Proceedings of the British Cardiac Society

THE 59TH ANNUAL GENERAL MEETING of the British Cardiac Society was held at the Royal Free Hospital, London on Wednesday and Thursday, 23 and 24 April 1980. The President, W SOMERVILLE, took the Chair during private business. At the scientific sessions the Chair was taken by CECIL SYMONS.

Abstracts of papers

Influence of changing antiarrhythmic drug policy on incidence and outcome of ventricular fibrillation complicating myocardial infarction

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We have assessed the effect of a progressive reduction in the use of antiarrhythmic drugs in the management of acute myocardial infarction over a 12-year period.

A total of 1481 patients were admitted to a coronary care unit during the three periods, 1967–8, 1972–3, and 1977–8. The age and sex distribution of the patient population remained constant. In 1967–8, 40 per cent of patients received intravenous lignocaine or alternative antiarrhythmic treatment, with only 21 per cent in 1972–3 and 10 per cent in 1977–8. The indication for antiarrhythmic drug treatment in 1967–8 was the presence of ventricular ectopic activity in 70 per cent of cases, whereas in 1977–8 the indication for treatment was a preceding episode of ventricular fibrillation in all but 35 per cent. The incidence of ventricular fibrillation occurring within the unit during the three periods under review was 13, 10, and 10 per cent, respectively. Direct current countershock resulted in restoration of spontaneous heart rhythm in 80 to 85 per cent of all patients, but only 39 per cent survived hospital admission in 1967–8, 55 per cent in 1972–3, and 50 per cent in 1977–8. Death after an initially successful resuscitation was almost invariably the result of heart failure rather than an arrhythmia. Suppression of ventricular ectopic activity by lignocaine, in the doses used at the time of the study, was of no benefit in either reducing the incidence of ventricular fibrillation or altering its outcome.

Comparison between oral mexiletine, disopyramide, and placebo used prophylactically after acute myocardial infarction

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The presence of ventricular premature beats on random electrocardiograms or 24-hour tape electrocardiograms is said to increase the risk of sudden cardiac death after acute myocardial infarction. Reducing or abolishing ventricular premature beats might therefore decrease the risk of sudden cardiac death. Ninety-five patients in hospital with proven acute myocardial infarction were randomly assigned to three oral, double blind treatment groups between six and 10 days after infarction. Thirty-one patients took mexiletine (600 to 750 mg/day) continuously for three months; 31 took disopyramide (300 to 600 mg/day); and 33 took placebo capsules. Twenty-four-hour electrocardiogram tapes were recorded before medication and after one, three, and four months.

The mean daily ventricular premature beat count per patient was not significantly different between the three groups either before, during, or after medication. No apparent change in mean daily ventricular premature beat frequency occurred in any group during the four months. No medication had significant effects on ventricular tachycardia or couplet frequency. Three patients in each group reinfarcted. Death occurred in five patients taking disopyramide, three taking mexiletine, and two taking placebo, only four of these being sudden coronary deaths. Side effects were common, resulting in eight patients stopping mexiletine, three stopping disopyramide, and two stopping placebo despite non-toxic plasma levels.
These results do not support the routine prophylactic use of disopyramide or mexiletine after myocardial infarction.

**Failure of predischARGE ambulatory electrocardiographic monitoring to predict sudden death after myocardial infarction**

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Recent studies have suggested that frequent or complex ventricular premature beats detected in the late hospital phase of myocardial infarction may identify patients at high risk of sudden death.

We have performed 24-hour ambulatory electrocardiographic recordings on 139 survivors of myocardial infarction 48 hours before discharge from hospital to select high risk cases for inclusion in a secondary prevention study. Using the Reynolds Pathfinder system for analysis, 42 patients had frequent (>30/hour) or complex (runs of two or more consecutive) ventricular premature beats and were classified as "high risk". Ninety-seven patients had less than 30 ventricular premature beats/hour and were classified as "low risk".

During a mean follow-up period of six months seven deaths have occurred in the high risk group. Five deaths were sudden and five occurred before discharge from hospital. Seven of the 12 deaths in low risk patients were sudden.

When restudied one month after discharge 51 per cent of "low risk" patients had developed "high risk" arrhythmias.

**Conclusions:**
(1) 24-hour electrocardiographic recordings made immediately before discharge identified patients in immediate danger of sudden death but failed to predict long-term risk. (2) Ventricular premature beats increase in frequency after discharge from hospital.

**Right ventricular outflow tachycardia: distinct clinical entity**

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Pacemapping for ventricular tachycardia has allowed the recognition of the surface electrocardiographic appearances of ventricular tachycardia originating in different parts of the ventricles. When cases of idiopathic ventricular tachycardia were analysed a disproportionate number arose from the outflow tract of the right ventricle.

Epi- and endocardial pacemapping (four cases) has shown that right ventricular outflow ventricular tachycardia is characterised by left bundle-branch block pattern and inferior frontal axis (+80° to +100°).

Ten cases (five men, five women) of right ventricular outflow arrhythmias are presented, ranging from ventricular fibrillation (one case) and monoform ventricular tachycardia (seven cases) to couplets (two cases).

The patients were young (mean age 26.9 years) and the histories were short (mean 17.8 months).

The QTc in sinus rhythm was prolonged in every case (mean 0.47 for men and children, and 0.44 s for the women).

In three cases an infectious illness (mumps, varicella, and mycoplasma pericarditis) preceded the onset of ventricular tachycardia, and one case was Kveim positive. Two cases showed congestive cardiomyopathy. Other cases had no structural heart disease.

No single treatment was effective in all cases. These arrhythmias proved refractory to disopyramide in seven cases, and to amiodarone in three cases. Amiodarone was successful in two cases, oxprenolol in one case, continuous atrial overdrive pacing in one case, and dual demand right ventricular pacing in two cases. Operative right ventricular pacemapping and excision of ventricular tachycardia origin proved successful in one case.

**Relation between symptoms, initiation zone, and oral antiarrhythmic treatment in re-entry atrioventricular tachycardia**

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Of 43 patients with paroxysmal reciprocating atrioventricular tachycardia who had undergone intracardiac electrophysiological testing, 31 were treated successfully either with slow-channel or fast-channel antagonists or a combination. Thirty-one patients had Wolff-Parkinson-White (WPW) syndrome—concealed in 13—the remainder had intra- AV nodal tachycardia. None had documented atrial fibrillation. During the electrophysiological study the widest zone over which single atrial premature
beats initiated tachycardia both during sinus rhythm and atrial pacing was measured.

The patients with concealed WPW syndrome had the widest initiation zones, exceeding 150 ms in six. These patients also tended to have the most frequent episodes of tachycardia, five had more than one per week. Successful treatment was achieved in seven, of whom five received slow-channel antagonists. The initiation zone was variable in the patients with overt pre-excitation, often related to the anterograde refractory period of the accessory pathway. In 10 the initiation zone was <20 ms and five had less than four attacks per year. Thirteen were treated successfully, a combination of slow- and fast-channel antagonists being most effective (six). In two, fast-channel antagonists alone succeeded. Intranodal re-entry was characterised by a variable initiation zone and variable frequency of tachycardias. Eleven were successfully controlled and in all but one this was achieved with slow-channel antagonists.

This study demonstrates the efficacy of specific channel antagonists in a high proportion of cases and may allow prediction of success when the mechanisms have been defined, which was often possible from clinical tracings.

Arrhythmia and mortality in hypertrophic cardiomyopathy

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Retrospective analysis of 216 patients with hypertrophic cardiomyopathy, follow-up one to 23 years (mean six), disclosed that 48 had died, 24 of them suddenly. The 168 survivors were compared with the 48 who died. The following were associated with poor prognosis: young age (p < 0.003), dizziness (p < 0.02), and severe dyspnoea (p < 0.02) at the time of diagnosis; and cardiac surgery (p < 0.01) and the onset of atrial fibrillation (p < 0.05) during follow-up. Neither a positive family history nor any electrocardiographic or haemodynamic measurement predicted mortality.

Ambulatory electrocardiographic monitoring in 30 unselected patients showed that 50 per cent had multiform or paired ventricular extrasystoles or ventricular tachycardia and 46 per cent had important supraventricular arrhythmias. Neither beta-adrenergic blocking treatment nor calcium antagonist treatment with verapamil (480 mg/day) reduced the incidence of arrhythmia.

Death in hypertrophic cardiomyopathy is most often sudden. Serious albeit asymptomatic arrhythmias are frequent: a trial of two conventional treatments showed that neither was effective. The detection of arrhythmia and its effective treatment may improve prognosis in this disease.

Regional variations in cardiovascular disease in Great Britain and prevalence of risk factors

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The British Regional Heart Study aims at determining the factors responsible for the pronounced regional variations in cardiovascular disease. Twenty-five towns have been selected to represent the full range of cardiovascular mortality and water hardness and the major geographic regions. Some 8000 men aged 40 to 59 years drawn from a representative general practice in each town are being studied to relate the prevalence of personal risk factors to cardiovascular mortality. A prospective study will relate incidence of cardiovascular events to personal and environmental risk factors. Preliminary results from the first 16 towns are presented.

Mean systolic and diastolic blood pressures vary widely and there is a strong relation between them and cardiovascular mortality rates in the towns. There is a positive relation between mean blood lead concentrations and mean blood pressures but no relation between water hardness and blood pressures. An inverse relation is seen between respiratory function and cardiovascular mortality rates. No relation is evident between mean plasma total cholesterol or mean high-density lipoprotein levels and cardiovascular mortality and there is little difference between towns in body mass index.

Social class and coronary heart disease

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Forty years ago death from coronary heart disease appeared to be much commoner in professional classes, whereas now it is much commoner in manual and unskilled classes. Changes in diagnostic
fashion account for only part of this reversal of the social class pattern. The worsening mortality in lower classes correlates statistically with more smoking and with various dietary changes.

The mortality differential is even wider in our study of 17,530 male London civil servants: in the lowest employment grade the age-adjusted rate is 360 per cent of that in the top (administrative) grade. Part of this large difference can be accounted for by higher levels of smoking and blood pressure and by lower levels of leisure-time exercise, glucose tolerance, and body height; but much of the high coronary heart disease mortality of working-class men remains unexplained.

Socioeconomic factors and coronary heart disease

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The relation between socioeconomic groups, the prevalence of coronary heart disease, and the presence of coronary risk factors was examined in 1568 male subjects who attended an Irish Heart Foundation industrial-based risk factor screening programme. One-third were in the higher and one-sixth were in the lower socioeconomic groups. Social class was defined according to the level of formal education, the subjects being divided into those with first, second, and third level of education.

A history of hypertension, coronary disease, and intermittent claudication was significantly associated with lower socioeconomic class (p < 0.05 in all cases). These findings may be explained by the distribution of coronary risk factors. Those in the lower socioeconomic group included more current smokers and less non-smokers. They had significantly higher blood pressure and cholesterol levels compared with the better educated groups and they were heavier, older, and exercised less.

Minor ST segment and T wave changes in resting electrocardiogram of asymptomatic subjects

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Minor T wave and ST segment changes in the resting electrocardiogram of asymptomatic subjects are a frequent and non-specific finding. As possible indicators of occult coronary artery disease they may be of significance in the routine examination of professional aircrew.

Routine scrutiny of 14,000 professional aircrew and air-traffic control officers over a two-year period yielded 192 subjects who underwent maximal treadmill electrocardiography at CAA House for the elucidation of possible cardiovascular disease. One hundred and seven (55.7%) of these had minor ST-T changes in the resting electrocardiogram. Further investigation of this group led to the permanent loss of licence in seven (6.5%) on account of proven or strongly suspected coronary artery disease and in one case from hypertrophic obstructive cardiomyopathy. Seven (6.5%) more licences had restrictions imposed on account of borderline exercise responses pending further investigation. Angiography was performed in 11 (10.3%) but only three had significant coronary artery disease. Of the remaining 93, 26 (28.0%) had non-diagnostic changes on exercise and 40 (43.0%) demonstrated a reduction in T wave voltage >50 per cent on hyperventilation at rest which was corrected by exercise.

It is concluded that minor ST-T changes are unusually caused by coronary artery disease in asymptomatic subjects and that the so-called labile T wave syndrome is considerably more common.

Replacement versus repair for severe mitral regurgitation caused by “floppy” valves

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Between September 1969 and September 1979, 120 patients underwent operation for severe mitral regurgitation caused by “floppy” valves. Valve replacement, using an inverted fresh aortic homograft, was performed in 45 patients (group A) all before 1974 and 75 patients (group B) had repair of their valves. The ages of the patients were between 7 and 71 years (mean 48). Five of the younger patients had Marfan’s syndrome and 17 patients had had bacterial endocarditis. There was rapid deterioration in symptoms before operation. Ruptured chordae to the posterior cusp was present in 72 patients (60%), to the anterior cusp in 15. Thirty-three patients had a combination of both, or elongated chordae. There was no significant difference in age, severity of symptoms, or type of lesion found at operation in either group. Additional procedures were performed in three patients in group A and 13 in group B.

The early mortality for isolated repair was 2 per
cent compared with 7 per cent for replacement. The overall late mortality was 21 per cent for group A (mean follow-up of 78 months) and 6 per cent for group B (mean follow-up of 38 months). The five-year actuarial survival for group A was 63 per cent and 89 per cent for group B. Twenty-seven patients in group A (93%) and 55 patients in group B (93%) moved to Class I or II of the NYHA Classification.

It is concluded that a valve conserving procedure is possible in almost all patients and appears to give better early and late results.

Identification of risk of thromboembolism from prosthetic cardiac valves
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The use of oral anticoagulants in patients with prosthetic cardiac valves has reduced the risk of thromboembolism. However, 10 per cent of patients with mechanical valves still have thromboemboli despite adequate anticoagulation. Abnormal platelet function has been shown in such patients. A radioimmunoassay for the platelet specific protein betathromboglobulin (BTG) has been developed. The plasma BTG is thought to measure the in vivo platelet aggregation and release reaction occurring at the time of sampling. We have studied 131 patients with valve replacements. Those with double valve replacements had a significantly higher plasma BTG (67.74 ± 5.42 ng/ml N = 18) than those with single metal valve prostheses (55.5 ± 2.3 ng/ml N = 69, p < 0.05). In turn, patients with single metal prostheses had significantly raised values compared with those with heterograft valves (45.7 ± 2.3 ng/ml N = 24, p < 0.05). This is in keeping with the known thrombogenicity of metal valves compared with heterograft valves. Patients with single metal valves who suffered a thromboembolic event while on warfarin had a nearly significantly higher BTG (65.0 ± 4.3 ng/ml N = 13, p < 0.1) than those with single metal valves who had no thromboemboli. We conclude that raised plasma BTG identifies those patients with prosthetic valves who are at risk from platelet thromboemboli.

Yield of coronary arteriography in patients before valve replacement
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Coronary arteriograms performed before valve replacement in 643 patients (age range 31 to 77 years; mean 54 ± 8 years) were reviewed in order to assess the value of this investigation in patients with valve disease with or without angina.

Significant coronary artery disease was more common in the 199 patients with angina (42%) than in the 444 patients without angina (14%) and was more common in the 417 patients who had one or more coronary heart disease risk factors (31%) than in those without risk factors (8%).

In the patients without angina, significant coronary artery disease was found more frequently in those with at least one risk factor (21%) than in those with no risk factors (4%), and progressively more commonly in those patients with increasing numbers of risk factors. All differences were statistically significant (p < 0.001).

Thus, the yield of abnormal arteriograms in patients in whom both angina and risk factors are absent is very small, whereas the yield becomes significantly greater in those with angina and in angina-free patients who possess risk factors.

Orthotopic heart transplantation after 16 hours of ischaemia
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Preliminary experiments with cardiopulmonary bypass showed that satisfactory preservation of the heart could be obtained for periods of up to four hours of ischaemia using single dose cold cardioplegia and rapid induction of local profound cardiac hypothermia. Thereafter morbidity from prolonged cardiopulmonary bypass became a limiting factor.

The present experiments were designed to test the efficacy of cardioplegia and rapid cooling for prolonged (16 hour) periods of myocardial ischaemia using orthotopic heart transplantation in pigs as the experimental model. The donor heart is excised after infusing cold cardioplegia into the aortic root during venous inflow occlusion and then rapidly cooled and maintained at 2 to 4°C in cardioplegic solution. Sixteen hours later it is transplanted orthotopically into the recipient animal.

Early graft function was good or excellent in 11 of 14 experiments, as judged by these animals being weaned satisfactorily from bypass with minimal inotropic support. Seven pigs subsequently lived between six hours and 83 days, the latter animal being sacrificed electively after immunosuppression with Cyclosporin A.
This simple and effective method for achieving extended periods of myocardial preservation has important implications with regard to heart donor procurement for clinical transplantation.

Value of computer digitisation of left ventricular echocardiogram in transposition of the great arteries

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Thirty-one patients with transposition of the great arteries had sequential M-mode echocardiograms recorded during the first year of life. Twenty-three had further sequential studies after a corrective Mustard procedure. Computer digitisation of left ventricular echocardiograms was carried out and the following indices measured, LVEDD; LVESD; max dd/dt and max dL/dt/d for both ventricular filling and emptying. The results obtained were compared with data from normal infants.

At birth, left ventricular dimensions, filling, and emptying characteristics were normal but all became significantly reduced by 2 months of age, suggesting abnormal left ventricular function. Normal or increased left ventricular dimension and filling/emptying rates were maintained only where there was a duct or ventricular septal defect with associated increased pulmonary blood flow. These abnormalities in left ventricular function indices persisted after a Mustard procedure. In three patients with documented post-Mustard caval obstruction, an extremely slow left ventricular filling profile was recorded, which we consider to be diagnostic of obstructed systemic venous return.

It is concluded that sequential analysis of left ventricular function by digitisation of the M-mode left ventricular echocardiogram is of considerable value in the management of infants with transposition of great arteries as it provides non-invasive evidence of abnormal left ventricular function and allows identification of a ventricular septal defect, persistent ductus arteriosus, or obstructed systemic venous return.

Accuracy of two-dimensional echocardiography in diagnosis of mitral stenosis

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Previous studies have shown a poor correlation between the severity of the degree of mitral valve stenosis using M-mode echocardiography with the haemodynamic assessment of the mitral valve area. The object of this study was to compare two-dimensional echocardiographic assessment with haemodynamic assessment of the mitral valve area in 15 patients with pure mitral stenosis.

Satisfactory two-dimensional echocardiograms of the mitral valve leaflets were obtained in 10 patients with the Smith Kline Instruments EkoSector System I. The echocardiograms were recorded on polaroid film, enlarged by a factor of 10, and the valve area estimated by planimetry. All patients underwent left and right heart catheterisation. Dye dilution cardiac outputs were performed and the mitral valve area was calculated using the Gorlin formula.

The degree of mitral stenosis ranged from trivial to severe (range 2.9 to 0.8 cm²) with a mean haemodynamic mitral valve area of 1.38 ± 0.21 cm² (SE) and by two-dimensional echocardiography (range 2.8 to 0.9 cm²) with a mean of 1.45 ± 0.21 cm² (SE). There was a linear relation of the valve areas by the two methods with a correlation coefficient of 0.88.

The results suggest the severity of mitral stenosis and the mitral valve area can be accurately assessed non-invasively by two-dimensional echocardiography.

Two-dimensional echocardiographic categorisation of univentricular heart: ventricular morphology, type, and mode of atrioventricular connection

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Most univentricular hearts have two chambers in their ventricular mass, only one of which possesses an atrioventricular connection. Categorisation into univentricular hearts of right or left ventricular type, or indeterminate type, using two-dimensional echocardiography has been successfully achieved in 80 patients to whom this technique has been applied. Thus, right ventricular rudimentary chambers in 59 univentricular hearts of left ventricular type were shown to be anterosuperior and either to right or left. In contrast, left ventricular rudimentary chambers in 10 univentricular heart of right ventricular type were posteroinferior. Eleven uni-
ventricular hearts of indeterminate type were characterised by absence of a rudimentary chamber. In addition the trabecular pattern of both main and rudimentary chambers was separately identified in some of the patients with univentricular hearts of right and left ventricular type, and 2-D echocardiography also illustrated the mode of atrioventricular connection, either via two valves, a common valve, or straddling valve, and in the latter demonstrated the orientation of the septum straddled. Finally, it was also possible to distinguish absent atrioventricular connection from an imperforate valve in five patients.

**Three-dimensional ambulatory monitoring for arrhythmias**

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Ambulatory monitoring of arrhythmias has become established in clinical medicine. The interpretation of single bipolar lead recordings may be difficult because of artefact, and the distinction between supraventricular and ventricular arrhythmias may be impossible. We have obtained three-dimensional recordings (X, Y, and Z co-ordinates) using a modified three-channel Oxford Medilog box. The most suitable of the three recordings is played back through an Oxford unit and Reynolds pathfinder. When an arrhythmia is detected or an artefact such as a dislodged lead is suspected the three lead recordings are played on to a three-channel tape-recorder, which is subsequently played back to display an X, Y, Z electrocardiogram. The best single lead for identification of P wave and QRS can at any time be changed for single lead write-out.

To date we have obtained these recordings in 32 patients. Twenty of these patients had arrhythmias, which were identified as ventricular in 10 and supraventricular in four from X, Y, Z recordings, though single lead recording was not diagnostic. In addition, five patients had one unsatisfactory recording out of the three and the redundancy of leads prevented repetition of the test. It is concluded that three-dimensional ambulatory monitoring is useful for identifying and studying arrhythmias.

**Is thallium-201 (**$^{201}$**TL)** tomography superior to standard digital $^{201}$TL scintigraphy in detection of patients with coronary artery disease?**

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A standard parallel-hole collimator was compared with a multi-pinhole tomographic collimator (12 slices) to evaluate $^{201}$TL myocardial scintigrams acquired during stress and tracer redistribution in 43 patients (14 normal coronary arteries; 12 coronary artery disease; 11 post coronary artery bypass surgery; six unknown coronary artery status). Tomograms and standard scintigrams were analysed independently from a colour digital display by four observers.

Of the 12 patients with coronary artery disease, 10 had an abnormal standard scintigram compared with nine with an abnormal tomogram (NS). In the 11 patients with coronary artery bypass surgery no preference could be shown for either collimator in the predictive evaluation of graft status or in the detection of ischaemia in diseased but non-grafted coronary arteries. Of the 14 patients with normal coronary arteries only seven had a normal standard scintigram, and eight a normal tomogram (NS). Finally, of the six patients without arteriographic data, five had an abnormal standard scintigram compared with four with an abnormal tomogram (NS). Standard scintigrams and tomograms were completely comparable in the detection of intra-myocardial tracer redistribution.

We conclude that $^{201}$TL tomograms are not superior to standard digital scintigrams in the detection of patients with normal and diseased coronary arteries.

**Biplane exercise radionuclide ventriculography in patients with coronary artery disease**

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Fifteen patients with coronary artery disease were investigated by exercise first pass radionuclide ventriculography in right and left anterior oblique projections. There was a fall in left ventricular ejection fraction (LVEF) on exercise for left anterior oblique ($p < 0.05$) and right anterior oblique ($p < 0.05$) projections, with no significant differences between the two obliques. For the eight patients with triple vessel disease mean LVEF fell from 64-1 to 52-5 in the right anterior oblique
(p < 0.01) and from 49.9 to 40.8 in the left anterior oblique (p < 0.02). Fall in LVEF was higher for patients with triple vessel disease than for those with less extensive lesions in right anterior oblique (p < 0.01) and left anterior oblique (p < 0.05). Rest and exercise regional wall motion abnormalities were assessed; 15/15 zones of exercise-induced regional wall motion abnormalities seen in the right anterior oblique and 21/25 seen in the left anterior oblique were in regions supplied by significantly stenosed vessels. Of 34 coronary artery stenoses, 22 were identified by regional wall motion abnormalities in the left anterior oblique and 22 in the right anterior oblique. Combined right and left anterior oblique analysis identified 28. Six of seven patients with triple vessel disease had a positive exercise study (exercise LVEF < 50%, exercise-induced regional wall motion abnormality or fall in LVEF on exercise > 10%, in the right anterior oblique, and six of seven in the left anterior oblique. All seven were identified by combined analysis.

Both right and left anterior oblique exercise first pass radionuclide ventriculography are of value in the assessment of patients with coronary artery disease. Biplane radionuclide ventriculography improves the detection of individual stenoses and may prove helpful in the identification of patients with triple vessel disease.

Nifedipine added to beta-blockade: beneficial effect in coronary artery disease

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The haemodynamic and metabolic effects of adding nifedipine to chronic beta-adrenergic blocking therapy were studied before and during atrial pacing to angina in 10 patients. All were taking propranolol 80 mg tds (or equivalent) and had proven extensive coronary artery disease. Heart rate at rest rose from 63 beats/minute on beta-blockade alone to 76 beats/min 20 minutes after nifedipine 20 mg sublingually (p < 0.02). Likewise, coronary sinus blood flow rose from 74 ml/min to 127 ml/min (p < 0.005) and coronary vascular resistance fell from 1.1 to 0.8 units (p < 0.005). Arterio-coronary sinus oxygen difference fell from 3552 to 3568 μmol/l. Cardiac output, total peripheral resistance, systolic blood pressure, and myocardial lactate metabolism were unchanged at rest.

Addition of nifedipine to beta-blockade prolonged pacing time from 363 to 494 seconds.

These results suggest that nifedipine produces an additional beneficial effect on myocardial function in patients with coronary artery disease already on beta-blockade; this appears to be a result in part of a coronary vasodilator property of the drug.

Anti-anginal effects of propranolol and nifedipine

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Using a double blind randomised clinical trial of balanced Latin square design, the antianginal effects of nifedipine (60 mg/day), propranolol (480 mg/day), and the combination were compared with placebo in 16 patients with severe angina pectoris. Response to treatment was assessed by exercise praecordial ST mapping, 48-hour ambulatory electrocardiographic monitoring, pain relief, and glyceryl trinitrate consumption.

There was a decrease in pain frequency from 22 ±4 attacks per patient per week (mean ± SEM) on placebo to 14 ±3 (nifedipine), 7 ±2 (propranolol), and 6 ±2 (propranolol and nifedipine) (p < 0.005, 0.001, and 0.001, respectively).

Objectively, the total area of exercise-induced ST depression was decreased from 20 ±3 mm per patient (placebo) to 14 ±3 (nifedipine), 10 ±2 (propranolol), and 2 ±0.7 (propranolol and nifedipine) (p < 0.005, 0.005, and 0.0005, respectively). Episodes of ST depression detected on ambulatory monitoring were reduced from 7 ±2 episodes per patient per 24 hours (placebo) to 3.5 ±0.8 (nifedipine), 1.3 ±0.4 (propranolol), and 0.25 ±0.2 (propranolol and nifedipine) (p < 0.025, 0.01, and 0.001, respectively).

Resting supine heart rate fell from 75 ±3 beats/min on placebo to 56 ±2 on propranolol (p < 0.0005) and 57 ±3 beats/min (p < 0.0005) on propranol and nifedipine, but remained unchanged on nifedipine (73 ±4 beats/min); similar effects were seen on the erect heart rate, the calculated mean rate from monitor tapes, and the maximum rate induced by exercise.

All three active treatments had significant anti-anginal effects, by all criteria; the objective methods of exercise praecordial mapping and ambulatory ST monitoring provided the only reliable indices that propranolol and nifedipine were significantly better than either drug.

Our observations show that the combination is a safe and effective form of treatment for angina.
Prostacyclin: haemodynamic and metabolic effects in patients with ischaemic heart disease

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Prostacyclin is a prostaglandin synthesised within the vascular endothelium. The objectives of this study were to examine the relative effects of an infusion of the drug, at doses of 2, 4, 6, and 8 ng/kg per min, on the coronary and systemic haemodynamics and its inhibition of platelet aggregation in patients with angiographically proven coronary artery disease. Eight patients have been investigated and dose related changes were observed. At 8 ng heart rate increased (71 to 84 beats/minute) while systolic (137 to 111 mmHg) and diastolic (70 to 61 mmHg) pressures fell. Total systemic vascular resistance fell (22.1 to 14.3 units) and cardiac output increased (4.23 to 5.30 l/min). Pulmonary artery pressures were unchanged. Coronary vascular resistance fell from 0.76 to 0.56 units, but the total coronary sinus blood flow was unchanged. Platelet aggregation (Born technique) was inhibited by 45 per cent at 6 ng. Lactate and oxygen extraction were unchanged at rest but pacing time to angina during prostacyclin infusion was prolonged in 60 per cent of patients.

These mild coronary and systemic haemodynamic effects with significant inhibition of platelet aggregation and prolongation of pacing time to angina suggest that prostacyclin should be evaluated in patients with unstable angina.

Autoimmunity—high prevalence in coronary artery disease: possible role in pathogenesis of atheroma

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This study was performed to test the hypothesis that preclinical hypothyroidism is a causative factor in coronary atheroma. Using patients undergoing coronary arteriography, 108 subjects with coronary atheroma were matched for age and sex with 108 subjects with no angiographic evidence of atheroma. At catheterisation each had the following tests: tissue autoantibody, thyroxin, triiodothyronine and thyrotropin releasing hormone stimulation test.

There was a highly significant difference in the prevalence of tissue autoantibody between the two groups (men p=0.003, women p=0.006). There were 67 men and 41 women in each group; 21 per cent of men (14) with atheroma had auto-antibodies compared with 4 per cent of controls (3); 46 per cent of women (19) with atheroma had auto-antibodies compared with 20 per cent of controls (8). The type of autoantibody differed between sexes. In women the commonest autoantibodies were against thyroid whereas non-thyroid auto-antibodies were predominant in men. No difference in thyroid function was found between the two groups; nor was there any difference in the serum cholesterol between those with normal and abnormal thyroid function.

Incidence studies have suggested that thyroid autoimmunity is a risk factor for coronary artery disease. This study has shown that tissue auto-antibody in general is associated with coronary artery disease and it is suggested that autoantibody may promote atheroma through intimal damage resulting from circulating immune complexes.

Heart rate response to glyceryl trinitrate as a test of beta-adrenoceptor blockade: a reappraisal

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The heart rate response to glycerly trinitrate has been claimed to be independent of vagal effects and has been used as a test of beta-adrenoceptor blockade. However, its usefulness has been questioned. Six normal men, mean age 28 ± 1.6 SEM years, had a mean response of 23 ± 1 beats per minute after placing a standard glyceryl trinitrate tablet (0.5 mg) under the tongue for four minutes while standing upright. Blockade of the cardiac autonomic nervous system by intravenous atropine 0.04 mg/kg and propranolol 0.6 mg/kg showed that the heart rate response resulted both from vagal withdrawal and reflex sympathetic stimulation of the heart, each contributing 50 per cent of the total heart rate response.

Beta-adrenoceptor antagonism was assessed by inhibition of heart rate response to glyceryl trinitrate and compared with reductions in exercising heart rates in 13 essential hypertensives, mean age 49 ± 2 years, who completed a double blind comparison of placebo, acebutolol 200 mg twice daily, and acebutolol 400 mg once daily. Both tests detected beta-
adrenoceptor antagonism at 12 and 24 h after the last dose of active drug and there was a significant correlation between the heart rate responses to both tests (control: \( r = -0.71, p < 0.001 \); 12 h: \( r = -0.75, p < 0.001 \); 24 h: \( r = -0.74, p < 0.001 \)). Furthermore, there was a significant correlation between the heart rate response to glyceryl trinitrate and serum acebutolol levels (\( r = -0.60, p < 0.001 \)). Therefore, the glyceryl trinitrate tests appear to be at least as effective as bicycle exercise in detecting levels of beta-adrenoceptor antagonism.

References


Late results of monocusp reconstruction of right ventricular outflow tract in patients with tetralogy of Fallot operated on under 2 years of age

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Seventeen children with tetralogy of Fallot, who underwent successful reconstruction of the right ventricular outflow tract with a monocusp of a fresh adult-sized aortic homograft, have been followed-up for between two and seven years (mean 4-25). Their ages were between 5 and 24 months (mean 13 months). The monocusp was used to enlarge the valve ring and at the same time to render the valve competent. There have been no late deaths and all children are asymptomatic and not on cardiac drugs. Five patients (29%) have developed a soft early diastolic murmur at varying intervals since operation. There is calcification in the free wall of the homograft in all patients. Fifteen patients have been reinvestigated two weeks to 44 months after operation. Five have been reinvestigated twice. Fourteen patients had a right ventricular outflow tract gradient of less than 15 mmHg, and the RV/LV ratio was less than 0·4 in 12 patients. The right ventricular end-diastolic pressure was less than 12 mmHg in all patients. In those patients investigated twice there was no change in right ventricular outflow tract gradient, RV/LV ratio, or right ventricular end-diastolic pressure. No patient had angiographic evidence of significant pulmonary regurgitation.

It is concluded that reconstruction of the right ventricular outflow tract in patients with tetralogy of Fallot, operated upon under the age of 2 years, gives good long-term results and appears to allow for growth.

Infradiaphragmatic total anomalous pulmonary venous drainage: surgical treatment and long-term results

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Since 1971, 20 infants (aged 1 day to 3 months) with infradiaphragmatic total anomalous pulmonary venous drainage have undergone repair. All patients presented with severe cyanosis (mean \( \text{PaO}_2 \) 35·8) and congestive heart failure. Right-sided pressures were equal to or greater than systemic in 18. All had a persistent ductus arteriosus. Surgical repair was accomplished using deep hypothermia with circulatory arrest. The confluence of pulmonary veins was anastomosed to the left atrium. The descending vein was ligated or divided in 15 and left open in five. Atrial septal defects were closed with a patch in six and sutured in 14. Eight patients died (40%). Acidosis upon admission was significantly greater among non-survivors (mean pH 7·29 ±0·03) than survivors (mean pH 7·37 ±0·02), \( p < 0·05 \). No differences were noted in catheterisation findings, timing of operation, or surgical techniques. Twelve survivors are well two months to seven years after operation. All are asymptomatic and none requires cardiac medication. Normal chest x-rays and cardiac rhythms are present in each. Five have undergone repeat catheterisation, demonstrating normal pressures and no shunts. It is concluded that the initial mortality of infradiaphragmatic total anomalous pulmonary venous drainage depends mainly upon the condition of the child on admission. Long-term results of surviving patients are excellent.

Filter films in infants with heart disease

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Determination of atrial situs is of cardinal importance in the analysis of complex congenital heart lesions, and is best predicted from bronchial situs.
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However, previous methods for assessing bronchial morphology are unsuited to the very young patient.

To assess bronchial morphology, 100 consecutive patients under 18 months of age (median 2 months) with suspected congenital heart disease were studied by high kilovoltage filtered beam radiographs, before cardiac catheterisation. This low radiation dose technique clearly defined bronchial anatomy in 95 patients. Bronchial lengths were compared and 10 cases had a ratio < 1.5 suggesting situs ambiguous. Discriminant function analysis based on tracheal width and bronchial length enabled clear distinction of right from left bronchi. Four patients had bilateral right and six had bilateral left bronchi. Three of these 10 cases died and there was necropsy confirmation of the radiological diagnosis.

Thus routine screening of bronchial situs in this age group has shown an unexpectedly high incidence (10%) of situs ambiguous. This is known to be associated with a constellation of cardiac anomalies, most importantly interrupted inferior vena cava with left isomerism and total anomalous pulmonary venous drainage with right isomerism. This simple technique therefore provides a useful basis for planning cardiac catheterisation.

Severe apnoea and prolonged duct patency after use of prostaglandin E₂

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The use of E-type prostaglandins to maintain patency of the ductus arteriosus in the ductus dependent pulmonary blood circulation is well established. Their use has been suggested to facilitate safe transfer of certain groups of critically sick and cyanosed neonates to regional centres. We report here complications of prostaglandin infusion in six patients (three pulmonary atresia with intact septum, two pulmonary atresia with ventricular septal defect, one tetralogy of Fallot) presenting in the first few days of life with severe cyanosis (PO₂ < 5 kPa).

All received prostaglandin E₂ (PGE₂) 0.05 to 0.1 μg/kg per min via a peripheral vein and a rise in arterial PO₂ resulted > 3 kPa. Three of four patients breathing spontaneously developed recurrent apnoea during PGE₂ infusion and one required ventilation. None had been apnoeic previously, and no other cause for apnoea was found.

A modified right Blalock Taussig anastomosis (five cases) or Waterston-Cooley anastomosis (one case) was performed within 24 hours of admission, and the PGE₂ infusion discontinued 24 hours post-operatively. Four cases were considered to have persistent duct patency after stopping PGE₂. In two of these with intractable pulmonary oedema, wide duct patency was confirmed two to three weeks later at subsequent operation to close the ductus. Both the apnoeic episodes and prolonged ductal patency were considered to be related to use of prostaglandin E₂.