0.02) of the denervated donor atrium were significantly prolonged by disopyramide whereas the recovery times of the innervated recipient atrium shortened slightly. During incremental pacing the atrioventricular Wenckebach cycle length (314±8 ms to 350±13 ms, p<0.01) increased after disopyramide, as did the ventricular arterial Wenckebach cycle length (419±62 ms to 500±61 ms, p<0.01). The drug had no effect on the effective refractory period of the atrium, atrioven-

tricular node, or ventricle though the functional refractory period of the atrioventricular node was prolonged (369±13 ms to 395±12 ms, p<0.001).

In comparison with effects on the innervated normal heart, the direct intrinsic effects of disopyramide on the transplanted denervated heart are conspicuously depressant.

Prognosis of chronic second degree atroioventricular block

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This paper presents the findings of the prospective follow-up of patients with second degree block seen in the Devon Heart Block and Bradycardia Survey started in 1968. Patients with conduction disturbance which occurred within 28 days of myocardial infarction or pericarditis are excluded, as are those with drug-induced block. Two hundred and seventy patients with second degree block have been seen in the survey; in 44 instances evidence of higher degree of block was available leaving 226 patients presenting with second degree block. The patients were divided into Mobitz I and Mobitz II groups according to the usual criteria, the mean age of the former group being four years less than the latter.

Temporary or sustained improvement in conduction was seen in 20% of patients and 46% progressed to third degree block. The five year survival for the whole group was approximately 50% and surprisingly it was similar for both of the Mobitz groups. Paced patients faced significantly better than unpaced, this difference being maintained even when corrected for age.

Comparative electrophysiological effects of novel antiarrhythmic drug, bepridil

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Bepridil is a novel, non-iodinated, fast and slow channel blocker that prolongs myocardial refractoriness
and depresses atrioventricular nodal function. We compared intravenous bepridil (2.0 mg/kg) with verapamil (0.15 mg/kg) in nine patients with reciprocating atrioventricular nodal tachycardia, and with ajmaline (0.75 mg/kg) in eight patients in whom re-entry tachycardia was associated with the Wolff-Parkinson-White syndrome; 12 of these patients were restudied three days after oral bepridil (1500 mg) when steady state had been achieved. Intravenous bepridil increased sinus cycle length in all patients (40 to 120 ms, mean 66) and increased the AH interval (0 to 20 ms, mean 8). No effect was seen on His-Purkinje conduction. The “pre-Wenckebach cycle length” of the atrioventricular node was prolonged after bepridil (45 to 150 ms, mean 95) as were the effective refractory periods of the atrioventricular node (50 to 90 ms, mean 74), atrium (10 to 50 ms, mean 28), ventricle (0 to 30 ms, mean 14), and accessory pathway retrograde (55 to 70 ms, mean 63). Tachycardia terminated in all patients after verapamil or ajmaline whereas failure occurred in three patients after bepridil: all had pre-excitation. At restudy after oral bepridil reinitiation was impossible in six patients; in the other six tachycardia was slower, and terminated spontaneously (two) or with single stimuli.

Bepridil thus possesses a combination of electrophysiological properties, each of its actions comparable to representative conventional agents: this broad spectrum of antiarrhythmic action is appropriate for the safe and effective treatment of supraventricular arrhythmias.

Electrophysiological effects of sotalol—more than just another beta blocker

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The electrophysiological effects of intravenous sotalol hydrochloride (0.4 mg/kg) were assessed in 24 patients, including 13 with the Wolff-Parkinson-White syndrome. Fifteen minutes after sotalol administration there was an increase in sinus cycle length (739±107 to 869±109 ms, p<0.001) and in sinus node recovery time (1084±302 to 1270±301 ms, p<0.01). The AH interval increased (82±28 to 94±32 ms, p<0.001), but the HV interval was unchanged. The QRS duration was also unchanged, but the QT (401±45 to 427±38 ms, p<0.01) and the JT (300±44 to 321±35 ms, p<0.02) intervals were both increased. The atrial (216±38 to 233±40 ms, p<0.01), ventricular (231±30 to 242±31 ms, p<0.01), and atrioventricular nodal (294±87 to 338±90 ms, p<0.001) effective refractory periods were all prolonged, as was the atrioventricular nodal functional refractory period (417±92 to 467±86 ms, p<0.001). In the 13 patients with ventricular pre-excitation there was an increase in the accessory pathway anterograde (317±88 to 350±81 ms, p<0.02) and retrograde (296±40 to 371±139 ms, p<0.05) effective refractory periods. In 12 of these 13 sotalol was given during atrioventricular re-entrant tachycardia, resulting in termination in five. Tachycardia cycle length increased in all patients (355±64 to 413±54 ms, p<0.001) with the major effect being in the atrioventricular direction (atrioventricular interval 230±69 to 286±54 ms, p<0.001). The effect on atrial, ventricular, and accessory pathway effective refractory periods and on ventricular repolarisation is not typical of that observed with other beta blockers but may be the result of lengthening of the action potential duration, as seen with amiodarone. These findings suggest that sotalol may be more versatile than other beta receptor antagonists in the treatment of arrhythmias.

Ventricular arrhythmia in tetralogy of Fallot: influence of age, haemodynamic factors, and surgery

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Serious ventricular arrhythmia occurs after correction of tetralogy of Fallot and may be associated with late sudden death. To determine the factors responsible for these arrhythmias, we studied 38 unoperated patients (age 2 months to 45 years) and 77 postoperative patients (follow-up three to 22, mean 14-6 years) using 48 hour electrocardiographic monitoring. Thirty-one of the postoperative patients had cardiac catheterisation and gated equilibrium radionuclide angiography using Krypton-81m (right ventricle) and Technetium-99m (left ventricle), at rest and after isometric exercise. None of the unoperated patients aged below 9 years had significant arrhythmia. Four of seven patients older than 10, however, had ventricular arrhythmia, of whom three had ventricular tachycardia. No other clinical or haemodynamic measurements distinguished these patients. Thirty-three postoperative patients (43%) had serious ventricular arrhythmia and four (5%) ventricular tachycardia. There was no significant difference in haemodynamic status or ventricular ejection fraction between patients with ventricular arrhythmia and those without. Ventricular arrhythmia was significantly more frequent in those operated on at an
older age. (One of 14 aged 2 to 7, 19 of 45 aged 8 to 15, 13 of 18 aged 16 or more; p<0.01).
Thus, ventricular arrhythmias cannot be predicted from the postoperative haemodynamic status of the patient. They are related to the timing of correction rather than to the operation itself.

**Increased atrial pacing threshold in heart transplant rejection**

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The pacing threshold of the donor right atrium was measured in eight heart transplant recipients for 27 to 46 days (mean 33) after transplantation. Threshold current and potential were measured at nine different pulse widths each day during the period of study and correlated with the degree of rejection diagnosed by right ventricular endomyocardial biopsy. Biopsies were performed each seven to 10 days or on suspicion of rejection. Histological grading was from 0 (normal) to 4 (severe rejection). The degree of rejection was correlated with the mean values of current, potential, power, and energy on the day of the biopsy. There were insufficient examples of grade 1 and grade 4 rejection for statistical analysis (paired Student’s t test).

During rejection there was significant increase in potential (p<0.02), current, power, and energy (p<0.01) compared with the values associated with normal biopsies. The values associated with grade 2 and grade 3 rejection were not significantly different. Similar results were obtained with all pulse widths.

Right atrial pacing threshold correlates well with rejection of the transplanted heart but does not indicate the severity of rejection.

**Haemodynamic and metabolic effects of diltiazem, a new calcium antagonist, compared with nifedipine in patients with coronary artery disease**

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Diltiazem is a new calcium channel blocking agent which may have value in patients with angina pectoris. The haemodynamic and myocardial metabolic effects of diltiazem have been compared with those of nifedipine at rest and during rapid atrial pacing in 20 patients with obstructive coronary artery disease. No patient was receiving a beta blocking agent at the time of the study.

Diltiazem, 0.25 mg/kg intravenously given over two minutes followed by 0.005 mg/kg per min, produced a fall in systemic vascular resistance from 20-1 to 15-7 units (p<0.002) with an increase in cardiac output from 5-5 to 6-5 l/min (p<0.01) and a fall in mean arterial pressure from 100 to 92 mmHg (p<0.005). Coronary sinus blood flow rose after both drugs. Comparable haemodynamic changes occurred after nifedipine 20 mg sublingually. The systemic vasodilator effects of diltiazem, however, were not associated with a change in resting heart rate, whereas after nifedipine it rose from 70 to 80 beats/min (p<0.001).

Importantly, after diltiazem, mean pacing time to angina increased from 174 to 356 seconds (p<0.02) and mean lactate extraction improved from −22% (ie production) to +2%. The atrial pacing time to angina and the myocardial lactate extraction ratio after nifedipine did not change significantly.

The effects of diltiazem differ importantly from those of nifedipine and may be advantageous in the treatment of angina pectoris.

**Comparison of “dipyridamole-exercise” thallium-201 imaging and standard exercise thallium-201 imaging in men with angina**

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Traditional thallium-201 myocardial imaging as performed with exercise or dipyridamole stress. We have devised a method for combining oral dipyridamole and treadmill exercise in one test: “dip-ex” testing. In 13 men with angina this was a more effective stress than exercise alone.

Thirteen men with mild to moderate angina and good exercise performance were selected. In seven, coronary artery disease had been demonstrated angiographically; in the remaining six, in whom angiography was inappropriate, the presence of coronary artery disease was accepted on the typical history combined with an ischaemic exercise electrocardiogram. (The prevalence of coronary artery disease in such men is 96 to 100%.)

Patients underwent thallium-201 imaging on two occasions, two weeks apart. On one occasion, dipyridamole 300 mg was taken by mouth 60 minutes before exercise. Thallium-201 2 mCi was given intravenously at maximal exercise.

Thallium-201 imaging was abnormal (regional
count deficit of >25%) in 12 patients after dip-ex testing and in eight after exercise alone. Dip-ex testing disclosed a total of 26 abnormal myocardial regions in the 13 patients, while exercise imaging showed 12. When only the dip-ex images were abnormal, angiography tended to show at least one occluded or critically narrowed vessel, and a well developed collateral circulation.

The mean myocardial to background ratio was 3.48±0.75 after dip-ex testing and 2.95±0.55 after exercise alone (p<0.01).

The dip-ex technique has now been used diagnostically in 60 patients. It is useful, simple, and safe.

Relation between episodes of reversible cardiac ischaemia and arrhythmias

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Cardiac arrhythmia is the presumed predominant cause of sudden death in patients with ischaemic heart disease; however, the precise relation between acute ischaemic episodes and cardiac arrhythmias in such patients is uncertain.

To examine this relation, 40 patients with angina caused by coronary artery disease were studied with continuous 24 hour electrocardiographic FM recordings, 28 of whom also had stress electrocardiograms that were analysed for both ischaemic and arrhythmic events. Only two patients (5%) had symptoms of cardiac arrhythmia. Patients with acute myocardial infarction within two weeks were excluded.

Twenty-six of 40 24 hour electrocardiograph tapes (65%) showed ischaemic episodes characterised by 1.5 mm or greater ST segment depression or elevation 0-08 s after the J point. Thirty-seven (92.5%) of these same tapes showed cardiac arrhythmias. Arrhythmias were immediately associated with episodes of ischaemia in six patients (16.2% of tapes showing arrhythmia, 15% total tapes); ischaemia precipitated arrhythmia in five (19.2% of tapes showing ischaemic episodes, 12.5% total tapes), and vice versa in one (2.7% of tapes showing arrhythmia, 2.5% total tapes). Of nine arrhythmias precipitated by ischaemia, two were ventricular tachycardia, two complex or early ventricular extrasystoles, three simple ventricular extrasystoles, and two conduction disturbances. Apparently similar episodes of ischaemia in the same patient did not consistently reproduce the cardiac arrhythmia. There was no significant difference in arrhythmias produced by either "demand" or "spontaneous" ischaemia but the incidence was greater with severe and prolonged ischaemia. Exercise testing produced angina and/or electrocardiographic appearances of ischaemia in 21 of 28 (75%) patients and cardiac arrhythmias in three of 28 patients (10-7%). Arrhythmias were immediately associated with episodes of ischaemia in two; ischaemia preceding arrhythmia in one, and following sustained arrhythmia in one.

In conclusion, the incidence of arrhythmias during episodes of reversible cardiac ischaemia is low in patients with angina resulting from coronary artery disease. Treatment that prevents ischaemia might be expected to reduce the incidence of fatal cardiac arrhythmias in such patients. Arrhythmias that precipitate ischaemia are rare but are important to suppress when they arise.

Reciprocal ST depression in myocardial infarction: relation to exercise-induced ST depression

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In acute myocardial infarction, ST depression in leads distant from those showing ST elevation has been considered "reciprocal" but could reflect local ischaemia. To examine this possibility, we have reviewed 103 consecutive patients who underwent exercise testing soon after infarction. Treadmill exercise testing was performed a mean of 12 (five to 30) days after infarction using a modified Naughton procedure. Thirty-five (34%) of these patients had had "reciprocal" changes within 48 hours of infarction defined as ST depression ≧1 mm at a distance from the infarct site. Twenty-one (61%) of the 35 had exercise-induced ST depression in the leads previously showing "reciprocal" change. Twelve of the remaining 14 subsequently had symptom limited exercise testing; two showed ST depression in the same site as the "reciprocal" change.

Thus, 66% of those with "reciprocal" change had ST depression on exercise in the same leads. Coronary anatomy was examined in eight of these by arteriography and in one at necropsy; all but one had a ≧50% stenosis in a coronary artery supplying the "reciprocal" territory additional to disease in the vessel to the infarct site.

These findings suggest that "reciprocal" change may reflect ischaemia in territory distant from the infarction.

Orthotopic vs. heterotopic cardiac transplantation: haemodynamic and physiological factors

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Heart transplantation has been successfully carried out since 1960 based on the technical procedure described by Lower and Shumway. It was not until 1967, however, that the procedure was attempted in humans and the surgical technique has been essentially unchanged since. Shortly after the initiation of human cardiac transplantation episodes of acute post-operative right sided heart failure were noted in some patients in whom the preoperative pulmonary vascular resistance was substantially raised. It seemed that the new heart could not adapt rapidly enough to the high pressures necessary to the right heart and thus rapidly failed. Research into a solution to this catastrophic complication led to the development of the heterotopic transplant in which a new heart was “piggy-backed” onto a left ventricle allowing the native right ventricle to continue to supply the pulmonary circuit at its own chronically high pressure. Some investigators felt this to be a superior technique to orthotopic transplant as it allowed for possible recovery of the damaged native heart and resulted in eventual removal of the transplant in one case as the native’s heart function improved. Heterotopic transplantation, however, is a more technically complex surgical procedure, leading to substantial alterations in flow characteristics and compliance between the two hearts. The potential benefit to the damaged native left ventricle is not guaranteed and there are significant risks of thrombus and embolus associated with the blood flow characteristics of the heterotopic procedure. A study was performed to outline the differences between the two procedures and shows a superior result with orthotopic. The two procedures were compared; echocardiographic features of the wall and valve motion were studied. Simultaneous phonocardiography, apexcardiography, and electrocardiography showed unique physiological features of the heterotopic transplant. Catheterisation studies corroborated these findings, and suggested progressive deterioration of a native heart in a heterotopic transplant because of disparate pressures and volumes. Thus it is shown that heterotopic transplant is not necessarily a superior technique and may in fact contribute to further deterioration of the native heart and necessitate further intervention.

We have studied six subjects with autonomic failure (Shy-Drager or idiopathic type) using ambulatory intra-arterial pressure monitoring. All were monitored for at least 24 hours during which they were fully ambulant. Four were studied for an additional 24 hours during which they were restricted to bed. Tape recordings were computed to obtain mean hourly values of heart rate, and systolic and diastolic blood pressure from which circadian curves were derived.

Heart rate curves were normal in shape but the amplitude of the day-night change was reduced. The pattern of blood pressure change was, however, completely inverted from normal, with highest pressures occurring shortly after retiring for the night and then falling steadily to the nadir shortly after awakening, with a gradual rise thereafter. This pattern was highly consistent among the group and was generally unchanged during the period of bed rest. There was little effect of awakening on the underlying trend of blood pressure.

The low pressures in the early morning coincided with the exacerbation of orthostatic symptoms that many such patients report. Also, the night time pressures were often surprisingly in the hypertensive range. The pattern demonstrated appears to be highly relevant to clinical features of this condition and suggests potentially valuable approaches to treatment.

Changes in plasma potassium and the electrocardiogram induced by adrenaline and the effect of beta blockade on them

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We have previously reported on transient hypokalaemia in acute myocardial infarction. To investigate our hypothesis that this might be the result of increased circulating catecholamines, we have infused adrenaline in normal volunteers to the levels observed after myocardial infarction.

Nine subjects were studied on three occasions after pretreatment with placebo, atenolol, or timolol. Adrenaline, 0.06 μg/kg per min, was infused over 90 minutes; plasma potassium was measured serially and a single lead electrocardiogram was recorded.

Pretreatment did not significantly alter plasma potassium (4.05, 4.03, and 4.09 mmol/l after placebo, atenolol and timolol, respectively). During infusion, plasma potassium fell to 3.21 mmol/l (p<0.001) after placebo, and to 3.67 mmol/l after atenolol; it rose to 4.25 mmol/l after timolol.
Pretreatment did not alter the QTc interval. During infusion QTc rose from 0.36 to 0.4 s (p<0.01) after placebo and was unchanged after atenolol and timolol. During infusion after placebo, T wave amplitude decreased and two subjects developed U waves; the decrease in T wave amplitude was less after atenolol and absent after timolol.

Thus, increased plasma adrenaline may be a factor in the production of both hypokalaemia and arrhythmias after myocardial infarction and the prevention of hypokalaemia and of abnormalities of repolarisation may contribute to the beneficial effects of beta blockade in this context.

Endogenous progesterone and blood pressure

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The amount of progestogen, as well as oestrogen, in oral contraceptives influences the risk of arterial disease in oral contraceptive users. The use of progestogens in hormone replacement regimens for menopausal symptoms is increasing, and there is added reason for assessing the effects of progestogens. The risk of ischaemic heart disease and stroke resulting from progestogens in oral contraceptive may be mediated through a rise in blood pressure. In the Northwick Park Heart Study, data from nearly 300 white women aged 44 years or less and not taking oral contraceptives show that blood pressure was significantly raised on those days of the menstrual cycle when progestone levels would be expected to be highest. There was a systolic pressure difference of about 10 mmHg between the highest and lowest mean values for individual days of the cycle. Differences in age, indices of obesity, and smoking habit were not responsible for the differences in pressure. There was no correlation between pressure and anticipated levels of hormones other than progestrone. The hypothesis that serum progesterone levels might be correlated with level of blood pressure had not been formulated when the pressure measurements were made, so that finding is unlikely to be the result of bias.

Cardiomyopathy in Friedreich's ataxia

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Cardiomyopathy occurs commonly in Friedreich's ataxia and is often the cause of death. Some echocardiographic studies, but not all, have suggested that the cardiac pathology may be identical to hypertrophic obstructive cardiomyopathy. It has been speculated that catecholamine imbalance in Friedreich's ataxia may stimulate the cardiac muscle abnormality. We elected to compare the M-mode echocardiograms of patients with Friedreich's ataxia with those of patients who had similar hereditary spinal degeneration syndromes. Analysis of echocardiograms was made by two observers without prior knowledge of the neurological disorder.

Thirty-three children aged 4 to 18 years were studied. Ten of 11 with classical Friedreich's ataxia and two of three with atypical ataxia had abnormal echocardiograms. None of the other 21 patients with neurological disorders had echocardiographic abnormalities. The abnormal echocardiograms all showed increased thickness of the ventricular septum and left ventricular posterior wall. Asymmetric septal hypertrophy and systolic anterior motion of the mitral valve were present in three patients. Early systolic closure of the aortic valve occurred in one.

This study has shown that cardiac involvement is almost invariable in Friedreich's ataxia but does not occur in other similar neurological disorders. The cardiomyopathy appears to be heterogeneous. Echocardiography is a sensitive method of diagnosis and may help differentiate Freidreich's ataxia from other disorders.

Changes in left ventricular mass, volume, and function after surgery for chronic aortic regurgitation

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In order to assess the reversibility of the myocardial adaptations and dysfunction accompanying chronic aortic regurgitation, we studied serial changes in left ventricular mass and volume in 67 patients with this chronic volume overload who survived aortic valve replacement. There changes were correlated with postoperative clinical, haemodynamic, and histological data. Patients were divided into two groups: those in whom the left ventricular echocardiographic diameters returned to normal after operation (group A), and those with postoperative dilatation (group B). The postoperative end-diastolic diameter returned to normal in 51 patients (group A); a parallel reduction of left ventricular voltages and echocardiographic estimates of ventricular mass was noted in 86% of these cases. Out of the 16 patients with postoperative ventricular dilatation (group B), 14 had satisfactory valve function. After valve replacement, patients in this group B had persistent or progressive
electrocardiographic abnormalities, unchanged estimates of ventricular muscle mass, altered segmental wall motion, and impaired haemodynamic responses to exercise.

Left ventricular biopsies were obtained before and one year after operation from four patients in group A and from eight patients in group B. Mean postoperative muscle fibre diameter had regressed significantly to 23.4 μ in cases from group A, but remained massively increased (mean 32.5 μ) in patients from group B. Increased interstitial collagen, degenerative ultrastructural changes, and reduced levels of myofibrill-associated ATPase in pre- and postoperative biopsies correlated with impaired ventricular function and persistent dilatation and hypertrophy after surgery.

Preoperative echocardiographic and angiographic data could define the type and degree of ventricular dysfunction which was irreversible. The histological alterations seen in pre- and postoperative biopsies from those patients who experienced no functional improvement suggest that irreversible morphological changes contribute to a depressed cardiac function after surgery.

Relation between alcohol intake, myocardial dysfunction, and myocardial tissue enzyme activities

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The quantity of alcohol responsible for heart muscle disease in man is unknown.

Thirty patients with suspected cardiomyopathy were studied by catheterisation and myocardial biopsy. Detailed drinking histories were taken by an independent observer. Myocardial tissue enzyme activities were measured. This study compared the results of these three independent investigations.

Analysis of the drinking histories showed a clear division into two groups. Eleven patients (36%) consumed more than 80 g alcohol daily for 10 years and 15 patients (50%) consumed less than 40 g alcohol daily for 10 years. Only four patients (14%) consumed 40 to 80 g daily. Sixteen patients (52%) consumed in excess of 500 kg total lifetime intake of alcohol.

Myocardial enzyme activities have previously been shown to separate alcoholic heart muscle disease and dilated cardiomyopathy. In this study creatinine kinase activity correlated with daily alcohol consumption (40 g p<0.02, 80 g p<0.005) and total cumulative alcohol intake (p<0.05). Furthermore, alpha hydroxybutyric dehydrogenase: lactate dehydrogenase ratio correlated with left ventricular ejection fraction (p<0.05).

In conclusion, drinking in excess of 80 g alcohol daily for 10 years or cumulative lifetime intake greater than 500 kg is likely to result in alcoholic heart muscle disease. Myocardial damage reflected in abnormal enzyme activity may be seen in patients consuming 40 to 80 g alcohol daily.

Effect of intravenous amrinone on resting haemodynamic function in patients with congestive cardiac failure

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The effect of intravenous amrinone on resting haemodynamic function was investigated in 15 patients with congestive cardiac failure. 3-5 mg/kg amrinone produce appreciable and significant changes in cardiac index (+102%), ejection fraction (+36%), systemic vascular resistance (−57%), mean arterial pressure (−20 mmHg), and left ventricular end-diastolic pressure (−9.6 mmHg). 1-5 mg/kg amrinone produced similar but smaller changes (p<0.01). These alterations were accompanied by only small increases in heart rate (p<0.01) and a small reduction in left ventricular end-diastolic volume (p<0.02). No change in max dP/dt, min dP/dt, [max (dP/dt)/P], max (dP/dt), KV max, or the ratio of left ventricular end-systolic pressure to left ventricular end-systolic volume occurred. It is concluded that the beneficial effects of intravenous amrinone on the resting haemodynamics in our patients were attributable to vasodilatation, with the drug having no demonstrable inotropic effect.

Interaction between inotropism and vasodilatation in heart failure

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Although drugs used in heart failure may have inotropic or vasodilator properties, their clinical effects in patients may be similar. Furthermore, a combination of drugs with different pharmacological actions may be used to advantage. To examine these possibilities, we compared a non-glycosidic non-adrenergic inotropic agent (amrinone) and a beta-
agonist (pirbuterol), with a venodilator (isosorbide dinitrate) added to each drug.

After control measurements, oral amrinone (100 mg) or pirbuterol (20 mg) were given in random order to each of 13 patients, on successive days with isosorbide dinitrate (20 mg) given orally after two and a half hours. Control values were not significantly different before amrinone or pirbuterol were given. Significant (p<0.01) increases in cardiac index (65% with amrinone, 55% with pirbuterol) and falls in wedge pressure (27%, 19%), right atrial pressure (16%, 21%), and systemic vascular resistance (33%, 32%) occurred. Heart rate and blood pressure remained unchanged. The magnitude of the changes caused by amrinone and pirbuterol were not significantly different. The addition of isosorbide dinitrate caused further (p<0.01) falls in wedge and right atrial pressures, and a fall (p<0.05) in heart rate with each drug. Other variables remained unchanged.

Although amrinone and pirbuterol have different pharmacological properties, their acute haemodynamic effects in patients with chronic heart failure are indistinguishable. Both drugs produce an increase in cardiac output at lower filling pressure and systemic vasodilatation; the submaximal venodilatation may be enhanced by nitrates.

Immunosuppressive therapy in acute inflammatory myocarditis

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This study describes the diagnosis of acute myocarditis and its treatment with immunosuppressive therapy. Twelve patients with a recent history of an infectious illness presented with acute dyspnoea and evidence of biventricular heart failure. Cardiac catheterisation and left ventricular biopsies were performed in all patients. Left ventricular angiography and echocardiography were compatible with dilated cardiomyopathy. Histology showed evidence of acute inflammatory myocarditis in nine patients. Serology suggested a viral aetiology in six patients (Coxsackie B in five, Herpes simplex in one), of whom two had negative biopsies. Seven patients were started on prednisone and azathioprine. Two patients received prednisone alone.

After two months treatment nine patients were restudied and eight showed symptomatic and haemodynamic improvement with a fall in left ventricular end-diastolic pressure from 26-4 to 15-2 mmHg, pulmonary artery systolic pressure from 40 to 27 mmHg, and a rise in ejection fraction from 26-8 to 49% and in cardiac index from 2-7 to 3-9 l/min per m. Histology in seven patients showed healing myocarditis. Two patients showed persisting acute myocarditis (one not treated, one on steroids alone).

Serology and myocardial histology are complementary in the diagnosis and management of this condition. The results of treatment suggest a role for combined immunosuppressive therapy.

Early and late results of surgical repair of lesions associated with corrected transposition

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Nineteen patients, 15 male and four female, aged 13 months to 47 years (mean 16 years) underwent surgical repair of lesions associated with corrected transposition. Ventricular septal defects were closed in 16 (multiple in two) and 11 had pulmonary stenosis. Seven of the 19 patients had important left atrioventricular valve regurgitation, five requiring surgical correction. Conduction disturbances or arrhythmias were present preoperatively in eight: congenital complete heart block or complete atrioventricular dissociation (five), established or intermittent atrial fibrillation (three). Four patients had previous surgery: banding of the pulmonary artery (one) and systemic-pulmonary shunt (three). Seven perioperative deaths occurred, six resulting from low output state: failure to close multiple ventricular septal defects (one), new and precipitous onset of complete heart block (two), poor systemic ventricular function (one), and progressive haemodynamic deterioration (two). One death followed septic meningitis complicating temporary transvenous pacing. Perioperative onset of complete heart block occurred in five requiring permanent pacing.

Twelve survivors were followed for three to eight years with postoperative cardiac catheterisation in 10 at one to 36 months in addition to assessment with M-mode and two dimensional echocardiography, ambulatory monitoring, and exercise testing. Left atrioventricular valve regurgitation was present in 10, with subsequent valve replacement in one. Four late deaths occurred at 15 months to four years resulting from indirect complications of permanent pacing (two), complex arrhythmias (one), and non-cardiac cause (one). Of the eight current survivors, four have severe residual left atrioventricular valve regurgitation (two with pacemakers), and only two are completely asymptomatic.

The presence of conduction system abnormalities and the function of the left atrioventricular valve and
morphological right ventricle influence not only the natural history of patients, but also the unnatural history of patients after surgical treatment of associated lesions in corrected transposition. The results of this series suggest that direct repair is indicated only in the severely symptomatic patients.

Complications of long-term prostaglandin E2 therapy in infants with complex heart disease

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The short term use of prostaglandin E2 to maintain duct patency is well established in the treatment of duct dependent congenital heart disease. Few reports, however, exist of the effectiveness and complication rate of long-term PGE2 therapy.

Over the past three years, 31 such infants (average gestation 39 weeks, birth weight 3-0 kg) were started on oral prostaglandin E2 therapy. Nineteen infants were treated for a period of less than seven days before palliative surgery. Apart from transient pyrexia these infants had no serious side effects. A further 12 infants were maintained on oral prostaglandin E2 long term (mean 28.5 days, nine with pulmonary atresia, two tricuspid atresia, one critical pulmonary stenosis). All developed side-effects attributable to oral prostaglandin E2 therapy. Six infants had severe apnoeic episodes requiring resuscitation. Ten infants had recurrent pyrexias. Eight had intermittent diarrhoea (three with melena). A further three infants developed a persistent severe metabolic acidosis (average duration of therapy 47 days) for which no other cause could be determined. All died as a result of this.

We conclude that short term prostaglandin E2 administration is both effective and safe. In our experience, however, its long-term use in infants with congenital heart disease is more hazardous than previously reported. The incidence and mechanism of the late spontaneous metabolic acidosis require further elucidation.

Role of suprasternal two dimensional echocardiography in assessment of neonate and infant with congenital heart disease

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Though two dimensional echocardiography has made a major impact on the assessment of the sick neonate and infant, the main emphasis has been on intracardiac anatomy demonstrated by subcostal and praecordial cuts rather than direct visualisation of supracardiac structures. The aims of the study were to evaluate the ability of suprasternal echocardiography to demonstrate normal anatomy and to determine which anomalies could be visualised from this approach. Studies were made on a total of 193 cases. In 50 cases with normal supracardiac anatomy reliable delineation was possible in all cases. In particular, the side of the aortic arch, brachiocephalic branching, and continuity of the pulmonary arteries could be shown. Specific patterns were present for the majority of cases with supracardiac abnormalities. In the group, 15 cases had total anomalous pulmonary venous drainage, four aortico pulmonary window, 13 truncus arteriosus, 30 coarctation of the aorta, 15 pulmonary atresia, 50 persistent ductus arteriosus, 10 left superior vena cava to coronary sinus, two anomalous origin of left pulmonary artery from the aorta, and four interrupted aortic arch.

Thus two dimensional echocardiography allows a reliable assessment of the normal supracardiac anatomy and enables the examiner to obtain detailed information about defects not available from the praecordial and subcostal windows.

Demonstration of defects of interventricular septum in adults by two dimensional echocardiography

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The ability of two dimensional echocardiography to identify and classify ventricular septal defects in adults was studied prospectively in 56 patients (age range 15 to 78 years). Included were 41 patients with congenital heart disease (24 with isolated septal defects) and 15 patients with post-infection defects. A multiplane scanning technique of examination was routinely recorded. Defects were considered identified only when consistently visualised in two echocardiographic planes. The echocardiographic findings were subsequently correlated with clinical, catheterisation, surgical, and postmortem information.

Twenty-one congenital defects were identified and correctly classified. Defects associated with complex lesions or isolated Eisenmenger defects were reliably identified, as were isolated defects with Qp:Qs>2:1. All 11 isolated defects not identified appeared clinically small and in eight catheterisation demonstrated a Qp:Qs>1-6:1.

Post-infarction defects in the trabecular septum
were identified in 13 patients, with the defect visualised in 10. In the remaining three patients contrast echocardiography demonstrated right to left ventricular shunting.

We conclude that two dimensional echocardiography is extremely effective in identifying and predicting the haemodynamic significance of adult congenital ventricular septal defects. In addition, this study emphasises the value of two dimensional echocardiography in demonstrating post-infarction defects, either by direct visualisation or by the use of contrast echocardiography.

Notices

The Fifth Symposium on Echocardiology will be held at the Erasmus University, Rotterdam, the Netherlands, 22 to 25 June 1983. For further details, please write to Mr H Rijsterborgh, Erasmus University, Ee 2302a, PO Box 1738, 3000 DR Rotterdam, the Netherlands.

Subacute bacterial endocarditis

A survey is currently being carried out by the British Cardiac Society and the Medical Services Study Group of the Royal College of Physicians. Though improvement of dental prophylaxis is one objective, the survey is already yielding other valuable information. It is hoped that proformas will be received in respect of a high proportion of patients with subacute bacterial endocarditis in the British Isles seen during 1981 and 1982 and readers are asked to arrange for them to be submitted in respect of any cases that come to their notice. Proformas can be obtained from Sir Cyril Clarke, Medical Services Study Group, King’s Fund Centre, 126 Albert Street, London NW1 7NF (tel. 01-267 6111, ext. 263) to whom they should be returned.

British Cardiac Society

The Autumn Meeting will take place at Wembley on 6 and 7 December 1982 and the closing date for receipt of abstracts is 11 August 1982.

The Annual General Meeting for 1983 will take place in Bristol on 12 and 13 April, and the closing date for abstracts will be 4 January 1983.

The Autumn Meeting will be held at Wembley on 21 and 22 November 1983, and the closing date for abstracts will be 28 July 1983.

International conference on cardiac arrest and resuscitation

This conference, sponsored by the British Heart Foundation in association with the Community Resuscitation Advisory Council, BASICS, and the Royal Postgraduate Medical School, Hammersmith, will be held in Brighton on 19 to 21 October 1982. Inquiries to: Conference Services Limited, 3 Bute Street, London SW7 3EY.