

Proceedings of the British Cardiac Society

THE AUTUMN MEETING of the British Cardiac Society (Chairman RW EMANUEL) was held at Wembley Conference Centre on Monday and Tuesday, 6 and 7 December 1982. The President, M F OLIVER, took the Chair during private business.

Abstracts of papers

Q wave changes during exercise: a valuable predictor of coronary artery disease

M J O'Hara, V Bala Subramanian, A B Davies, E B Raftery
Northwick Park Hospital and Clinical Research Centre, Harrow, Middx

To improve the accuracy of the stress test for predicting coronary disease we studied the change of Q wave amplitude during exercise. Of 158 subjects who had coronary arteriograms and exercise tests, normal coronaries were found in 31 and arterial disease in 127. Immediately before and immediately after treadmill exercise Q wave amplitude was measured in lead CM5 from the computer-derived average of 25 consecutive beats. Whereas Q wave amplitude was greater in normal subjects at rest and increased with exercise, the reverse occurred in those with coronary disease. Using the criterion of decrease or no change in Q wave amplitude during exercise as indicating a positive test the sensitivity, specificity, and predictive value for detecting coronary disease were 83, 58, and 89%, respectively. The corresponding values for ST depression were 57, 71, and 89%. When either a positive ST or Q wave response was used the sensitivity increased to 91% with a loss of specificity (39%) but no change in predictive value. Though the mechanism of the observed changes of Q wave amplitude is unclear, its measurement adds considerably to the accuracy of the stress test for predicting coronary artery disease.

Role of early postinfarction exercise test in identifying candidates for early coronary surgery

K Jennings, D S Reid, D G Julian
Freeman Hospital, Newcastle upon Tyne

ST changes on postmyocardial infarction exercise testing have been reported to predict death in the

succeeding year; it has been deduced that they could be an indication for early coronary surgery because they represent hazardous but reversible ischaemia.

To evaluate exercise testing in this context, we exercised 103 consecutive patients able to perform a limited Naughton protocol, a mean of 12 days after infarction. No patient experienced complication within 48 hours of exercise. Eight patients died during the one year follow-up. Deaths were associated with exercise-induced reduction in blood pressure ($p < 0.01$); all were identified by poor exercising haemodynamics (heart rate > 130 /beats per minute or reduction in blood pressure). ST depression or arrhythmias on exercise were not significantly associated with death. Inability to complete the test for any reason was associated with left ventricular failure, non-fatal infarction, or death ($p < 0.05$). Three patients died within three weeks of discharge, before they would have attended for follow-up review. Fifteen patients with normal tests (other than angina in four) had uncomplicated follow-up apart from refractory angina in the four who had angina on exercise testing.

ST changes on postinfarction exercise testing appear less predictive of later complications than haemodynamic observations, which may indicate irreversible left ventricular damage rather than ischaemia.

Assessment of success of coronary angioplasty by use of maximal ST segment/heart rate slope

N P Silverton, D R Smith, M S Elamin, M Kardash, M I Ionescu, W Whitaker, D A S G Mary, R J Linden
Department of Cardiovascular Studies, The University of Leeds, and Department of Cardiology, Leeds General Infirmary

Percutaneous transluminal coronary angioplasty has been shown to be effective in improving the symptoms of angina pectoris in patients with fixed coronary stenoses. Long term management may require regular coronary angiography to assess possible restenosis and to aid in the interpretation of any recurrent chest pain in patients who have more than single vessel coronary disease. The present study shows that a non-invasive exercise test (maximal ST segment/heart rate slope), which has been shown to predict accurately the extent and severity of coronary artery disease, can be used to assess the outcome of angioplasty.

Eleven patients (seven men, four women), mean

age 51.7 years (33.7 to 62.5 years) underwent angioplasty for severe proximal left anterior descending stenoses; four patients had significant lesions in other vessels, two unsuitable for grafting and two associated with previous documented myocardial infarction. Angioplasty was successful in 10 patients with an improvement in the angiographic narrowing from a mean of 92% (80 to 95%) to a mean of 45% (15 to 90%) and a reduction in the trans-stenotic gradient from a mean of 55 mmHg (39 to 90) to 16 mmHg (5 to 35). The exercise test was performed before, and serially after, the manoeuvre, including one at the time of a six-month follow-up coronary angiogram. The max ST/HR slope was always reduced immediately after the dilatation (from a mean of 24.6 mm. beat⁻¹. min. 10⁻³; $p < 0.05$, paired t test). In addition, at six months, the max ST/HR slope always correctly predicted the state of the vessels, including a late post-operative occlusion in one patient, and refuted the clinical diagnosis of a restenosis in another patient who experienced recurrent angina.

Therefore, the maximal ST segment/heart rate slope may be used as an accurate and reproducible indicator of the continued success, or failure, of coronary angioplasty.

Maximal ST/heart rate slope: a reliable predictor of severity of coronary artery disease?

Charles Ilsley, Rudolph Canepa-Anson, Anthony Rickards
The National Heart Hospital, London

The maximal rate of change of the ST segment with heart rate (max ST/HR slope) has been advocated as a totally reliable indicator for the presence and severity of coronary artery disease. The max ST/HR (mm. beat⁻¹. min. 10⁻³) was calculated in 30 men (age 40 to 65) who had undergone both 12 lead treadmill exercise electrocardiography and coronary angiography for the investigation of chest pain. Results were assimilated independently. Exercise was symptom-limited, with resting heart rate of 48 to 110 (mean 68) and peak heart rate of 74 to 150 (mean 116). Five patients had normal coronary angiography and all had normal max ST/HR slopes with no ST segment depression during exercise. The predictive accuracy for the presence of coronary artery disease was 92% (23/25) using the max ST/HR slope and 84% (21/25) for conventional ST analysis. Only 50% (4/8), however, of those with single vessel, 64% (7/11) with double, and 83% (5/6) with triple vessel disease were correctly predicted by the max ST/HR slope. The predictive accuracy for disease severity was therefore only

70% overall (21/30).

In contrast with the Leeds group, this study uses treadmill exercise, a modified Bruce protocol, and does not include CM5 lead. While there is a broad relation to previously defined results, this study suggests that the max ST/HR slope cannot reliably differentiate one, two, and three vessel coronary disease.

Prognostic implication of clinical presentation with hypertrophic cardiomyopathy in childhood

W J McKenna, J E Deanfield, Diane England, Celia Oakley, J F Goodwin, K A Hallidie-Smith
Royal Postgraduate Medical School, London

Retrospective analysis was performed to assess the natural history in relation to clinical and haemodynamic features in 37 patients in whom the diagnosis of hypertrophic cardiomyopathy had been made in childhood. At diagnosis they were aged 1 to 14, mean 9 years. All were studied because of symptoms or abnormalities on physical examination. For the purpose of this study we excluded seven cases in whom the initial presentation was sudden death and 10 in whom the diagnosis had been made during the screening of the families of those probands with a family history of "malignant" hypertrophic cardiomyopathy. During a mean follow up of nine years, only five experienced severe dyspnoea or chest pain; of these, two had progressive dyspnoea and died in cardiac failure and three died after myectomy. The 19 survivors were compared with the 11 sudden deaths. Eleven of the survivors and five of the sudden deaths were asymptomatic, and only syncope ($p < 0.03$) was associated with sudden death. All patients were in sinus rhythm, bundle-branch block was rare (two patients), and voltage criteria for left ventricular hypertrophy were not related to poor prognosis. Haemodynamic data in the survivors and the sudden deaths were not significantly different for pulmonary capillary wedge pressure (12.7 ± 4.1 v 14 ± 3.8), left ventricular end-diastolic pressure (14.1 ± 5.5 v 16.0 ± 3.8), left ventricular outflow tract gradient at rest or after provocation (59% v 56%), right ventricular end-diastolic pressure (6.5 ± 2.2 v 6.4 ± 3.5), and right ventricular gradient (41% v 56%). Most deaths were sudden and better predicted by the history than electrocardiographic or haemodynamic measurements. Thus, for a child to present clinically with hypertrophic cardiomyopathy indicates a poor prognosis even if symptoms are absent or mild.

Analysis of factors that predict mortality in patients with coronary artery disease using a statistical model

M Cattell, S Peters, R Balcon
The London Chest Hospital, Bonner Road, London

Data were analysed from 1749 male patients followed for a maximum of 10 years; 804 were treated surgically and there were 191 deaths (86 surgical). Univariate analysis involved 33 clinical variables including age, symptoms, treatment, risk factors, and exercise data (surgery was a single variable), and 17 angiographic variables including a coronary index. Age (<50) had a negative effect on survival and patients were divided into groups above and below 50 years. A parametric model was chosen to express survival, the best fit being exponential for patients <50, Weibull for >50 years. Individual variables and cross products that do not deviate the model significantly ($p > 0.05$) are rejected. Low coronary index, global left ventricular contraction abnormality, and the presence of peripheral arterial disease correlated with mortality ($p < 0.001$) in patients under 50. Surgery correlated significantly with survival ($p < 0.01$). In patients over 50 the same correlates existed together with combinations of coronary index and the presence of dyspnoea, and pulmonary venous congestion on x-ray film ($p < 0.001$). Collateral filling of the right main coronary artery enhanced survival ($p < 0.002$). There was a good correlation between deaths observed and predicted by the model. For patients <50 there were 97 observed deaths and 91.41 predicted, and >50 there were 94 observed and 86.54 predicted deaths. Once patients with coronary disease present, the most important predictors of survival are angiographic severity of disease, indicators of left ventricular dysfunction, and peripheral arterial disease. Classical risk factors were not good predictors of mortality.

Animal model for studying role of platelets in histopathological and mechanical changes in autogenous vein grafts

A H Gershlick, A J Murday, Denise Syndercombe Court, Margaret S Newell, N Betts, A Thomas, C T Lewis, P G Mills
The London Hospital, and St George's Hospital, London

We present a new animal model in which the pathophysiological processes in autogenous vein grafts may be studied. The external jugular vein is grafted to the ipsilateral carotid artery in rabbits. Smooth muscle hyperplasia is present in the graft at one month (9/9 animals) and two months (10/10 animals). Distensibility, as assessed by measuring incre-

mental strain, is reduced in 4/4 vein grafts at one month.

Autoradiography and in vivo gamma-camera scanning after ^{111}In Indium-oxine platelet labelling indicate that platelets are deposited on the graft wall at one day (8/9 animals), one week (4/5 animals), and one month (4/5 animals) postoperatively. Platelet activity has been assessed by measuring the dose-response variability of platelet aggregation to standard aggregating agents. There is a significant increase in platelet activation in blood samples taken distal to the graft as compared with those taken proximally ($p < 0.01$, $n = 10$). Sampling from the central ear artery supplied by the graft shows increased platelet activity one week ($p < 0.05$, $n = 6$), one month ($p < 0.02$, $n = 10$), and two months ($p < 0.05$, $n = 8$) after operation.

We have thus established an animal model in which platelet function, histopathological processes, and mechanical variables can be measured concurrently. Smooth muscle cell proliferation has been shown and quantified, and platelet function is altered by the presence of the graft.

Histamine and catecholamine responses to physiological stress

J G F Cleland, F Nilam, G C Inglis, K McLeod, S G Ball, H J Dargie
Department of Cardiology and MRC Blood Pressure Unit, Western Infirmary, Glasgow

Histamine has cardiovascular actions both direct and through the sympathetic nervous system. Administered intravenously it can provoke ischaemia in patients with coronary atheroma; physiological release of histamine has not been investigated previously in patients with angina.

We measured plasma noradrenaline, adrenaline, and histamine, by radio-enzymatic techniques, in venous blood samples during lying, standing, isometric exercise, cold pressor testing, and upright bicycle exercise in 16 patients with angina pectoris taking no active medication.

On standing, noradrenaline increased from 438 ± 54 (mean and standard error of the mean) to 564 ± 64 pg/ml ($p < 0.001$) and histamine from 407 ± 35 to 621 ± 60 pg/ml ($p < 0.005$). During the cold pressor test similar rises in noradrenaline (425 ± 49 to 507 ± 53 pg/ml, $p < 0.005$) and histamine (428 ± 32 to 526 ± 39 pg/ml, $p < 0.02$) occurred. Noradrenaline and histamine increases during isometric exercise were not statistically significant (438 ± 50 to 450 ± 57 and 482 ± 44 to 526 ± 74 pg/ml, respectively).

Bicycle exercise caused much larger rises in noradrenaline (611 ± 57 to 1921 ± 373 pg/ml, $p < 0.005$) than histamine (481 ± 41 to 633 ± 55 pg/ml, $p < 0.02$). There

were significant correlations between rise in noradrenaline, but not histamine, and exercise time ($r=0.769$) ($p<0.001$) and rise in double product ($r=0.064$) ($p<0.02$). Though there were pronounced individual rises in adrenaline no overall significant change was noted.

Histamine is released in patients with coronary artery disease under various physiological stresses; its role in the development of angina requires further investigation.

Right ventricular diastolic collapse: an echocardiographic sign of tamponade

G J Williams, J B Partridge

Non Invasive Cardiac Investigation Unit, Killingbeck Hospital, Leeds

Sixty seven real time and M-mode echocardiographic studies were obtained in 52 patients with pericardial effusions, seven of the patients having cardiac tamponade. The real time studies were analysed frame by frame using a video disc system permitting accurate correlation with the electrocardiogram. The M-mode recordings were examined for previously reported signs of effusion and tamponade such as reduced mitral opening slopes and reduced left ventricular posterior wall movements. M-mode traces had no correlation with the presence of tamponade. Similarly, the generally accepted "swinging" heart and reversal of septal movement on real time studies of effusion did not correlate with the presence of tamponade. Abnormal right ventricular diastolic collapse, however, was noted on real time studies in those patients with tamponade, and the same movement, to a lesser extent, was seen in some other large effusions. The abnormality of right ventricular movement resolved with the resolution or removal of the effusion, and its timing was independent of respiration.

Our explanation of the movement is that during diastole the intrapericardial pressure is greater than right ventricular pressure and prevents filling, until such time as left ventricular systole occurs. This reduces cardiac size within the tense pericardium and thereby permits brief and reduced filling of the right ventricle before right ventricular systole starts. Inspiration exaggerates the effect, resulting in minimal right ventricular ejection and hence subsequently reduced left ventricular stroke volume (paradoxical arterial pulsation). The timing of diastolic right ventricular collapse was not reliably detected on M-mode.

Cross-sectional echocardiographic assessment of interrupted aortic arch

J F Smallhorn, R H Anderson, F J Macartney

The Hospital for Sick Children, Great Ormond Street, London

Interrupted aortic arch is exceptionally difficult to diagnose in infancy without catheterisation. Cross-sectional echocardiography was performed in 10 patients aged 1 day to 7 months. In all, the interruption was between the left carotid and subclavian arteries. The arterial connection was concordant in six, double outlet right ventricle in two, and truncus in two.

The ascending aorta was small in each and terminated in the left carotid artery. The ductus arteriosus continued into the descending aorta with no vestige of upper descending aorta in eight. In two, both blind ends of the aorta could be visualised simultaneously, separated by the interruption. The left subclavian artery was seen distal to the ductus in all but one case. In one patient the right subclavian artery also arose below the interruption. The position of the associated ventricular septal defect was predicted in all, as was the presence of subaortic stenosis resulting from posterior infundibular septal displacement. Cross-sectional echocardiography provides an accurate diagnosis and permits early treatment with prostaglandins to prevent ductal closure.

Functional and anatomical correlates in interatrial shunts: an echocardiographic analysis

J C Forfar, M J Godman

Department of Cardiology, The Royal Infirmary, and Royal Hospital for Sick Children, Edinburgh

Intracardiac contrast echocardiography and balloon sizing techniques have examined the relation between defect size and patterns of interatrial shunting in 30 consecutive patients (1 to 14 years) evaluated for a possible secundum or sinus venosus atrial septal defect. Echocardiography before catheterisation positively identified an atrial septal defect in 17/19 patients with a left-to-right shunt but was not diagnostic in one sinus venosus defect and one fenestrated septal aneurysm. Echocardiography showed an intact septum in 10/11 patients with a probe-patent foramen ovale. Contrast studies showed variable left-to-right shunting in all patients with atrial septal defect. A right-to-left shunt and negative contrast echoes were observed in 10/19 patients and 7/19 patients with atrial septal, respectively, but in no patients with patent foramen ovale. Echocardiographic estimation of defect diameter correlated quantitatively with direct balloon measurement, though the latter proved unreliable in fenestrated and sinus venosus defects. In contrast, however, no correlation was observed between defect diameter and the extent of interatrial shunting

assessed by oximetry or contrast echocardiography. Two dimensional echocardiography is a sensitive and specific technique for the identification of atrial septal defects. The disparate relation between the diameter of the defect and pulmonary blood flow suggests that the latter may not be the most important determinant for surgical management.

Diagnosis of complete transposition of great arteries by 2D echocardiography

J V De Giovanni, M F Shiu, E D Silove
The Children's Hospital, Birmingham

The key to the 2D echocardiographic diagnosis of complete transposition of the great arteries is the identification of the aorta arising from the right ventricle and of the pulmonary artery from the left ventricle. These features can be reliably demonstrated from the subcostal approach. We used two principal subcostal planes, approximately at right angles to one another. The first displays the left (posterior) ventricle giving rise to the posterior, bifurcating pulmonary artery. The second shows the parallel course of the great arteries in their anteroposterior plane (a "double sausage" appearance) and the aorta originating anteriorly from the anterior right ventricle and ascending to its arch.

Of 563 infants examined consecutively by 2D echocardiography, the criteria for the diagnosis of transposition of the great arteries were met in 36. There were no false negative or false positive diagnoses. The application of the two subcostal planes and strict criteria ensured that transposition of the great arteries was correctly differentiated from other complex malformations such as congenitally corrected transposition, persistent truncus arteriosus, and various types of univentricular heart. Other relevant information concerning the atria, ventricles, their connections, and septa was obtained from conventional echocardiographic windows.

The diagnostic accuracy simplifies cardiac catheterisation, performed primarily to create an atrial communication.

Late haemodynamic evaluation of Mustard operation for transposition of great arteries

H S Joffe, J D Wisheart, S C Jordan
Bristol Royal Hospital for Sick Children and Bristol Royal Infirmary

Detailed haemodynamic studies were performed in 19 asymptomatic patients 34.2 ± 3.9 months (mean \pm SEM) after successful repair of transposition of the great arteries by a uniform Mustard technique to

establish (i) frequency and degree of obstruction in venous pathways, (ii) correlation of pressure gradients with calibre of these pathways, and (iii) influence of azygos vein run-off.

Investigations were performed under general anaesthesia using standard techniques. Withdrawal pressures from the superior vena cava to systemic venous atrium and inferior vena cava were obtained in 19, and simultaneous pulmonary venous atrial and pulmonary arterial wedge pressures in 18 patients. Angiography in the superior, inferior vena cavae, and pulmonary artery permitted direct measurement of the diameter of pathways and the extent of azygos vein flow.

Mean pressure gradient (mmHg) was mild (0-3), moderate (4-6), and severe (>6) in 11, five, and three patients, respectively, across the superior vena cava pathway; in 17, two, and no patients across the inferior vena cava pathway; and in 16, two, and no patients across the pulmonary venous pathway. There was significant negative correlation between pressure gradient and diameter of the superior vena cava pathway ($y = 12.77 - 0.90x$; $r = 0.68$, $p < 0.01$) and inferior vena cava pathway ($y = 3.33 - 0.14x$; $r = 0.51$, $p < 0.05$), but not pulmonary venous pathway ($y = 1.16 + 0.03x$; $r = 0.12$, $p > 0.05$). Maximal azygos flow was associated with most severe stenosis in the superior vena cava pathway.

Severe superior vena cava obstruction occurred in 16% of clinically well patients, and azygos vein run-off did not relieve superior vena cava hypertension.

Natural history of ventricular septal defects—long term prospective two dimensional echocardiographic study

G R Sutherland, H H Bain, R H Anderson, S Hunter
Regional Cardiographic Centre, Freeman Hospital, Newcastle upon Tyne

Since two dimensional echocardiography can reliably identify and classify ventricular septal defects in children, it seemed logical to study prospectively a group of infants with isolated ventricular septal defects to determine which defects tend to close and by which pathological mechanism this is achieved. One hundred and seventeen infants, all with haemodynamically significant defects (42 perimembranous inlet, 31 perimembranous outlet, 18 single trabecular, 15 muscular inlet, six muscular outlet, and five subarterial defects) were serially studied over a mean period of 19 months using two dimensional echocardiography.

During the study period, 13 defects closed and a further 31 defects clearly showed evidence of partial closure. Differing closure mechanisms were clearly

established which appeared to be specific for each type of defect. Perimembranous inlet defects tended to close from their posterior aspect by incorporating tricuspid septal leaflet tissue, thus forming a posterior "pseudo-aneurysm of the membranous septum". Perimembranous outlet defects closed by true membranous septal aneurysm formation. Single trabecular defects closed spontaneously from their right ventricular aspect. Muscular inlet defects closed by incorporating tricuspid chordae into the defect. Neither muscular outlet nor subarterial defects showed any evidence of closure.

We conclude that serial two dimensional echocardiographic studies have clearly established which ventricular septal defects will tend to close and the specific pathological mechanisms by which this is effected.

Short term use of prostaglandin E₁ (Prostin VR) in early management of critically ill newborn infant with duct dependent congenital heart disease

Katherine Hallidie-Smith
Royal Postgraduate Medical School, Hammersmith Hospital, London

A three year experience with the use of prostaglandin E₁ has resulted in the establishment of a safe and effective regimen which can be instituted before transfer to a paediatric cardiac centre.

Forty-one infants aged 6 hours to 5 days have been given prostaglandin E₁ dissolved in 5% dextrose by continuous peripheral venous infusion at a dose ranging from 0.05 µg/kg per min (first 23 patients) to 0.02 µg/kg per min (current patients), with beneficial effects in all babies and no serious side effects. Prostaglandin E₁ was started within two hours of admission (35 patients) and before transfer (six patients). It was continued until catheter diagnosis, atrial septostomy, or emergency surgery (6 hours to 5 days). Three broad groups were treated: (1) 17 hypoxic infants with poor pulmonary blood flow, (2) eight hypoxic infants with poor mixing (transposition of the great arteries), and (3) 16 infants with left heart obstructive lesions. Clinical variables, blood pressure, and arterial blood gases were monitored. A beneficial response was noted in less than 30 minutes (groups 1 and 2) and in less than 1.5 hours (group 3). Arterial PO₂ rose by 2.1 to 5.9 kPa (oxygen saturation 20 to 60%) in groups 1 and 2 and arterial pH was improved or corrected in all groups. In group 3, cardiac output (assessed clinically) and urinary output improved dramatically. There were no major side effects. It is concluded that pre-catheter prostaglandin E₁ treatment for infants suspected of having duct dependent congenital heart disease can be both safe and effective.

Changes in glucose oxidation by autotransplanted baboon heart

A J Drake-Holland, T English, R Medd, M I M Noble, J Wallwork
Department of Medicine I, St George's Hospital Medical School, London; Huntingdon Research Centre, Cambridgeshire; Midhurst Medical Research Institute, Midhurst, Sussex; Heart Transplant Research Unit, Papworth Hospital, Cambridge

Chronic denervation of the heart leads to depletion of tissue catecholamines, giving rise to metabolic abnormalities including a reduction in cardiac glucose oxidation. With denervation after cardiac autotransplantation there is a possibility of abnormal metabolism of glucose or lipids. Patients as a result of allotransplantation can develop accelerated coronary artery disease and are unable to convert glucose to lactate during ischaemic pacing tests. Impaired oxidation of glucose implies an increased oxidation of fat, which could lead to development of coronary artery disease in the transplanted heart. Cardiac glucose oxidation (using ¹⁴C-labelled D-glucose) was studied in six female baboons, before and three to five weeks after autotransplantation. A technique was developed to sample, simultaneously, systemic arterial and coronary sinus samples percutaneously after the radioactive infusion. Samples were analysed for total CO₂, O₂ content, ¹⁴CO₂, glucose, lactate, pH, PCO₂, and O₂. In every case there was a distinct decrease in the oxidation of glucose after autotransplantation (p<0.05). This indicated that the removal of the sympathetic and parasympathetic nerve supply to the heart affects the ratios of the glucose oxidised to other substrates, for example non-esterified free fatty acids.

Role for ¹²⁵I-antimyosin (FAB')₂ in early detection of myocardial necrosis

Adam D Timmis, J Antonio Lopez, John T Fallon, Ban An Khaw, Edgar Haber, Wm John Powell Jr
Massachusetts General Hospital, Boston, USA

Low flow myocardial ischaemia in the distribution of the left anterior descending coronary artery was established in 19 anaesthetised dogs. The time course of irreversible myocardial injury was determined using ¹²⁵I-antimyosin (Fab')₂—a specific immunological marker of myocardial necrosis. In order to prevent recirculation of the (Fab')₂, thereby limiting the time of exposure to the myocardium, the fragments were injected directly into the coronary circulation during diversion of the coronary sinus effluent. The simultaneous injection of ¹³¹I-nonspecific (Fab')₂ controlled for variables unrelated to specific antimyosin activ-

ity and enabled calculation, by gamma scintillation counting, of the relative uptake of ^{125}I -antimyosin (Fab')₂ in the ischaemic area. The antibody fragments were given either two, three, or five hours after the onset of low flow in different groups of dogs, and animals were sacrificed shortly thereafter. Selective accumulation of ^{125}I -antimyosin (Fab')₂ in the ischaemic area occurred at between two and three hours (relative uptake 0.9 ± 0.1 at two hours, rising to 1.65 ± 0.15 at three hours, $p < 0.05$), indicating that necrosis was already established at this time. Macroautoradiographs of microscopical sections of the ischaemic myocardium independently confirmed selective accumulation of ^{125}I -antimyosin (Fab')₂, and hence necrosis, at three hours after the onset of low flow. In this study the use of ^{125}I -antimyosin (Fab')₂, rather than histology, as a marker of necrosis avoided error resulting from sampling and also permitted the detection of cell death early during the ischaemic process. The demonstration, within a narrow time frame of early necrosis in this low flow preparation, provides a potential model with which to evaluate agents for myocardial preservation in obstructive coronary disease.

Natriuretic activity of extracts of human and baboon atrium

A A MacPhee, N C Trippodo, F E Cole
Alton Ochsner Medical Foundation, New Orleans,
La, USA

We assayed natriuretic activity of extracts from human and baboon atria to determine if primate heart contained a substance similar to that found in rat atria. Small fragments of the right atrial appendage were obtained from 36 patients undergoing surgery for coronary artery disease. Atrial and ventricular tissues were obtained from 3 adult male baboons. The tissues were extracted twice with 10 vol. 1N acetic acid followed by centrifugation at 12 000 g for 10 minutes. The combined supernatants were lyophilised, resuspended in 0.5N acetic acid, and fractionated on a column of Sephadex G-75. Fractions eluting with molecular weights between 5000 and 40 000 daltons were pooled and lyophilised. Natriuretic activity was assayed by measuring changes in urinary sodium excretion after intravenous injection of the chromatographed extracts into anaesthetised rats. Injection of 5.3, 2.6, and 1.9 mg protein of atrial extract increased urinary sodium excretion 5909, 973, and 366%, respectively, and urine output 2328, 683, and 151%, respectively. Natriuretic activity of human atrial extract was unaffected by heating on a boiling water bath for 10 minutes or incubation with plasma at 37°C but was destroyed by treatment with trypsin.

No natriuretic activity was found in fractions eluting with molecular weights $< 5\ 000$ or $> 40\ 000$ daltons. While extracts of baboon atria give results similar to those of human, baboon ventricle was devoid of natriuretic activity.

The data suggest that primate atrial tissue contains an endogenous natriuretic substance similar in nature to that found previously in rat atrial tissue.

Ethanol reduces calcium content of aortic tissue in vitro: its relevance to atherosclerosis

I J Lloyd, R Weston, T P L Thomas
Department of Pharmacology, Welsh National School
of Medicine, Cardiff

There is now a large body of evidence suggesting that ethanol confers a degree of protection against atherosclerosis, stroke, and myocardial infarction, and that this effect may only be seen in low to moderate alcohol consumption. There is currently no explanation for this effect.

An early change in atherosclerosis is an increase in calcium content of the vasculature, an increase in the "primary calcification". A reduction in calcium content is thought to result in a reduced incidence and severity of atherosclerosis.

Pig aortic tissue was incubated in physiological solutions at 37°C for three hours in the absence of alcohol and also in the presence of varying amounts. After incubation the tissue was dried, digested, and the calcium content measured.

In the presence of low concentrations of alcohol (4 mg%) there was a reduction in calcium content of 7.4% ($p < 0.05$). At higher concentrations the effect was not maintained.

These data firstly further strengthen the link between alcohol and decreased atherogenesis, secondly show a direct effect on arteries, and thirdly offer support for the suggestion that it is only low doses that are effective.

Dependence of reperfusion ventricular fibrillation on action potential shortening

W J Penny, D J Sheridan
Department of Cardiology, Welsh National School of
Medicine, Heath Park, Cardiff

To assess the arrhythmogenic potential of cellular electrophysiological changes associated with myocardial reperfusion we used isolated guinea pig hearts to record action potentials and electrocardiograms during periods of reperfusion in which the incidence of ventricular fibrillation was modified by altering the

duration and severity of preceding ischaemia, or by antiarrhythmic doses of phentolamine (5×10^{-6} M). Ischaemia was induced for periods of five to 60 minutes by reducing coronary flow to 10% of control (LFI) or to zero (ZFI). In a separate group, hearts were reperfused in the presence of phentolamine after 30 minutes of LFI. In untreated hearts ventricular tachycardia and ventricular fibrillation occurred after 10 minutes of ZFI (40% and 20%, $n=5$) or 15 minutes of LFI (40% and 40%, $n=5$), but not with shorter periods. Ventricular tachycardia and fibrillation were most frequent after 20 to 30 minutes of ischaemia and were similar after LFI (94% and 88%, $n=21$) and ZFI (95% and 95%, $n=25$), but were less after 60 minutes of LFI (40% and 0%, $n=5$) and ZFI (40% and 0%, $n=5$). Phentolamine also reduced the incidence of ventricular tachycardia and ventricular fibrillation (14% and 29% compared with 94% and 88%).

Reperfusion induced electrophysiological recovery in all hearts; the occurrence of ventricular fibrillation, however, was associated with further reperfusion-induced shortening of action potential duration from 98 ± 7 ms to 86 ± 6 ms ($p < 0.05$), in contrast to hearts free from ventricular fibrillation in which lengthening was observed from 137 ± 8 ms to 143 ± 6 ms and from 86 ± 12 ms to 100 ± 10 ms after five and 60 minutes of ischaemia, respectively, and from 99 ± 5.9 ms to 120 ± 6.5 ms in the presence of phentolamine. Thus, reperfusion-induced shortening of action potential duration preceded ventricular fibrillation, but was not observed after short or long periods of ischaemia, or in the presence of phentolamine when ventricular fibrillation was significantly reduced.

Effects of selective and non-selective beta blockade on reperfusion-induced ventricular fibrillation

A S Manning, K Isted, R Crome, D J Hearse, D J Coltart
The Rayne Institute, St Thomas's Hospital, London

We have assessed the relative protection against reperfusion-induced ventricular fibrillation afforded by two non-selective beta blocking agents (oxprenolol and timolol) and two cardioselective agents (metoprolol and acebutolol) and have related this to levels of cyclic AMP, cyclic GMP, and high energy phosphates within the previously ischaemic tissue. Isolated, left atrially perfused, "working" rat hearts were perfused with equipotent concentrations of beta blockers (oxprenolol 300 ng/ml; timolol 50 ng/ml; metoprolol 300 ng/ml; acebutolol 2000 ng/ml) in the presence of 5×10^{-6} M adrenaline, acting as exogenous sympathetic support. Cardiac function was assessed before and during a 15 minute period of coronary artery ligation.

The occlusion around the artery was then released, thereby reperfusing the ischaemic zone. After two minutes of reperfusion hearts were frozen rapidly for later assay of metabolites. Incidence of reperfusion ventricular fibrillation in the control group was 97% (33/34 hearts). Neither non-selective beta blocker altered this incidence (93% in the timolol-treated group, 12/13; 92% in the oxprenolol-treated group, 11/12). Both cardioselective beta blockers, however, reduced this incidence: 41% in the metoprolol-treated group (9/22); 50% in the acebutolol-treated group (6/12). Thus cardioselective beta blockade partially reduces the incidence of reperfusion ventricular fibrillation while non-selective blockade is ineffective. Neither changes in cardiac function during the ischaemic period nor cellular levels of cyclic AMP, cyclic GMP, or high-energy phosphates within the previously ischaemic zone, however, could be correlated with the incidence of fibrillation.

Myocardial clearance of digoxin

B E Griffiths, D Buss, G J Grotte, M J Lewis, A H Henderson
Departments of Cardiology and Pharmacology, Welsh National School of Medicine, Heath Park, Cardiff

The plasma pharmacokinetics of digoxin in man are well described but no information is available on its myocardial kinetics. We have studied the decline in serum and myocardial levels of digoxin in 45 patients undergoing open heart surgery after withdrawal of digoxin therapy up to 20 days before operation. All patients had been taking digoxin for at least six months. Serum digoxin was measured while on treatment (six hours after the last tablet) and again at the time of operation (immediately before cardiopulmonary bypass). At operation papillary muscle and/or right atrial appendage were removed and assayed for digoxin levels. All digoxin assays were performed using a commercially available radioimmunoassay kit. The decline in serum digoxin levels was exponential with a half life of 48 hours. In contrast, the decline in both ventricular and atrial digoxin levels was bi-exponential with a fast (alpha phase) elimination up to day 3, followed by a slow (beta phase) elimination. The alpha phase half lives were seven and 12 hours and the beta phase half lives three-and-a-half and four-and-a-half days for papillary muscle and right atrial appendage, respectively, with no significant difference between the clearance from the two types of myocardium. Measurable levels of digoxin were still present in both tissues 20 days after stopping treatment. These data have obvious and important clinical implications.

Relation between myocardial amiodarone concentration and QT interval

N M G Debbas, R S Bexton, C du Cailar, P Puech, A J Camm

The Cardiac Department, St Bartholomew's Hospital, London; and Service de Cardiologie, Hôpital Saint Eloi, Montpellier, France

This study was performed to assess the correlation between plasma level of amiodarone, myocardial concentration, and QTc lengthening which has been reported to correlate with antiarrhythmic action. Nine patients, seven with angina and two with paroxysmal ventricular tachycardia, were treated with oral amiodarone (200 to 400 mg daily) for at least three months before undergoing cardiac surgery. QTc intervals were measured from lead II of surface electrocardiograms recorded before amiodarone and immediately before surgery. Patients with prominent U waves after amiodarone were excluded. Both plasma levels and myocardial biopsy concentrations were estimated by the HPLC technique from samples taken at the beginning of the surgical procedure.

There was significant lengthening of QTc after the administration of amiodarone (454 ± 34 ms to 533 ± 61 ms, $p < 0.01$). There was a good correlation between the plasma levels and the myocardial biopsy concentrations ($r^2 = 0.85$, $p < 0.001$) and both correlated well with the percentage increase in QTc (plasma: $r^2 = 0.84$, $p < 0.001$; myocardium: $r^2 = 0.93$, $p < 0.001$). Though there was a good correlation between dosage administered (mg/kg per day) and both plasma level ($r^2 = 0.88$, $p < 0.001$) and myocardial concentration ($r^2 = 0.86$, $p < 0.001$), the correlation with the percentage increase in QTc was weaker but still highly significant ($r^2 = 0.77$, $p < 0.005$).

It can be concluded that the plasma level of amiodarone appears to correlate well with myocardial concentration and that the myocardial concentration of amiodarone can be estimated clinically from lengthening of QTc.

Amiodarone tissue distribution: relation to adverse effects

P C Adams, M R Nicholson G C A Storey, D W Holt, R W F Campbell

Academic Department of Cardiology, Freeman Hospital, Newcastle upon Tyne, and Poisons Unit, Guy's Hospital, London

Tissue is difficult to obtain for the study of drug distribution in man. Yet this is an important determinant of drug efficacy, toxicity, and pharmacokinetics. We

studied the differential tissue distribution of amiodarone and its major metabolite, desethylamiodarone, in seven subjects, using enzymatic digestion of 37 biopsy, necropsy, and surgical specimens, followed by high performance liquid chromatography. Concentrations (mg/kg wet weight of amiodarone and desethylamiodarone, respectively) were *high* in liver (610,4010), lung (180,794), and spleen (114,385), and *low* in heart (28,92), skeletal muscle (12,28), thyroid (14,66), and brain (6,46). In fat, the concentration of amiodarone was high (260 mg/kg) but that of desethylamiodarone low (72 mg/kg), the mean ratio being 3.6:1 compared with 0.18:1 for other tissues. Plasma concentrations (amiodarone 2 mg/l, desethylamiodarone 2 mg/l) were much lower than tissue concentrations. In two patients, skin from areas of amiodarone-induced pigmentation contained high concentrations of drug and metabolite (119,539), but concentrations were much lower (17,72) in unaffected skin from these patients. Abnormal skin contained excess pigment, localised in dermal macrophages.

Extensive tissue binding explains the long terminal half life of amiodarone. Adverse effects in lung, liver, and skin, where metabolite concentration is highest, may result from local accumulation.

Comparison of effects of sotalol, disopyramide, and metoprolol on potential re-entry circuits in experimental canine ventricular tachycardia

S M Cobbe, J Senges, E Hoffman, A Ritzenhoff, W Kübler

Cardiology Department, University of Heidelberg, W Germany

It has recently been suggested that the beta adrenergic blocker sotalol has clinically significant antiarrhythmic properties by virtue of its class III (action potential prolongation) effect. We have compared the effects of sotalol, disopyramide, and metoprolol on the refractoriness of normal myocardium and potential re-entry circuits in ischaemic myocardium in 17 conscious dogs three to eight days after experimental myocardial infarction. Epicardial recordings from the infarct zone were made by a large implanted "composite" electrode. Myocardial refractoriness was determined and ventricular tachycardia provoked by programmed ventricular stimulation. Electrophysiological studies were carried out before and after intravenous sotalol 4.5 mg/kg ($n = 19$), disopyramide 2 mg/kg bolus, 2 mg/kg per h infusion ($n = 8$), or metoprolol 0.45 mg/kg ($n = 14$).

Sotalol prevented or significantly slowed ventricular tachycardia in 11/19 experiments (58%), dis-

opyramide in 6/8 (75%), and metoprolol in only 1/14 (7%). Ventricular effective refractory period was increased $14.1 \pm 1.3\%$ (mean \pm SEM) by sotalol, $11.5 \pm 4.4\%$ by disopyramide, and $5.4 \pm 1.4\%$ by metoprolol. Sotalol and disopyramide increased infarct zone refractoriness by $41.0 \pm 12.5\%$ and $37.5 \pm 7.5\%$, respectively, both values significantly greater than the effect on normal myocardium, while metoprolol had no effect.

Despite different basic electrophysiological properties, sotalol and disopyramide both selectively increase refractoriness in potential re-entrant circuits in ischaemic myocardium. The action of sotalol appears to be related to its class III properties rather than beta blockade.

Changes in "in vitro" serum protein binding of disopyramide and flecainide after acute myocardial infarction

J L Caplin, A Johnston, A J Camm
St Bartholomew's Hospital, London

Alpha-1 acid glycoprotein is one of a number of acute phase reactant proteins in serum which tend to rise after acute myocardial infarction. This protein is a major determinant of the serum binding of basic antiarrhythmic drugs. Therefore the "in vitro" binding of disopyramide and flecainide, and the alpha-1 acid glycoprotein levels were measured in patients after acute myocardial infarction. Eleven patients (10 male) were studied, average age 56.7 years. Blood samples were obtained for five consecutive days after admission. On the first day alpha-1 acid glycoprotein levels were raised compared with normals (laboratory controls), 1.03 ± 0.37 g/l versus 0.87 ± 0.32 g/l (mean \pm SD), $p < 0.01$. They continued to rise significantly each day, being 1.75 ± 0.42 g/l on the fifth day ($p < 0.001$). Similarly, protein binding of disopyramide was raised on the first day, $80 \pm 7\%$ versus $68 \pm 8\%$, $p < 0.001$, and remained high during the study. Though protein binding of flecainide was up on the first day, $61 \pm 10\%$ versus $48 \pm 4\%$, $p < 0.01$, it did not remain significantly high. Serum albumin and total proteins were within normal ranges. We conclude that there is a significant rise in alpha-1 acid glycoprotein after acute myocardial infarction and that protein binding of disopyramide (more so than flecainide) is increased after acute myocardial infarction. The effectiveness of antiarrhythmic agents may be altered by changes in protein binding after acute myocardial infarction.

Role of computerised tomography in diseases of heart and thoracic aorta

D L Stone, A K Dixon, G I Verney, M C Petch
Departments of Cardiology and Radiology, Papworth and Addenbrooke's Hospitals

Computerised tomography is a new imaging technique with potential application to the diagnosis of cardiovascular disease. We have studied 49 patients (32 men, 17 women, age range 18 to 76, mean 53.6 years) with a Somatom 2 scanner capable of rapid sequence scans. Images were enhanced with intravenous contrast medium and the results were compared with echocardiography and contrast angiography.

Twenty-two patients has suspected disease of the thoracic aorta, 10 had dissection, five were normal, and seven had other pathology (for example, pheochromocytoma). Eleven patients had pericardial disease: four had effusions, four had malignant infiltration, two had a thickened pericardium, and one appeared normal. Ten patients had myocardial disease; the free wall and septum were seen in all cases, the septum being much thickened in those with hypertrophic cardiomyopathy. Six patients had coronary artery bypass surgery; assessment of graft patency was unreliable.

Computerised tomography is of doubtful benefit in assessing coronary vein graft patency, offers little advantage over accepted techniques in the study of myocardial disease, but is of considerable value in the diagnosis of pericardial and aortic abnormalities, especially suspected aortic dissection.

Evaluation of computerised tomography in the diagnosis of left ventricular aneurysms

C J Foster, T Sekiya, I Isherwood
Manchester Royal Infirmary, Department of
Diagnostic Radiology, University of Manchester

In order to evaluate the accuracy of computerised tomography in diagnosing left ventricular aneurysms, 19 patients with clinical evidence of poor left ventricular function, some of whom were suspected of having an aneurysm, were studied. At angiography 15 patients had aneurysms (14 anterior, one posterior) and four diffusely hypokinetic ventricles. Five patients with angiographically normal left ventricular function were also studied.

A series of computerised tomographic scans of the ventricle from base to apex during intravenous contrast infusion were performed. The scans were studied for a change from the predictable contour of the left ventricle and the equivalent of an LAO short

axis measurement was made. The patients with normal ventricles and those with dilated ventricles had a smooth predictable contour to the left ventricle. All 15 patients with aneurysms showed a localised change from the predicted contour of the ventricle. The computerised tomographic short axis measurements were normal in patients with normal ventricles (4.2 to 5.1 cm), increased in those with dilated ventricles (6.5 to 7.5 cm), and varied widely between the patients with aneurysms (4.4 to 7.2 cm).

From this small series computerised tomography shows a 100% specificity and sensitivity in the diagnosis of left ventricular aneurysm.

Using bipolar pacing wire in pulmonary artery to monitor oxygen tension and cardiac output

P J Bourdillon, Jennifer Becket, R Walesby, S Edmundson, P Stinton, P Duffin
Royal Postgraduate Medical School, London

Mixed venous oxygen tension and cardiac output are two of the more useful variables for monitoring patients after cardiac surgery. We have developed a technique which enables both variables to be monitored without the need to withdraw blood.

A standard bipolar pacing wire placed in the pulmonary artery is used to obtain the signals. To record cardiac output a 9 kHz sine wave is passed between the electrodes and the change in impedance recorded as a bolus of hypertrophic saline passes the electrodes. To record oxygen tension, pulsed polarography at a frequency of 0.1 Hz has been used.

One-hundred-and-ten output measurements have been compared with green dye measurements in 21 patients after cardiac surgery, and 126 oxygen tension measurements have been compared with those of an automatic blood gas analyser in 12 of these patients. Multiple regression analysis explained 81% of the variance of the cardiac output measurements made in any one individual, and 75% of the variance of the oxygen tension measurements.

It is concluded that for monitoring changes occurring in the individual patient, this economical approach is practical.

Clinical evaluation of ambulatory pulmonary artery pressure monitoring

A W Nathan, S G Perry, T Cochrane, R S Bexton, K J Hellestrand, S O Banim, R A J Spurrell, A J Camm
St Bartholomew's Hospital, London

Traditional measurement and recording methods are

inadequate for continuous monitoring of ambulatory pulmonary artery pressure. Therefore a new miniaturised solid state system has been developed and assessed in 17 patients. A manometer tipped catheter, inserted via a subclavian or cephalic vein, is used together with an isolated amplifier and peak detectors to determine systolic and diastolic pressures. Pressures are averaged over 30 seconds and stored in digital memory. After a 24 hour recording period data are rapidly transferred to a microcomputer for numerical or graphical display.

Seventeen patients had continuous ambulatory monitoring performed for between 24 and 96 hours, in seven to evaluate symptoms of dyspnoea in subjects with valvular or coronary disease (group 1), and in 10 to optimise oral treatment for left heart failure (group 2). The catheter was calibrated before insertion and was rechecked after removal. Five patients had both rest and ambulatory studies performed, and during the resting period luminal pressures were recorded for comparison. Satisfactory recordings were obtained in 13/17 patients, with less than 1% zero level drift and similar gain stability. Systolic pressures ranged from 10 to 97 (mean 40) mmHg, and diastolic from 1 to 46 (mean 15) mmHg, with good correlation between luminal and digital recordings. Four patients in group 1 had symptoms of dyspnoea associated with normal pressures, while three had raised pressures. Four of the six patients successfully monitored in group 2 had major alterations in their treatment based on data obtained during monitoring. There were no complications.

This system, which allows safe, reliable, and prolonged recording of ambulatory pulmonary artery pressure, improves the clinical assessment and management of left heart failure.

Coronary angioplasty for multiple disease

Edgar Sowton
Guy's Hospital, London

Twelve patients with multiple stenoses were treated by angioplasty as a single procedure. Four patients had triple vessel disease, five had double vessel disease, and the remainder had multiple discrete stenoses in one artery. In four patients dilatation of a proximal stenosis allowed sufficient contrast medium to flow and show a previously unknown distal stenosis. Two of the patients had twice undergone saphenous vein bypass grafting with recurrence of angina.

Fifteen left anterior descending lesions, 12 right coronary artery, three circumflex, and two saphenous grafts were all dilated. A double balloon catheter was

needed to cross two of the tight stenoses and the others were crossed with a 3.7 mm Dilaca. Each lesion was dilated for an average of 6.2 times and the maximum number of dilatations in a single patient was 27.

No patient was referred for immediate surgery and no infarctions occurred in relation to the procedure. Severe spasm was present in two cases requiring intracoronary isosorbide of up to 200 mg.

One patient had an exacerbation of angina with no change in his electrocardiogram, one patient with three stenoses in the left anterior descending redeveloped pain after two months and was again dilated, and one of the patients with previous cardiac surgery developed a tight new lesion which was also dilated. The remaining patients were symptom free after a mean follow-up time of four-and-a-half months by August 1982 (range one to 12 months).

Changes in haemodynamics and coronary flow during transluminal angioplasty of left main coronary artery

Ivo Amende, Rüdiger Simon, Paul R Lichtlen
Medical School Hannover, Hannover, West Germany

Successful transluminal coronary angioplasty was carried out in two patients with a significant isolated left main coronary artery stenosis. Both patients had normal left ventricular function and volumes at rest. Coronary angiography revealed absence of collateral circulation. A 3.7 mm balloon was repeatedly inflated within the left main coronary artery. The duration of the occlusion time was between 20 to 35 seconds. Simultaneous measurements of left ventricular haemodynamics and great cardiac vein flow using the thermodilution technique were performed continuously before, during, and after each balloon inflation. After inflation, great cardiac vein flow dropped immediately, fell to 34% of the control flow after 15 seconds, and remained constantly reduced until balloon deflation. Left ventricular and aortic pressures did not alter initially. After 15 seconds peak systolic pressure decreased slowly and was lowered by 25% at 30 seconds, whereas left ventricular filling pressure increased steadily to 150% of the control value. These changes were associated with ST segment elevation and ventricular extrasystoles in the electrocardiogram. After balloon deflation, electrocardiographic alterations disappeared and left ventricular haemodynamics returned to control, whereas great cardiac vein flow increased by 63% because of reactive hyperaemia.

In conclusion, regional coronary flow did not fall to zero during transient occlusion of the left main coronary artery though angiography did not show collater-

als before angioplasty. The remaining coronary flow, however, did not protect the postocclusion myocardium from ischaemia since severe impairment in left ventricular function occurred.

Ventricular fibrillation and polymorphic ventricular tachycardia mapping and surgery

R W F Campbell, C J Hilton, P C Adams,
M R Nicholson, C J Griffiths, D G Julian
Department of Cardiology, Freeman Hospital,
Newcastle upon Tyne

Cardiac surgical techniques for managing monomorphic ventricular tachycardia are well established but ventricular fibrillation and polymorphic ventricular tachycardia are less amenable to investigation, mapping, and surgical control. Three patients with such arrhythmias have been investigated. Case 1, a woman aged 31, had intractable polymorphic ventricular tachycardia (180 to 250/min). The arrhythmia could not be initiated at electrical study or intraoperatively but mapping to detect fragmented electrograms identified an abnormal left ventricular septal area which was resected. Case 2, a woman aged 33 with a structurally normal heart, had her polymorphic ventricular tachycardia and ventricular fibrillation induced at electrical study but not intraoperatively. The "fragmentation map" was abnormal throughout the left ventricle. A total left ventricular endocardial resection was performed. Case 3, a man aged 60, with polymorphic ventricular tachycardia (140 to 200/min) after infarction, was mapped during the arrhythmia at electrical study and intraoperatively. Sites of origin on both sides of the septum were identified and resected. All operations were successful, and postoperatively no arrhythmias could be initiated by programmed stimulation. Follow-up for the three patients was 28, five, and five months, respectively. We conclude that medically intractable ventricular fibrillation and polymorphic ventricular tachycardia can be managed surgically, that "fragmentation maps" are useful in directing surgery, and that endocardial resection for these arrhythmias may need to be extensive and involve the whole ventricle or both ventricles.

Ventricular arrhythmias in normal heart

P Holt, P V L Curry, D B O'Keeffe, R J Wainwright
Department of Cardiology, Guy's Hospital, London

Ventricular tachycardia in patients with ischaemic and non-ischaemic heart diseases has been investigated in many studies. We report on the features of ventricular arrhythmias occurring in the structurally

normal heart.

We studied 26 people (12 male, 14 female, aged 12 to 53 years). Twelve were asymptomatic with ventricular extrasystoles only. They were normal volunteers or people undergoing routine medical examination. The remaining 14 patients had paroxysmal ventricular tachycardia. All were normal on physical examination. Simultaneous 12 lead electrocardiograms were recorded at rest, on exercise, during breath holding, and during the Valsalva manoeuvre. M-mode, two dimensional echocardiograms, and gated cardiac scans were also performed. Cardiac catheterisation was only performed in those patients with life-threatening ventricular tachycardia. All investigations were normal.

The QRS morphology of the ventricular arrhythmias was virtually identical in all 26 cases: left bundle-branch block pattern, with a limb lead QRS vector of $+85^{\circ}$ - $+100^{\circ}$, mean amplitude 1.7 mV, and duration 0.12 to 0.14 seconds, indicating a right ventricular outflow tract site of origin. During exercise ventricular arrhythmias were suppressed in 13, increasing in frequency in the postexercise period in seven (ventricular tachycardia occurred in three). Inspiration and breath-holding reduced ventricular arrhythmia frequency in three. Valsalva manoeuvre caused ventricular tachycardia in one. Electrophysiology studies were undertaken in three patients, suggesting a re-entry mechanism in one, and confirming right ventricular outflow tract origin in all three. Two remained refractory to medical treatment, undergoing surgery for their life-threatening arrhythmias. Pace mapping localised the site of origin to the right ventricular outflow tract in both.

We have identified a group with structurally normal hearts who have arrhythmias arising from the right ventricular outflow tract. These ventricular arrhythmias are affected by exercise, and may not always be the result of a re-entry mechanism. They encompass a wide clinical spectrum, from the asymptomatic to those requiring surgical treatment for life-threatening arrhythmias.

Rapid ventricular response in WPW syndrome enhanced during exercise

J C P Crick, W Davies, P Holt, P V L Curry, E Sowton
Guy's Hospital, London

In patients with Wolff-Parkinson-White syndrome (WPW) atrial fibrillation may be conducted to the ventricles at a very high rate, inducing ventricular fibrillation. In a standard cardiac programmed stimulation study, the ventricular response to atrial fibrilla-

tion is tested only in the supine position at rest, and this may not identify the risk in the ambulant patient.

Ten patients with WPW and arrhythmias underwent cardiac programmed stimulation study including induction of atrial fibrillation at rest. A temporary bipolar atrial electrode was inserted via the subclavian vein and the patient exercised to limiting fatigue on a cycle ergometer. While exercise continued, atrial pacing was started and the rate increased until atrioventricular block occurred and atrial fibrillation was induced.

Eight patients were taking no drugs. Their maximum rate of conduction via the accessory pathway increased on exercise by 11% to 54%, mean 30%, exceeding 300/minute in three patients. In two other cases, conduction continued via the atrioventricular node after block occurred in the accessory pathway. In one patient treated with beta blocker the maximum rate increased by 9%. In the other patient, treatment with amiodarone had blocked conduction via the accessory pathway and this remained blocked on exercise.

No disorganised ventricular activity occurred. Only one patient felt faint during the procedure; all others were able to continue pedalling unaided. There were no adverse consequences of the test.

We conclude that atrial pacing on maximal exercise is a feasible procedure and identifies some patients in whom the accessory pathway conducts at a considerably higher rate than at rest.

Serological studies in congenital heart block

P J Maddison, R P Skinner, P V Taylor, O Scott, J S Scott, and E Esscher
Royal National Hospital for Rheumatic Diseases,
Bath; University of Leeds; and University Hospital,
Uppsala, Sweden

About one third of mothers delivering a baby with congenital heart block have, or will develop, a connective tissue disease, especially systemic lupus erythematosus. The heart block may be the result of transfer of maternal IgG autoantibody. This study aimed to define this autoantibody more clearly. Sera from 45 mothers of babies with heart block were tested for antibodies characteristic of systemic lupus erythematosus and other connective tissue diseases. Sera from affected children were also examined. Antibodies to Ro (SSA) were detected by immunodiffusion in 25 mothers (56%), a finding associated with systemic lupus erythematosus and, more frequently, Sjögren's syndrome. Anti-Ro was present in mothers with systemic lupus erythematosus, in one with recurrent parotitis, and in half the asymptomatic mothers.

Anti-Ro was detected in affected children up to six months but thereafter no serological abnormalities could be detected. There is therefore circumstantial evidence to associate congenital heart block with maternal transfer of anti-Ro, and patients with connective tissue disease who have this serological finding appear to be at risk of delivering an infant with congenital heart block. Anti-Ro, or a closely related antibody, may have a pathogenic role in connective tissue disease and congenital heart block.

Incidence and mechanism of left ventricular disease in mitral stenosis

L Cotter, K Dawkins, D Gibson
John Radcliffe Hospital, Oxford; and Brompton Hospital, London

In order to assess the incidence and mechanism of abnormal left ventricular systolic function (the myocardial factor) in mitral stenosis, digitised echocardiograms of the left ventricular cavity were obtained in 40 patients. Systolic function was abnormal in 28%. In nine patients peak Vcf was $<1.7 \text{ s}^{-1}$, in six patients shortening fraction was $<25\%$, and in four patients end-diastolic dimension was $>5.5 \text{ cm}$. In these patients peak lengthening rate was $1.5 \pm 0.5 \text{ s}^{-1}$ compared with $2.3 \pm 0.6 \text{ s}^{-1}$ in the other 29 patients ($p < 0.001$). Throughout the group peak Vcf correlated with peak lengthening rate ($r = 0.61$, $p < 0.001$). In 22 patients after surgery, change in peak Vcf correlated with change in peak lengthening rate ($p < 0.01$), and change in peak lengthening rate correlated inversely with change in end-diastolic dimension ($p < 0.02$).

Conclusions: (1) Abnormal left ventricular systolic function is common in mitral stenosis and is related to the disturbance of filling. (2) These abnormalities regress after surgery and are therefore not necessarily a result of irreversible left ventricular disease. (3) Left ventricular disease in mitral stenosis is not simply a result of underfilling since end-diastolic dimension falls as peak Vcf increases, the reverse of the change expected because of Starling's Law.

Results of new valve conserving operation for treatment of aneurysms or acute dissection of aortic root

A Fagan, R Pillai, R Radley-Smith, M H Yacoub
Harefield Hospital, Harefield, Middlesex

A technique for Dacron replacement of the diseased ascending aorta and sinuses of Valsalva with preserva-

tion of the patient's own aortic valve has been developed. After excision of the sinuses 1 mm above the aortic annulus, the scalloped ends of a 30 to 35 mm Dacron graft are sutured to the annulus, the coronary ostia are then anastomosed to the Dacron tube. Between December 1978 and February 1982, this technique was used in 23 patients with severe aortic regurgitation caused by large aneurysms of the ascending aorta and root in 16 and acute dissection in six. Their ages were between 9 and 65 years (mean 44). Seven had skeletal manifestations of the Marfan syndrome. Extension of one or more of the aortic cusps, using homologous dura mater, was necessary in four. Two patients (9%) operated on as an emergency, in a low output state, died early. There have been no late deaths with a follow-up of three to 38 months (mean 19). One patient required cusp extension after one year. Four patients have residual aortic diastolic murmurs resulting from mild regurgitation. There was significant decrease in heart size as assessed by radiographic and echocardiographic measurements. Repeat angiography performed in six showed "normal" appearances of the aortic root and coronary ostia. All surviving patients have evidence of a continuing good haemodynamic result.

It is concluded that conservation of the aortic valve is possible in patients with aneurysms or dissection of the ascending aorta and appears to give good early and late results.

Clinical and angiographic findings after perioperative myocardial infarction in patients undergoing coronary bypass grafting

S A Qureshi, M A Halim, C Ilsley, M H Yacoub
Harefield Hospital, Harefield, Middlesex

Between October 1969 and December 1979, 106 patients (12%) sustained perioperative myocardial infarction after coronary artery bypass grafting. Perioperative myocardial infarction was defined by (1) evolution of new Q waves, (2) poor progression of R waves across chest leads, or (3) appearance of persistent bundle-branch block. There were four (3.8%) early and five (4.8%) late deaths during a mean follow-up of 60 months (range 24 to 144 months). The five year actuarial survival was 90%. At the last follow-up 62 patients (70%) were asymptomatic, 18 (20%) were improved, and eight (10%) were unchanged, of whom two required reoperation. Graft patency was assessed in 82 patients (77%) with perioperative myocardial infarction. Seventy patients (83%) had patent grafts to the area of the infarct while

12 (17%) had occluded grafts. Ejection fraction, assessed angiographically, showed a change from 0.68 ± 0.09 preoperatively to 0.64 ± 0.16 postoperatively. In the patients with a patent graft to the infarcted territory the ejection fraction changed from 0.69 ± 0.14 preoperatively to 0.67 ± 0.16 postoperatively. In the patients with an occluded graft to the infarcted territory, the preoperative ejection fraction of 0.65 ± 0.11 decreased to 0.61 ± 0.18 postoperatively. (Figures are mean \pm SD.) It is concluded that in this series perioperative myocardial infarction was associated with slightly reduced graft patency and had little influence on left ventricular function and long term prognosis.

Early reperfusion after selective intracoronary thrombolysis using BRL 26921

W S Hillis, C R Jones, B C Campbell, W F M Fulton
Department of Materia Medica, University of Glasgow, Stobhill General Hospital, Glasgow

BRL 26921 is a complex of acylated streptokinase and plasminogen with pronounced fibrin binding capacity. Intracoronary thrombolysis was performed in 12 patients (mean age 63, range 42 to 75) admitted with chest pain of less than six hours' duration (mean three hours 20 minutes), with electrocardiographic confirmation of acute myocardial infarction.

Selective coronary arteriography, Judkins technique, was performed. The right coronary artery was the site of occlusion in seven, the left anterior descending in six. BRL 26921, 15 mg, was injected intracoronary over 45 minutes. Serial coronary artery injections were performed.

Early coronary artery reperfusion was obtained in six right and four left anterior descending coronary arteries. This was associated with a reduction in the sum of ST segment elevation, mean 43.3 mm ($p \pm 0.02$ paired *t* test). Late reocclusion occurred in two left anterior descending and one right coronary artery. Treatment was associated with a reduction in fibrinogen mean to 130 mg/100 ml (\pm SD 79.8), normal range 200 to 400 mg/100 ml.

Reperfusion arrhythmias included self terminating ventricular tachycardia, multifocal ventricular extrasystoles, supraventricular tachycardia, and reversal of bradycardias including complete heart block in right coronary reperfusion.

These results show the efficacy of BRL 26921 in establishing early reperfusion in the acute stage of myocardial infarction.

Development and clinical validation of gold-195m: a new short half-life radiopharmaceutical for rapid, sequential first pass radionuclide angiography in man

D S Dymond, A T Elliot, W D Flatman, D L Stone, R Bett, J G Cuninghame, H E Sims
St Bartholomew's Hospital, London, and Atomic Energy Research Establishment, Harwell

A portable mercury-195m/gold-195m generator has been developed capable of producing 17-20 mCi aliquots of the short half-life (30.5 seconds) radionuclide gold-195m for first pass radionuclide angiography (FPRA). The gold-195m is eluted with 2.5mM sodium cyanide solution, mercury breakthrough being $<0.01\%$. Safety of the eluate has been established in the experimental animal and in man, with no significant alterations in plasma cyanide or thiocyanate levels after repeated administrations. In 15 patients, left ventricular ejection fraction measured from first pass radionuclide angiography with gold-195m correlated closely with technetium-99m values ($r=0.99$, SEE 3.1%). Interobserver and sequential reproducibility of gold studies were high ($r=0.98$ and $r=0.99$, respectively), with mean \pm SD variability of $2.0 \pm 2.9\%$ and $0.6 \pm 2.7\%$, respectively. Statistical reliability of the gold studies, assessed from the observed left ventricular end-diastolic counts, matched that of technetium-99m studies (mean \pm SD counts 5040 ± 3108 and 5169 ± 1450 , respectively). Wall motion images obtained with the two radionuclides were identical. Residual count rates five minutes after data acquisition with gold were $<1\%$ of those after technetium-99m. The suitability of gold-195m for rapid, sequential first pass radionuclide angiography has been shown in patients undergoing cold pressor stimulation or dynamic exercise. Accurate, reproducible, high count rate studies are obtainable with gold-195m, and it is now possible to perform rapid sequential imaging without the constraints of an unacceptably high radiation burden.

Left heart transfer function: important index of cardiac performance

S Walton, S R Underwood, P J Ell, R H Swanton, R W Emanuel
Department of Cardiology and Institute of Nuclear Medicine, Middlesex Hospital and Medical School, London

In this study delayed transit of a radionuclide bolus through the left heart is used to quantify abnormalities of cardiac performance.

One-hundred-and-eight subjects with a variety of cardiac disorders were studied by first pass and equilibrium radionuclide angiography. The ratio of the washout slopes of the pulmonary and left ventricular activity time curves during the first pass study—left heart transfer function—was used as an index of flow through the left heart. Ejection fraction and the right to left ventricular stroke volume index, both calculated from the equilibrium study, were used as indices of left ventricular contraction and left sided valvar regurgitation, respectively.

In 31 subjects with normal equilibrium studies the variation of left heart transfer function was 1.45 ± 0.10 (mean \pm SD). Values of 1.90 ± 0.40 were obtained in 57 with depressed ejection fraction. High values were also found in 10 subjects with valvar regurgitation (2.65 ± 0.50) and the highest of all in a further 10 with both valvar regurgitation and depressed ejection fraction (3.35 ± 0.80). In 23 subjects there was a difference of $5 \pm 5\%$ between serial estimations of left heart transfer function.

Left heart transfer function defines cardiac function in terms of the ability of the heart to produce flow, a property of fundamental importance. It is simple to measure and highly reproducible.

New method for measuring myocardial perfusion and wall motion simultaneously with thallium-201 tomography

C E Handler, R G Ardley, D A Brennand-Roper, A J W Hilson, P Paraskevas, M N Maisey, E Sowton, R Wainwright
Guy's Hospital, London

Our preliminary communication showed no improvement in the detection of coronary heart disease by thallium-201 7-pin-hole emission tomography (7-PHET) compared with conventional four-view planar imaging. We have attempted to improve the accuracy of 7-pin-hole emission tomography by including a perfusion profile analysis, and to study wall motion by using the accumulated data during the entire cardiac cycle gated with the electrocardiographic signal.

Using profile curves to measure changes in thallium distribution in the myocardium we have improved the detection of coronary disease. The sensitivity increased from 67% to 89% with profile analysis in 33 patients who had had coronary arteriography. From the gated study each slice was displayed as a moving image, and as end-diastolic and end-systolic outlines. Using this new technique we have been able to show

characteristic wall motion abnormalities which are associated with perfusion defects in the majority of patients.

We postulate that simultaneous measurement of myocardial perfusion and wall motion studies using thallium 7-pin-hole tomography provides improved detection and localisation of coronary disease and shows the effect of reversible ischaemia on regional myocardial contractility.

Global and regional left ventricular contractile reserve detected by intervention radionuclide angiography

R G Murray, S Chandler, Z Drolc, R E Nagle, W A Littler
University Department of Cardiovascular Medicine,
Queen Elizabeth Hospital, Edgbaston, Birmingham

The contractile reserve of the left ventricle was investigated in 29 patients with coronary artery disease by intervention radionuclide angiography. Equilibrium image data were collected in the left anterior oblique projection at rest and after sublingual nitrate. Global left ventricular ejection fraction and three regional ejection fractions (septum, free wall, apex) were derived from global and regional activity time curves.

Although global left ventricular ejection fraction increased after nitrate from $46\% \pm 3.6$ to $49\% \pm 3.9$ ($p < 0.001$) the individual response was variable. Global ejection fraction increased in 16 patients with normal ($>45\%$) ejection fraction from $60\% \pm 1.9$ to $66\% \pm 1.8$ ($p < 0.001$) but not in 13 patients with depressed ejection fraction ($28\% \pm 3.8$ to $30\% \pm 4.2$; $p = \text{NS}$). Those 13 patients with depressed global ejection fraction displayed impaired contraction in 27 regions. In 15 regions this was moderate (regional ejection fraction more than one third normal) and in 12 severe (less than one third normal). After nitrate, regional ejection fraction improved in 13 of the 27 regions suggesting functional reserve, but not in 14 suggesting irreversible dysfunction. Improvement was seen in 11 of 15 regions with moderate contractile abnormality, but only in two of 12 with severe abnormality ($p < 0.025$).

Thus, intervention radionuclide angiography provided a non-invasive description of ventricular potential. Contractile reserve was seen in the normal ventricle and regions with moderate dysfunction, but seldom in regions with severe dysfunction.