Method of head up tilt testing in the investigation of syncope

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Prolonged 60° head up tilt is gaining acceptance in the investigation of unexplained syncope, identifying the malignant vasovagal syndrome. Numerous protocols for tilting are in use but the most clinically useful is not yet defined. To try to do this several groups of patients and controls were tilted according to different protocols. Seventy one patients with unexplained recurrent syncope were tilted at 60° with a footplate support for a planned maximum of 60 minutes and 53 (75%) were syncopal at 24 (10) mins. A random 31 of these were tilted again and 24 (77%) were syncopal; a random 16 of these were tilted again and 13 (81%) were syncopal; a random 10 of these were tilted to 45°, and only three (30%) were syncopal. Sixteen patients with syncope due to atioventricular block were tilted and three (19%) were syncopal. Eighteen patients with syncope related to sinus node disease were tilted and two (11%) were syncopal. Twenty seven age matched non-syncopal controls were tilted and two (7%) were syncopal. A random 12 of these were tilted with a saddle support and seven (67%) were syncopal.

Reproducibility of tilt testing in patients with unexplained recurrent syncope is 80%. The rate of tilt syncope was significantly higher in patients with unexplained recurrent syncope than in controls or patients with syncope related to conduction tissue disease (p < 0.001). Saddle tilt results in loss of specificity, tilting to less than 60° results in loss of sensitivity. Tilting should be for 45 minutes (mean time of syncope plus 2 SD).

Differential response of repolarisation to changes in ventricular loading in patients with abnormal wall motion

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Changes in ventricular loading conditions may influence the time course of repolarisation (and hence refractoriness). This study aims at examining a possible differential response in patients with abnormal wall motion compared with those with normal wall motion. We used the Valsalva manoeuvre to manipulate pressure and volume and recorded monophasic action potentials from the left ventricular endocardium as a measure of the time course of repolarisation during right atrial pacing. Twenty three patients were studied undergoing routine cardiac catheterisation for chest pain. Seven had neither angiographic evidence of abnormal wall motion nor a history of myocardial infarction (group 1); five had a history of myocardial infarction but normal wall motion (group 2); and 10 showed evidence of abnormal wall motion either with or without previous infarction (group 3). During the forced expiratory phase of the Valsalva manoeuvre venous return is impeded and systolic pressure falls. In group 1 systolic pressure fell from 138 (SD 31) mm Hg to a plateau of 97 (37) mm Hg (p < 0.02). After release of the forced expiration during the rapid recovery phase it increased from 66 (26) mm Hg to 109 (32) mm Hg (p < 0.0001). During the forced expiratory phase in group 1 monophasic action potential duration shortened from 311 (47) ms to 295 (47) ms (p < 0.001) and lengthened during the rapid recovery phase from 285 (44) ms to 304 (44) ms (p < 0.0001). Monophasic action potential changes in the opposite direction occurred in six of the 10 patients in group 3. An in between pattern was seen in the patients in group 2. It is unlikely that autonomic effects associated with the Valsalva manoeuvre would account for these findings.

Our results provide further evidence that changes in ventricular loading influence repolarisation in humans. With abnormal wall motion the effects on repolarisation were often opposite to those with normal wall motion. Regional differences in wall motion could by this mechanism generate local electrical gradients that may be relevant to the association of arrhythmia with impaired left ventricular function.

Pulmonary extraction and left atrial secretion of atrial natriuretic factor

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Atrial natriuretic factor (ANF) concentrations are similar in pulmonary arterial and systemic arterial samples, so it is thought that the lungs do not extract a significant amount of the peptide. We tested this hypothesis by measuring ANF concentrations in samples taken from multiple sites of the central circulation in 12 patients undergoing cardiac surgery. We also investigated the effects of cardiopulmonary bypass on ANF concentrations as any deficiency of the peptide could contribute to the risk of renal ischaemic injury. The mean age of the patients was 59 years (range 43–68), and there were three women. All patients had a history of angina, and five had had a previous myocardial infarction. The operation consisted of up to three vein grafts, either alone (three patients) or combined with an internal mammary artery graft (nine patients). Mean (SD) ANF concentrations were lower in pulmonary venous samples (41 (20) pg/ml) than pulmonary arterial samples (54 (18) pg/ml; p < 0.001), showing 24% extraction of ANF by the lungs. Both left atrial (47 (23) pg/ml) and systemic arterial concentrations (52 (25) pg/ml) were higher than pulmonary venous concentrations (p < 0.05), indicating secretion of ANF into the left side of the heart. Plasma ANF concentration fell from 68 (23) pg/ml before aortic crossclamping to 35 (13) pg/ml and 28 (9) pg/ml 10 and 30 minutes after the application of clamps respectively (both p < 0.005). A rebound rise to 123 (33) pg/ml followed the release of the clamp (p < 0.001).

We conclude that ANF is extracted in the lungs and that plasma concentrations are restored by direct secretion of the peptide into the left side of the heart. As ANF protects against renal ischaemic injury the considerable fall in plasma concentrations observed during cardiopulmonary bypass may contribute to this complication of cardiac surgery.
Cerebral blood flow autoregulation in complete heart block

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Patients with chronic complete heart block are known to have a reduced cerebral blood flow of up to 20%, associated with a reduction in cardiac output of 30% despite a normal blood pressure. The time course of these changes is unknown, but they are reversed within a few minutes when VVI pacing at 70/min is started. We measured left and right carotid and vertebral artery flow in five patients (mean age 69 years) with a 7.5 MHz Doppler probe and Acuson 128 ultrasound machine. All patients had permanent pacemakers (four VVI one DDD) with no detectable underlying cardiac rhythm and were in VVI pacing at a heart rate of 70/min for at least one hour before being studied. None had evidence of carotid or vertebral artery stenoses. Patients were rested for 15 minutes before measurements were taken. After baseline readings heart rate was reduced to 40/min and measurements repeated after 15 minutes. Total cerebral blood flow fell by 3-3% (SD 8-1%) when pacing rate was reduced to 40/min. Mean ratio of carotid to vertebral flow (total carotid flow + total vertebral flow) was 3-6 (SE 0-94) at 70/min and 3-0 (SE 0-37) at 40/min (difference not significant).

There is no evidence of an acute change in cerebral blood flow, or its distribution, on reduction of heart rate from 70/min to 40/min during VVI pacing. This shows that cerebral autoregulation is well able to cope with sudden reductions in heart rate. The failure of autoregulation in complete heart block develops more gradually and is likely to be associated with a long term reduction of cardiac output.

Angiotensin converting enzyme inhibitors and magnesium conservation in patients with congestive cardiac failure

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Patients with congestive cardiac failure treated with long term diuretics are at risk from hypomagnesaemia. Angiotensin converting enzyme inhibitors may attenuate diuretic induced hypomagnesaemia and therefore we investigated their effect on diuretic induced magnesium excretion in patients with congestive cardiac failure. Nineteen patients (group 1) taking diuretics alone (frusemide or bumetanide) were compared with 15 patients (group 2) taking diuretics plus either captopril or enalapril. Drug doses were stable for three months. Patients received an intravenous loading dose of magnesium sulphate (30 mmol/l) to minimise variability in baseline magnesium state after which urine was collected for 24 hours. The two groups were well matched for age, weight, and diuretic dose. Plasma magnesium concentrations were similar in the two groups (0-87 (0-02) and 0-86 (0-02) mmol/l). Twenty-four hour urine magnesium excretion was significantly lower in group 2 (18-5 (1-4) mmol/24/h) than in group 1 (26-0 (1-0) mmol/24/h) (p < 0-0003). Creatinine clearance was significantly lower in group 2 (49 (5-0) ml/min) than in group 1 (74 (5-9) ml/min) (p < 0-002). Creatinine clearance correlated strongly with magnesium excretion in group 2 (p < 0-001) but not in group 1.

The results suggest that angiotensin converting enzyme inhibitors have an important magnesium conserving effect. The likeliest mechanism is through a reduction in glomerular filtration rate, though their antialdosterone action may contribute.

Impaired left lower lobe ventilation: an isotope study of mechanisms

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We previously showed a significant correlation between cardiac enlargement and reduced left lower lobe ventilation on routine V/Q scanning. In a prospective study on 19 patients with large hearts a considerable improvement in left lower lobe ventilation was seen in the prone compared with the supine position. Although there was a similar change in normal volunteers, this was less noticeable. To elucidate the mechanism of this change 11 patients with enlarged hearts were studied, the change in the difference in signal at right compared with the left base being expressed as a ratio on passing from supine to prone. In those showing a reduction in ventilation at the left bases with inhaled krypton-81m the ratio on moving from supine to prone was 2-40 (0-46), representing a real increase at the left base (no changes were seen at the right base). No change was seen with intravenous 99mTc-MAA acting as a marker of lung position (0-96 (0-08) or in regional lung perfusion with intravenous 99mTc-MAA and the peak of the injected xenon-133 curve (1-1 (0-21)). There was also no change in ventilatory turnover, and thus no evidence of air trapping, from the injected xenon-133 washout curve (1-35 (0-71)). Combining the xenon washout and krypton data to produce an index of volume change produced a significant reduction at the left base (3-05 (1-7)). This suggests that the mechanism of the phenomenon may be due to lung compression and alveolar closure and that a change in position reverses this closure and thereby improves lung ventilation and gas exchange.

Effect of ischaemia on the relation between monophasic action potential duration and cycle length in the human left ventricle

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The duration of the monophasic action potential is shortened by both an increase in heart rate and ischaemia. Any protocol devised to study ischaemia is thereby complicated by the effect on the action potential duration of changes in cycle length. The aim of the study was to see whether it was possible to dissociate these two effects.

Left ventricular monophasic action potentials were recorded in 12 patients after routine coronary angiography during incremental; atrial pacing to their angina threshold or loss of 1:1 conduction. Each pacing rate was maintained for two minutes, thereby establishing steady state conditions. The monophasic action potential recording catheter was in a non–ischaemic area in six patients and in an ischaemic area in the other six patients, as shown by the use
of isotope myocardial perfusion imaging. We observed a linear relation for steady state monophasic action potential duration—that is, for values obtained at the end of each two minute pacing train—between cycle lengths of 850 ms and 461 ms in both ischaemic (r = 0.93) and non-ischaemic regions (r = 0.82). The slope of the regression line for the ischaemic areas was greater than that for the non-ischaemic areas (28.6 ms v 23.5 ms per 100 ms cycle length decrease; p < 0.05). Rate correction algorithms such as the Bazett’s formula are unreliable in non-steady state conditions but may be useful under steady state conditions when restitution is complete. Applying Bazett’s formula to our data, we observed that changes in action potential duration in the ischaemic area showed a significant deviation from that in the non-ischaemic area, particularly at the shorter cycle lengths (288 ms v 312 ms at a cycle length of 500 ms; p < 0.006).

We conclude (a) that—ischaemia shifts the slope of the regression line relating action potential duration to cycle length while preserving the linear relationship and (b) that the rate correction algorithm applied to steady state values enables changes due to ischaemia to be differentiated from those due to changes in cycle length.

Effects of early captopril administration on left ventricular dilatation and function after acute myocardial infarction

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In a double blind study 99 patients (aged 40–75, 82 men) with acute myocardial infarction and a Norris score >3.5 were randomly assigned to receive captopril or placebo within 24 hours. Left ventricular (LV) volumes, ejection fraction, segment lengths, and cardiac output were measured serially by cross sectional and Doppler echocardiography. There were no differences in clinical and echocardiographic variables between the groups at baseline except for an excess of previous myocardial infarction in the placebo group (13/50 v 2/49; p = 0.002). By two months, compared with placebo, the captopril group had a lower LV systolic volume index (mean (SE) 45.6 (3.3) (ml/m² v 54.7 (2.8) ml/m², 95% confidence interval –17.8 to –0.6; p = 0.04) a higher LV ejection fraction (41.0 (2.1)% v 35.2 (1.7)%; 0.5 to 11;2; p = 0.03), and a shorter anterior segment length (87.3 (4.7) mm v 101.0 (3.6) mm, –25.7 to –1.8; p = 0.02). There was a non-significant trend towards a lower LV end diastolic volume index in the captopril group (75.7 (3.5) ml/m² v 83.6 (2.6) ml/m², –16.7 to 0.8; p = 0.08). No differences were identified in stroke volume index or cardiac index. In the placebo group there were significant increases in the anterior and posterior segment lengths from baseline to two months which did not occur in the captopril group.

This study provides further evidence that captopril can attenuate LV enlargement and improve LV function after myocardial infarction.

Continuous ST segment monitoring in the acute phase after admission to hospital with chest pain

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It has been reported that silent ischaemia occurring in unstable angina or after myocardial infarction is common and associated with an adverse short and medium term prognosis; most studies, however, have been carried out after stabilisation. To assess the frequency and prognostic implications of early ischaemic change in patients presenting with acute coronary syndromes we studied 248 patients (mean age 57) who presented to the accident and emergency department with chest pain assumed to be ischaemic in nature. Continuous electrocardiographic monitoring (CM5 + inferior lead) was started within six hours after admission with an FM recorder (mean 40 h, total 101.9 h). Strict criteria were used to define ischaemic change to avoid especially overdagnosis on the basis of baseline ST segment elevation. Of the 248 patients, 99 (39%) had an acute myocardial infarction and 109 (43%) had unstable angina. During the 101.9 hours of taping 52 (21%) patients showed evidence of ischaemia during electrocardiographic monitoring and 29 (56%) had more than 60 minutes of ischaemia. At a mean follow up of 13 weeks (range 2–52) six out of 29 (20%) patients with more than 60 minutes of ischaemia had died and a further five (16%) had interventions (four coronary artery bypass grafting, one percutaneous transluminal coronary angioplasty). Of the 196 patients without ischaemia, six (3%) had died.

About a fifth of patients presenting with acute coronary syndromes have evidence of ischaemia in the acute phase. Continuous monitoring identifies a subgroup at significantly increased risk of an early unfavourable outcome. Early identification, investigation, and treatment of such a subgroup may improve their prognosis.

Collateral flow after acute myocardial infarction

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Left ventricular function is thought to improve after thrombolytic treatment in patients with myocardial infarction, but the mechanisms are not fully understood. Angiography was performed at 24 hours in 14 patients presenting with a first myocardial infarction who had been treated within three hours of onset of symptoms with streptase and heparin; treatment was repeated at 5–7 days in 10 of them. At the time of angiography myocardial flow was assessed by the xenon clearance technique. After intracoronary injection of xenon under direct vision scans were obtained with a mobile gammacamera fitted with a biplane collimator, which allows simultaneous acquisition in the 30° and 70° left anterior oblique projections. In four patients the infarct vessel was totally occluded at initial angiography; in one patient this was patent at 5–7 days and a further two patients developed totally occluded vessels. Ventricular function was unchanged (left ventricular ejection fraction 24.5% (5–9%) at 24 hours, 25.7% (3–1%) at
5-7 days) in the whole group, but in five of the six patients with occluded vessels and angiographically demonstrated collaterals left ventricular function tended to improve (23% (3-9%) to 27-3% (4-5%)). Xenon flow showed improved collateral flow from 43-1 (10-2) ml/100 g/min to 65-9 (11-4) ml/100 g/min and increased distribution to the left ventricle (14% (3%) to 21% (4%) from the collaterals.

These results suggest that after myocardial infarction collateral flow tends to improve with time in patients with occluded vessels, and this may help to preserve ventricular function.

Prolonged anginal perceptual threshold in diabetes: effects on exercise capacity and myocardial ischaemia

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Anginal perceptual threshold (APT)—the time from onset of 0-1 mV ST depression to onset of angina during treadmill exercise—is prolonged in diabetes. We evaluated the functional importance of this perceptual abnormality by analysing its effect on exercise capacity and myocardial ischaemia in 32 diabetic patients and 36 non-diabetic controls. APT was prolonged in the patients by a mean of 86 s (p < 0.001) and correlated closely with exercise capacity (r = 0.8, p < 0.001), although in the controls these variables were unrelated. In both groups the time to onset of electrocardiographic ischaemia was related to exercise capacity (r = 0.8 and 0.9, p < 0.001), but the slope of the regression was significantly flatter in the patients because APT was prolonged, allowing exercise to continue as ischaemia intensified. This permissive effect of prolonged APT on exercise capacity had unfavourable consequences as reflected by its correlation with ischaemia at peak exercise (r = 0.6, p < 0.001)—the longer the threshold the greater the exercise capacity and the more severe the ischaemia. Indeed, the normal inverse relation between the severity of exertional ischaemia and exercise capacity seen in the non-diabetic controls (r = 0.4, p < 0.02) was completely lost in the diabetic group.

In conclusion, APT is a major determinant of exercise capacity in diabetes: prolongation has important functional consequences, depriving the patient of the signal to stop exercising as regional ischaemia intensifies. The effects of this process on arrhythmogenesis and myofibrillar damage remain to be determined.

Prognostic value of baroreflex testing early after myocardial infarction

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Baroreflex sensitivity (BRS) testing was performed in 99 patients 6-10 days after myocardial infarction with bolus doses of intravenous phenylephrine and intra-arterial monitoring (femoral or radial line). The mean rise in systolic blood pressure was 23 mm Hg and the mean dose of phenylephrine used on each injection was 0.8 mg. All

patients tolerated the procedure well. The mean left ventricular fraction of the study group was 51.5% (14.8%), mean age was 56.4 (9.8) years, and the mean BRS was 7.06 (4.7) ms/mm Hg. BRS was inversely correlated with age (r = -0.424, p < 0.0001) but not with ejection fraction or variability in heart rate. Infarct site or type (Q wave) had no significant effect on BRS. During follow up seven patients developed arrhythmic events (ventricular tachycardia or sudden death) and BRS in this group was considerably reduced (7.44 (4.65) v 3.85 (1.34); p < 0.002). On 24 hour electrocardiographic analysis nine patients had non-sustained arrhythmias and BRS was again significantly reduced in this group (7.52 (4.65) v 3.6 (2.78); p = 0.018). BRS was not significantly reduced when all cause cardiac mortality was analysed (7.3 (3.97) v 7.4 (4.65)).

In conclusion, BRS testing can be safely performed in the early period after infarction, is well tolerated, and gives important prognostic information on arrhythmic risk.

Exertional ST elevation after infarction: wall movement abnormality, reversible ischaemia, or both?

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Exertional ST elevation after myocardial infarction is a bad prognostic sign but its mechanism is obscure. We examined its relationship to regional and global left ventricular wall movement and reversible ischaemia (angina or ST depression, or both) in 42 consecutive patients without previous infarction by echocardiography, radionuclide angiography (multiple gated acquisition), and symptom limited exercise testing. The 17 patients who developed ST elevation had lower regional (anterior: 2.1 v 6.0, p < 0.005; inferior: 1.3 v 2.8, p < 0.01) and global (10.1 v 13.4, p < 0.05) wall movement scores. In 14 of these 17 patients with ST elevation the electrocardiographic location of ST elevation corresponded to underlying regional wall movement abnormalities (hypokinesia or dyskinesia, or both). Patients with ST elevation had lower radionuclide ejection fractions (33% v 47%, p < 0.04) and shorter exercise duration (11.0 v 13.1 min, p < 0.03) compared with the 25 patients without ST elevation. The frequency of reversible ischaemia was not significantly different between the two groups.

We conclude that exercise induced ST elevation after infarction is related to underlying left ventricular wall movement abnormalities and associated poor left ventricular performance but not with reversible ischaemia.

β-Endorphin release after acute myocardial ischaemia

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Plasma concentrations of β-endorphin (BE), an endogenous opioid peptide, increase in response to various stressful stimuli and are also raised in animal models of heart failure. In these models opioid antagonists improve cardiac performance, suggesting that BE may have a patho-
physiological role. Plasma BE concentrations were measured serially in 55 patients (aged 37–75, 37 men) admitted to the coronary care unit with acute myocardial ischaemia. Myocardial infarction was confirmed in 42 patients, 31 (74%) of whom had at least one measurement outside the normal range of 2.5–7–2 pmol/l. The mean (SE) peak value for all patients with myocardial infarction was 22.3 (3.7) pmol/l, significantly higher than the peak value of 5.1 (1.0) pmol/l in the 13 patients with unstable angina (95% confidence interval for difference of means 9-4 to 24-9).

The 12 patients with myocardial infarction who developed cardiac failure had a higher peak BE concentration than those without this complication (34.3 (8-3) vs 17.4 (3.8) pmol/l, - 32-8 to - 0.9). Univariate analysis indicated significant correlations between peak BE concentration and creatinine kinase activity and adrenocorticotropic hormone, cortisol, and glucose concentrations. Although pain is a major stimulus to BE release, there was no difference in the pain scores of the patients with and without myocardial infarction (70(4) vs 76(4), - 19 to 6) or between patients with and without cardiac failure (79(11) vs 72(4), - 19 to 34).

BE is another component of the neuroendocrine activation associated with myocardial infarction and cardiac failure.

Can we predict which cardiac arrests outside hospital are ventricular fibrillation?

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Only an occasional patient with asystole outside hospital will survive, so extended trained ambulance staff should concentrate on ventricular fibrillation (VF). We analysed 1196 cardiac arrests in adults attended by extended trained staff in West Yorkshire to assess whether VF can be predicted. Fibrillation was the initial rhythm in 456 patients (38%); 64 survived to leave hospital. Only one of the remaining patients (585 asystole, 155 electromechanical dissociation) survived—an 18 year old patient with asthma who developed asystole in transit. Five factors were positively associated with VF: age less than 70 (predictive accuracy 43%), location of arrest in a public place (36%), arrest occurring in presence of paramedical staff (46%) or bystanders (42%), bystander resuscitation (58%), and response time shorter than six minutes (45%). When all five associated factors were present VF was found in 74% of the arrests; if none was present VF accounted for 9%.

Fibrillation occurring after arrival of the ambulance or during transit was followed by 56-5% survival, but for those patients found in VF only a response time shorter than six minutes was associated with improved survival (14%, vs 5%).

Some factors are associated with VF, but their predictive value is not sufficient to be of much practical use.

Reactivity of eccentric and concentric coronary stenoses in chronic stable angina

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 Eccentric coronary stenoses are generally thought to be capable of changing their calibre in response to constrictor and dilator stimuli thus leading to a variable anginal threshold in patients with chronic stable angina. On the other hand, concentric stenoses are believed not to react in a similar manner. In 44 patients (34 men, 10 women age 55 (11) years) with chronic stable angina and angiographically documented coronary artery disease (> 50% coronary luminal diameter reduction) we studied the response of 55 coronary stenoses (50-90% diameter reduction) to the administration of 1 mg intracoronary isosorbide dinitrate (54 stenoses) and intravenous ergometrine (12 stenoses). Computed quantitative angiography was used to assess the degree of eccentricity of each stenosis and to measure the coronary diameter of reference segments (angiographically normal segments proximal to the stenosis) and stenotic segments during baseline and after isosorbide dinitrate and metrine. Twenty six of the 55 stenoses were eccentric (47%) and 29 (53%) concentric. After isosorbide dinitrate coronary stenosis diameter increased > 10%, compared with baseline, in 18 of the 26 (69%) eccentric stenoses and in 11 of the 29 (38%) concentric stenoses (p < 0.05). Mean diameter of eccentric stenoses increased from 1-11 (0-25)
mm during baseline to 1·32 (0·32) mm after isosorbide dinitrate (19% (14%) increment), whereas diameter of concentric stenoses changed from 1·10 (0·37) mm to 1·19 (0·38) mm (10% (15%) increment) (p < 0·05). Average dilatation of reference segments was not significantly different in patients with concentric and eccentric stenoses (7% (15%) and 10% (14%) respectively). Ergometrine, which did not produce angina or ST segment shifts in any patient, reduced stenosis diameter by ≥ 10% in four out of five eccentric stenoses (mean diameter reduction = 17 (9)% and in four out of seven concentric stenoses (mean reduction = 12 (10)% (NS). Constriction of reference segments with ergometrine was similar in patients with eccentric and concentric stenoses (11 (8)% and 12 (7)% respectively).

Thus, in patients with chronic stable angina eccentric stenoses have a significantly larger ability to dilate in response to isosorbide dinitrate than concentric stenoses. Although a significantly larger proportion of eccentric stenoses have the potential for dynamic changes of calibre, however, a sizeable proportion of concentric stenoses also have this potential.

Time course of ultrastructural injury and repair to pulmonary capillaries after experimental unilateral lung transplantation

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A donor lung is injured during preservation and is generally thought to be injured by reperfusion. Donor lungs from rats preserved by flush perfusion with cold Marshall’s solution at 4°C were examined by electronmicroscopy after two, four, or seven hours’ storage at 4°C and after transplantation (syngeneic) at four or 12 hours (six animals per time interval). During preservation rapid capillary remodelling occurred. Both endothelial and epithelial components of the blood-gas barrier thinned (surface to volume ratio increased by two hours; p < 0·001). Pericapillary oedema developed involving the blood-gas barrier when basement membrane thickness increased significantly (p < 0·001). Occasional breakage of the endothelial cell sheet occurred after four hours’ preservation. Even after seven hours’ preservation there was no evidence of irreversible cell damage. After transplantation type I and type II pneumonocytes recovered after 12 hours. Endothelial cell cytoskeletal remodelling took longer. Oedema decreased rapidly during the first four hours, despite the number of adherent neutrophils increasing threefold. Findings were similar in the allogeneic transplanted dog lung.

Thus the pulmonary capillaries of transplanted lungs showed no structural evidence of reperfusion injury; rather a gradual resolution of the changes incurred during preservation injury.

Fatal complications as a result of underestimated coronary artery disease at the time of corrective cardiac surgery

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Data from 321 postmortem reports (between 1970 and 1989) were analysed to obtain information about the fatal complications after open heart surgery in adults. The indications for surgery were: valve disease (n = 203, group I); ischaemic heart disease (n = 86, group II); combination of the two (n = 30, group III), and miscellaneous (n = 2, group IV). In all, 147 patients were studied within 24 hours of operation and 128 (40%) between one and 30 days after operation, and there were 46 (14%) late deaths. The main cause of death was cardiac in origin in 204 cases (63%), thoracic bleeding in 28 cases (9%), other organ complications in 45 cases (14%) and multigorgan failure in 44 cases (14%). The most frequent pathological finding was myocardial infarction or signs of subendocardial injury (n = 158). In the ischaemic groups (II and III) cardiac deaths n = 90 it was the result of incomplete myocardial revascularisation in 25 cases (27%). In the non-ischaemic groups (I and IV; cardiac deaths n = 114) in 36 cases (32%) it was as a consequence of unidentified coexisting coronary artery disease.

These data suggest that all adults should have complete visualisation of their coronary artery tree at the time of preoperative investigations and in case of existing coronary artery disease they should undergo complete myocardial revascularisation in addition to corrective cardiac operation.

Warm cardioplegic induction improves rate of recovery of myocardial function after prolonged storage for transplantation

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Cooling blood has detrimental effects on its perfusion characteristics. During the early moments of cold cardioplegic infusion the crystalloid solution cools the residual blood in the coronary vasculature, which may adversely affect the distribution of the cardioplegic solution. To investigate whether such an effect jeopardises myocardial preservation for transplantation cardioplegic induction was performed in rat hearts infused (60 mm Hg) with St Thomas’s Hospital cardioplegic solution. Two infusion conditions were studied: (a) one minute infusion at 22-24°C followed by two minutes at 7·5°C and (b) three minutes at 7·5°C. For each condition three groups of hearts (six/group) were studied after 0, four, and eight hours of storage at 7·5°C, after which they were heterotopically transplanted into the abdomen of recipient rats. With implanted fluid filled intraventricular balloons cardiac function was assessed by constructing pressure-volume curves one, four and 24 hours after transplantation. The groups with the initial warm infusion accepted a greater volume of cardioplegic solution than the cold groups (29 (1·7) ml v 22·3 (1·6) ml, p < 0·05). After one hour of reperfusion the recovery of heart rate was poor in all six groups (NS between groups), but precontrol values were attained by 24 hours. In the eight hour storage group the recovery of systolic pressure (measured at 90 ml balloon volume) recorded one hour after reperfusion was significantly better in the warm than the cold infusion groups (111·3 (7·5) mm Hg v 87·4 (6·4) mm Hg; p < 0·05), so too were diastolic (11·2 (0·9) v 20·0 (5·6) mm Hg; p < 0·05) and developed pressures (100·2 (7·2) v 69·3 (7·2) mm Hg; p < 0·05). After four hours reperfusion these differences in function were still apparent (91·7 (9·2) v 73·6 (5·3) mm Hg, 14·7 (1·3) v 23·7 (4·8) mm Hg, and 77·0 (8·7)
Growth pattern of paediatric hearts after transplantation

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Growth pattern of the heart structures after paediatric transplantation is of great interest. To evaluate the possibility of cardiac growth after cardiac transplantation 29 patients followed up for a minimum period of 18 months were studied by serial echocardiography. The recipients’ and donors’ mean age at time of transplantation was 9 (0-5–16) years and 12 (2-5–35) years respectively. All patients were treated with cyclosporin and azathioprine without the routine use of steroids. Echocardiographic assessment was performed at intervals of three months after transplantation. Patients’ weight increased from 40 (SD 11.6) kg to 49-8 (15.3) kg during the period of follow up, ranging from 18 to 72 (mean 48) months. Left ventricular dimensions in diastole and systole, left ventricular posterior wall thickness and mass, and aortic root diameter were measured and plotted against body weight. Growth patterns of cardiac dimensions in each patient were compared with published growth patterns in normal children. The initial left ventricular dimension in diastole was 39-8 (3-9) mm or 94-3% (9-1%) of predicted. At last examination left ventricular dimension in diastole was 41-5 (4-3 mm) or 93-8% (18.3%) of predicted.

It is concluded that paediatric cardiac allografts are capable of growth. This includes cavity dimensions, left ventricular mass, and aortic root diameter. The rate of growth of the different structures is variable and may be influenced by the discrepancy in size between donor and recipient, as well as blood pressure. Longer periods of follow up are required to define the full growth potential of the transplanted paediatric heart.

Controlled trial of physical training in chronic heart failure

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In a controlled trial of eight weeks duration home-based bicycle exercise training in patients with moderate to severe chronic heart failure (mean age 61.8 (1.5), left ventricular ejection fraction 0.20 (0.02) exercise duration and peak oxygen uptake were increased by about 20%. Exercise heart rate and rate x pressure product and 24 hour ambulatory heart rate and blood pressure were all significantly reduced, consistent with reduced myocardial oxygen requirement. Variability in heart rate was increased and resting noradrenaline spillover was reduced, both suggesting a reduced sympathetic to parasympathetic autonomic balance after training. Training increased cardiac output at rest and on exercise primarily owing to an increase in stroke volume, with systemic vasodilatation. The increase in exercise tolerance after training was closely linked to compliance with the training programme, indicating the specificity of the response.

These results suggest that carefully selected patients with moderate to severe heart failure can achieve significant and worthwhile improvements with exercise training and support the hypothesis that physical deconditioning may be partly responsible for some of the associated abnormalities and exercise limitation in chronic heart failure. They refute the frequent but unsupported recommendations that regular exercise should be avoided in chronic heart failure.

Inspiratory muscle fatigue and limitation of exercise by dyspnoea in chronic heart failure

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The mechanisms limiting exercise capacity in chronic left heart failure (CHF) are not known, and it seems that dyspnoea does not simply relate to increased pulmonary wedge pressure. Fatigue of the respiratory muscles has been described in chronic lung disease and might contribute to dyspnoea in CHF. We evaluated respiratory muscle function in CHF with a novel non-invasive index of inspiratory muscle fatigue (SR-τao). Peak transdiaphragmatic pressure and relaxation rate (τa0) during nasal sniffs are accepted indices of respiratory muscle fatigue, but their measurement requires gastric and oesophageal intubation. The time constant of pressure relaxation during gasps through a Starling resistor (SR-τao) was compared with standard nasal sniffs in normal subjects at rest and during maximal gasps. SR-τao correlated well with sniff τa0 (R = 0.76, p < 0.02). Ten patients with CHF (New York Heart Association grade III) and 10 age matched controls performed maximal symptom limited treadmill exercise. Maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), SR-τao, and maximum hand grip strength were recorded. At peak exercise MIP and MEP decreased significantly in the patients with CHF but not in the controls (p < 0.01), SR-τao became prolonged at peak exercise in the patients but not in the controls (p < 0.02) and hand grip did not change significantly with exercise in either group.

These data provide evidence of respiratory muscle weakness and fatigue in CHF when exercise is limited by dyspnoea whereas the strength of non-exercising muscle (hand grip) is not reduced. These changes are not seen in normal subjects and might contribute to the limitation of exercise capacity in CHF.

Interlead QT variability as a measure of temporal dispersion of ventricular recovery

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A simple non-invasive measure of time dispersion of ventricular recovery would be of great clinical importance. Increased dispersion is thought to be an important basis for ventricular arrhythmias, and a decrease in dispersion probably explains the action of class III antiarrhythmic drugs. QT interlead variability (dispersion) on the surface electrocardiogram may have potential as a measure of time dispersion of ventricular recovery. To examine this hypothesis QT dispersion was measured in three groups of patients. Each study entailed a situation in which dispersion of recovery time was expected to be minimal and one in which dispersion was expected to be large. In patients randomised to treatment with placebo or sotalol after myocardial infarction QTc dispersion (calculated as maximum QTc – minimum QTc) was significantly less in those receiving sotalol. In patients with a long QT interval associated with a history of ventricular arrhythmia (arrhythmogenic QT prolongation) QT dispersion was significantly greater than that in patients in whom a long QT was due to sotalol (antiarrhythmic QT prolongation). In patients with normal hearts QT dispersion was significantly less in sinus beats that with ventricular extrasystoles.

Thus all three studies provide strong support for the hypothesis that interlead QT variability reflects temporal dispersion of ventricular recovery.

The calcium release channel from cardiac sarcoplasmic reticulum. Characterisation of the channel from human hearts and its function in acute ischaemic injury

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The release of calcium from the sarcoplasmic reticulum (SR) is central to excitation-contraction coupling. In previous animal experiments the physiological release pathway has been identified as a calcium permeable ion channel in the SR membrane. In this study purified SR membrane vesicles were isolated from human hearts and, by fusing these vesicles with artificial planar phospholipid bilayers, single channel recordings were obtained under voltage-clamp conditions. The results provide the first report of the calcium release channel from human tissue and suggest that the channel is similar to that reported in other species. In addition, altered channel function does not seem to contribute to the impairment of calcium release in SR in end stage cardiac failure. Experiments also performed to investigate the effects of acute ischaemia on the calcium release channel from sheep hearts show that the channel is a target for early degradation during ischaemia. The effects of proteolysis and exposure to free radicals in vitro provide evidence that degradation of the channel leads to a phase of increased opening followed by loss of function.

These results suggest that damage to the calcium release channel may contribute to myocardial stunning.

Excess insulin secretion: a powerful new predictor of myocardial infarction of particular importance in Asians

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Increased insulin concentrations have been found in survivors of myocardial infarction, and in some prospective studies insulin has predicted subsequent cardiac events, but its independent role and mechanism of action are unclear. Insulin and C peptide are secreted by the pancreas in equimolar concentrations, insulin being subject to considerable first pass removal by the liver and C peptide being unaffected. The association between these peptides and the relative risk of myocardial infarction were examined in 150 consecutive male survivors of first infarction and in controls marked for age and ethnic origin. The subjects were either white (n = 76) or Asian (n = 74), the Asians having an excess rate of ischaemic heart disease and diabetes. Higher concentrations of C peptide (p < 0.001) and triglyceride (TG) (p < 0.01) and lower concentrations of high density lipoprotein cholesterol (HDL) (p < 0.001) were found in the patients. In a multivariate analysis the C peptide concentration and cholesterol/HDL ratio emerged as the most powerful independent predictors of cases in both ethnic groups. The C peptide concentration was independently associated with TG concentration (p < 0.001), which itself was associated closely with the cholesterol/HDL ratio (p < 0.0001).

These data suggest that the cluster of risk factors that include high insulin secretion, high TG concentration, and low HDL concentration may be important to the development of coronary artery disease (CAD). As established risk factors for CAD are lower in Asians, C peptide, a new marker of risk of myocardial infarction, which was higher in Asian than in white subjects, may explain both the excess of CAD and diabetes in Asian people.

The heart after direct current countershock: a novel myocardial syndrome?

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The mechanisms of myocardial injury after direct current countershocks from a hospital defibrillator were investigated in adult greyhounds. At one minute after five transthoracic shocks (400 J, damped sine wave, 0-5 minutes interval) lactate production occurred (mean lactate extraction – 193 (SE 135)(%) and mean peak noradrenaline concentration in coronary sinus blood was 916 (313) pg/ml. Coronary sinus oxygen saturation rose from 42 (4)(%) to 63 (2)(%) and mean global left ventricular myocardial blood flow rose from 156-9 (18-7) ml/minute to a peak value of 221-0 (38-7) ml/minute after five shocks. Glutamate-, but not succinate-supported, oxidative phosphorylation in mitochondria isolated from hearts after five lethal shocks was significantly lower than that in controls (50-7 (4-9) nanoAtoms oxygen (nAO)/mg mitochondria/minute v 86-6 (13-6) nAO/mg/minute, p < 0-02). Free radicals of the peroxyl group were detected in heart tissue by electron spin resonance spectroscopy after two internal shocks (50 J), although there was no rise in coronary sinus malondialdehyde concentrations in the dogs after five transthoracic shocks. Though a dramatic rise in noradrenaline concentration was observed in coronary sinus blood after five shocks, there was no accompanying rise in neuropeptide Y concentration.

It is proposed that this combination of physiological changes, comprising reduction of oxygen utilisation, production of lactate, mitochondrial depression, free
radical generation, and increased blood flow with a rise in coronary sinus noradrenaline but not in neuropeptide concentration are characteristic of the heart after direct current countershock.

Equivalent efficacy of single bolus and infusion dosing of recombinant tissue plasminogen activator in a canine model of coronary artery thrombotic occlusion and reperfusion

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In the treatment of acute myocardial infarction thrombolysis is now accepted as being of value in salvaging ischaemic myocardium and reducing mortality. Recent clinical evidence has suggested equivalent efficacy in terms of early coronary patency with bolus dosing of recombinant tissue plasminogen activator (rt-PA) compared with infusion dosing. The aim of this study was to evaluate the utility of single bolus administration of rt-PA compared with an infusion. Anaesthetised dogs were subjected to 90 minute's thrombotic occlusion of the left anterior descending coronary artery (LAD) after introduction of a copper coil on a guide wire. rt-PA (Dutepase, Wellcome Foundation) was administered at the same dose (0.6 MIU/kg) over six minutes (group 1, n = 8) or 60 minutes (group 2, n = 8). LAD patency was assessed arteriographically and microvascular coronary flow by radio-labelled microspheres. Infarct size was determined histochemically after 120 minutes of reperfusion and plasma fibrinogen monitored throughout. LAD patency was restored in 43-1 (7-0) min and 42-9 (7-4) min in groups 1 and 2 respectively. Patency after 60 minutes was 88% for both groups. Subendocardial microvascular coronary flow was restored to 102-6% (27 8%) and 114-3% (9-4%) (of control) in groups 1 and 2 respectively. There was no significant difference in infarct size expressed as percentage of area of risk (group 1, 42-1% (9-1%); group 2, 46-3% (8-4%)) or in circulating fibrinogen concentrations.

Thus, in an anaesthetised dog model of coronary arterial thrombotic occlusion and reperfusion single bolus administration of rt-PA achieves equivalent efficacy (LAD patency and microvascular coronary flow) to infusion dosing.

Free radical activity at the time of successful thrombolysis: relation to left ventricular function

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Although thrombolytic treatment of acute myocardial infarction often restores coronary patency and improves prognosis, improvement in left ventricular function is small. Experimental data suggest that residual impairment of left ventricular function after successful thrombolysis is due to reperfusion injury involving free radicals, as well as to damage accrued during ischaemia, but there is no clinical data on this point. In 50 patients given streptokinase for myocardial infarction peripheral venous blood samples before streptokinase and two hours later were centrifuged and frozen for assay of a marker of free radical activity: thiobarbituric acid reactive material (TBA-RM) reflects lipid peroxidation by free radicals. Coronary arteriography was performed within 72 hours of thrombolysis to determine coronary patency. The infarct related artery was patent in 42 (84%) patients and occluded (TIMI grade 0 or 1) in eight. In the 42 with a patent artery the concentration of TBA-RM increased after streptokinase by 105 (96) ng/nl compared with the 8 patients with an occluded artery TBA concentration decreased by 147 (80) (p < 0.01 between groups). In those with a patent artery there was a weak correlation between the rise in TBA-RM and left ventricular ejection fraction (R = 0.3; p < 0.02).

These data show that at the time of successful thrombolysis there is an increase in lipid peroxidation, which is not seen in patients in whom the artery remains occluded. This is the first demonstration in humans of free radical activity associated with documented myocardial reperfusion and provides indirect evidence of reperfusion injury, supported by the association between a large rise in TBA-RM concentration and low left ventricular ejection fraction.

Prediction of arrhythmic events in patients after infarction by heart rate variability and signal averaged electrocardiogram

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A total of 387 consecutive patients admitted with an acute myocardial infarction were assessed before discharge. Holter recordings were analysed for ventricular ectopic frequency >10/h (VE) and heart rate variability. Signal averaged electrocardiograms were analysed for late potentials. Clinical data and left ventricular ejection fraction were also recorded. Mean age was 59.2 (10.6); ejection fraction 50.43 (14.9); and heart rate variability 27.6 (11.4). Late potentials were present in 79 of the 387 patients and VE in 49 of the 387 patients. During follow up 20 patients had arrhythmic events, including sudden death or sustained ventricular tachycardia. These patients had reduced heart rate variability (10.2 (6.9) e 27.75 (11.2); p = 0.0001) and ejection fraction (40.7 (15.4) v 50.9% (14.8%); p = 0.001). Stepwise multivariant analysis showed that heart rate variability followed by VE, late potentials, and Killip class were independent predictors of arrhythmic events, whereas ejection fraction, age, infarct site, and Q waves were not. Heart rate variability was only weakly correlated with age (r = 0.19; p = 0.001) and ejection fraction (r = 0.27; p = 0.001). Whereas reduced heart rate variability (<20) was the most sensitive predictor of arrhythmic events (17/20), the positive predictive accuracy was 15.2% (17/112 patients). A combination of heart rate variability and late potentials yielded a higher positive predictive accuracy (32.4% (12/37 patients)) than any other combination.

In conclusion, a combination of heart rate variability and late potentials identifies a small subgroup of patients at high risk of arrhythmic events after acute myocardial infarction. These tests offer a simple non-invasive method of risk stratification independent of ejection fraction and can be obtained from a single ambulatory electrocardiogram.
Early coronary bypass surgery after acute myocardial infarction

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This is a randomised study of patients (men or women ≤65) surviving acute myocardial infarction and having a positive exercise test before discharge. The aim was to evaluate the effect of coronary bypass surgery on mortality. Those with a positive exercise test were considered for coronary angiography and for inclusion in the study when (a) left ventricular ejection fraction was >30% and (b) one coronary artery was narrowed by >70% and not supplying a dyskinetic ventricular segment. Patients randomised to surgery were operated on as soon as possible. Follow up was five years. All patients meeting clinical criteria but otherwise excluded were registered, and information on survival was obtained at two years. In all, 4658 patients were assessed and 3334 (71%) had an exercise test. This was positive in 728 (22%) and 598 had coronary angiography. Seventy patients did not wish to take part and 18 had severe angina requiring intervention. A total of 348 were randomised. Baseline characteristics of each treated group were similar. At two years the survival in the medical group was 96% and in the surgical group 93%. At five years the figures were 88% and 91%. Thirty patients in the medical group required surgery within five years. In those patients with a negative exercise test the two year mortality was 8%, with 8% requiring coronary bypass surgery. Thus, a negative exercise test does not allow complacency whereas a positive exercise test does not imply that surgery is inevitable.

Cardiac catheterisation 1988–9: the RITA trial coronary arteriogram register

RITA Trial Steering Committee

The Randomised Intervention Treatment of Angina (RITA) trial compares the long term effect of coronary bypass surgery and coronary angioplasty in patients treatable by either procedure. In addition, a register of patients undergoing cardiac catheterisation is maintained in the RITA trial centres to assess the overall context of patient recruitment. The first 21 months of register forms (21 881 patients) have been analysed. Cardiac catheterisation was performed during day case (14%), overnight (24%), or longer (62%) hospital admission. Reasons for investigation were angina (69%), myocardial infarction (10%), and valvar or other cardiac disease (21%). In patients with angina coronary arteriography showed single vessel disease in 20%, two vessel disease in 22%, and more extensive coronary disease in 41%. The planned management of patients with angina included elective coronary surgery (39%), elective coronary angioplasty (12%), or RITA randomisation (3%). But in 42% revascularisation was considered to be unnecessary. Disease in more than three major coronary vessels (5%), left main stem disease (4%), unsuitable coronary anatomy (3%), and a fatal complication of coronary arteriography (0.1%) were all criteria for exclusion from RITA. Randomisation was refused by 2% of patients with angina and by the referring physician in 3% of cases.

The RITA coronary arteriogram register has produced important information about current British cardiac practice. Around half of the patients catheterised for angina at RITA centres were referred for a revascularisation procedure, of whom 27% were suitable for coronary angioplasty.

Does epidural neurostimulation have an anti-ischaemic as well as analgesic effect in patients with angina?

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We studied 11 patients with epidural neurostimulators implanted for intractable severe angina to determine whether epidural stimulation reduces myocardial ischaemia as well as relieves pain. All patients showed improvement in symptoms. Right atrial pacing and treadmill exercise testing were performed with the neurostimulator off, on, and off. The main results (mean (confidence interval)) are comparing off and on. With right atrial pacing, maximum pacing rate increased from (143 (9-5) to 150 (6-7) beats/min; p < 0.02); total ST segment depression at 90% maximum control (off) was reduced from 6.4 (4-0) to 5.2 (3-3) mm (p < 0.02), and at rates of 120, 130, and 150 beats/min (p < 0.05). Maximum RPP was not significantly different despite higher heart rate (HR) because of a fall in maximum systolic blood pressure (135 (14) to 124 (12) mm Hg; p < 0.05) during stimulation. With exercise testing (n = 9) exercise duration was increased from 445 (156) to 507 (163) (p < 0.05); total ST segment depression at peak exercise was less, 5.6 (3-6) to 3.9 (3-3) mm (p < 0.01) and at 90% maximum control (off) HR, 3.7 (3-0) to 2.8 (3-5) mm; p < 0.01. Maximum RPP was not significantly different despite increased work and HR.

These results indicate that epidural neurostimulation increases exercise duration and time to angina (right atrial pacing) with less ST segment depression at comparable RPP and therefore has an anti-ischaemic effect, which may in part be due to peripheral vasodilatation reducing cardiac work.

Critical aortic stenosis diagnosed prenatally

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Of over 450 structural cardiac abnormalities detected antenatally, critical aortic stenosis was diagnosed in 26 cases at presentation. The cardiac sign on the echocardiogram common to all cases was a poorly contracting left ventricle. Other features, often present but not consistent, included cardiac enlargement, aortic hypoplasia, restricted mitral excursion, an intact atrial septum, increased myocardial echogenicity, and abnormal aortic Doppler flow. Eight fetuses showed evidence of intrauterine cardiac failure. Sequential echocardiographic studies in three cases showed reduced or no growth of the mitral valve orifice, aortic valve size, and left ventricular dimensions so that these measurements became smaller for gestational age as pregnancy progressed. This observation was also noted in four fetuses in whom there was a time delay between the
scan and postmortem examination. Pregnancy was terminated in 13 patients. One fetus is not yet delivered, but of the remaining 12 continuing pregnancies there are no survivors. There were two spontaneous intrauterine deaths and 10 neonatal deaths, six of which occurred on the first day of life. The diagnosis was confirmed in 22 cases at postmortem examination and in a further case at cardiac catheterisation.

Critical aortic stenosis diagnosed prenatally includes a range of abnormalities, with some cases progressing to the hypoplastic left heart syndrome with advancing gestational age. This would account for the poor range of age. This would account for the poor range of Age.

Doppler echocardiographic detection of anthracycline induced changes in diastolic ventricular function in children

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Anthracycline drugs produce dose dependent myocardial damage—monitoring their incremental effect on ventricular performance provides a model for comparison of ventricular function assessment techniques. Preliminary results from a serial Doppler echocardiographic study are presented. Ninety Doppler echocardiographic examinations were performed in 51 patients aged 5 months to 22 years between one and five times each who had received 0 (pretreatment) to 580 mg/m² anthracyclines. Left ventricular ejection fraction was calculated from M mode dimensions. Peak early (e) and late (a) transmural flow velocities were measured by pulsed wave Doppler sampling at the mitral valve leaflet tips and the ratio of e to a was calculated. Patients were divided into a pretreatment group and five groups of 100 mg/m² dose increments. Mean left ventricular ejection fraction was 72–73% in all groups except that receiving > 400 mg/m², in which it was 67% (p = 0.015). There was a biphasic trend of e/a ratio with dose. The initial mean (SD) in the pretreatment group (n = 16) was 1.73 (0.4), falling to 1.42 (0.3) by 100 mg/m² (n = 11), p = 0.02; the 35 patients receiving < 200 mg/m² had a ratio of e/a of 1.37 (0.03) and those receiving > 200 mg/m² (n = 39) a ratio of 1.49 (0.3) (p = 0.04), with a peak of 1.54 (0.2) at 300–400 mg/m² falling to 1.46 (0.3) at higher doses.

Anthracycline treatment produces changes in left ventricular diastolic filling patterns detectable by Doppler echocardiography before abnormalities of systolic function occur. Further serial echocardiographic studies of this model of progressive ventricular dysfunction are indicated.

Comparative values of intraoperative transoesophageal and epicardial ultrasonography in surgery for congenital heart disease

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Both intraoperative transoesophageal (TOE) and epicardial (EPI) ultrasonography (two dimensional imaging, colour flow mapping, and spectral Doppler) were attempted in 26 patients undergoing intracardiac correction for congenital heart disease to determine the relative advantages and limitations of either technique in assessing both the underlying morphology and the immediate surgical results. Introduction of the TOE probe was successful in 24 patients (92%). TOE studies were restricted to studies before bypass alone in nine children who were intubated with an uncuffed endotracheal tube. Twelve patients were studied before and after bypass and three patients were studied after bypass alone. In a 4·7 kg infant introduction of the probe raised ventilation pressures dramatically and required anaesthetic management. No other complications were encountered during TOE. Complete EPI studies were performed in all patients without complications. The assessment of the intracardiac morphology before bypass was more complete with EPI. In particular the right ven-

Transoesophageal echocardiography (TOE) in children with congenital heart disease

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TOE with a dedicated single plane paediatric probe was performed prospectively in 57 anaesthetised children before either cardiac catheterisation or cardiac surgery to evaluate the potential of this new technique in (a) the initial diagnosis, (b) perioperative management, and (c) the postoperative follow up of children with congenital heart disease. Age at study ranged from 9 months to 14·8 years (mean 5·6 years) and body weight from 4·7 kg to 52 kg (mean 19·7 kg); 38 children weighed less than 20 kg. All studies were successful; no complications were encountered. The TOE findings (imaging, pulsed Doppler, colour flow mapping) were correlated with the results of previous precardiac studies and cardiac catheterisation or surgical inspection, or both. TOE consistently provided more detailed insights into the morphology and function of systemic and pulmonary venous return, both atria, the intrapulmonary septum, Mustard baffles, both atrioventricular valves and their subvalvar apparatus, and the left ventricular outflow tract. Additional information was obtained in 31 of the 57 (54%) patients. Follow up studies after atrioventricular valve repair or replacement, or both, and after a Mustard or Fontan procedure were particularly rewarding. During aortic valve valvuloplasties TOE permitted the immediate exclusion of aortic regurgitation and monitoring of ventricular function. Intraoperative TOE was a valuable complementary technique to epicardial ultrasonography as it allowed the continuous monitoring of ventricular function and volume state immediately after bypass surgery. Problem areas for single plane TOE visualisation were the apical interventricular septum, the right ventricular outflow tract, and the left pulmonary artery. This experience suggests that the main indications for TOE studies in children are (a) specific atrial or atrioventricular junction lesions, (b) in perioperative monitoring, and (c) in the late follow up of atrial baffle procedures, Fontan procedures, and atrioventricular valve repair or replacement, or both.

In anaesthetised children with congenital heart disease TOE is an important and safe diagnostic and perioperative monitoring technique. It complements precardiac studies, providing more detailed information on specific lesions and cardiac function in many instances.
tricular outflow tract, the pulmonary artery system, the muscular ventricular septum, and arterial override (five patients) could be more reliably assessed. Major disadvantages of TOE were the limited number of obtainable scan planes, the limited haemodynamic information that could be derived, and the inferior image quality. Exclusion of residual interventricular shunting or residual outflow tract gradients after bypass was impossible with TOE but was reliably performed with EPI. In contrast TOE provided an improved insight into atioventricular valve function after bypass and permitted continuous monitoring of ventricular function during the immediate and early postoperative period, which was not feasible with EPI.

We conclude that intraoperative TOE and EPI in surgery for congenital heart disease are complementary rather than alternative techniques. The definite advantages of TOE are that it permits continuous monitoring of ventricular function and detailed assessment of atioventricular valve function; EPI is feasible in every patient, provides almost unlimited scan planes, and allows complete haemodynamic evaluation.

**Intraoperative epicardial echocardiography in surgery for subaortic obstruction**

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Intraoperative epicardial imaging, colour flow mapping, and pulsed Doppler were used to assess surgical repair in 15 patients with a preoperative precordial echoangiographic diagnosis of subaortic obstruction (14 “discrete” fibromuscular membranes, one tunnel obstruction; age range 2–30 years; mean 11 years). In all patients with surgically proved membranes epicardial imaging correctly identified the septal and lateral insertions of the membrane. Multiple levels of insertion in two patients and the lateral insertions in six patients were shown only by epicardial imaging, as was the precise extent of the tunnel obstruction. These findings modified the surgical approach in three patients. Additional defects were recognised in four patients: (one associated ventricular septal defect, one calcified spur on the aortic valve mimicking a membrane, and two perforated aortic valve cusps). Two wrong echoangiographic diagnoses were made: a reduplicated anterior mitral leaflet was identified as the cause of subaortic obstruction in one patient (diagnosed by epicardial imaging as having a discrete membrane) and reduplicated echoes from a calcified aortic valve leaflet were wrongly interpreted as a calcified membrane in another. Epicardial imaging after bypass showed remnants of the membrane in three patients and confirmed complete enucleation in others. Although colour flow mapping after bypass showed evidence of residual outflow tract turbulence in 13 out of 15 patients, peak systolic velocities by pulsed Doppler after bypass were <2.5 m/s in all cases (confirmed on follow up precordial echocardiographic studies). In two patients, mild residual dynamic gradients due to persistent septal hypertrophy were recorded, which disappeared on subsequent follow up. Pre-existing mitral regurgitation (4/15 patients) and aortic regurgitation (11/15 patients) remained unchanged in the postbypass studies.

Epicardial imaging after bypass provides superior morphological information about the precise extent and attachments of subaortic obstructive lesions and of associated defects when compared with precordial echocardiography. Epicardial imaging, pulsed Doppler, and colour flow mapping after bypass permit immediate assessment of surgical repair and the exclusion of significant residual obstruction, mitral regurgitation or aortic regurgitation.

**Value of intraoperative epicardial ultrasonography in Fontan type procedures**

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We used intraoperative epicardial imaging, colour flow mapping, pulsed and continuous wave Doppler before and after repair in 24 consecutive patients (median age 3 years 9 months) undergoing a Fontan type procedure in order to evaluate any potential value of this technique for surgical decision making and perioperative management. The preoperative diagnosis was tricuspid atresia in 13 patients, double inlet left ventricle in seven patients, and miscellaneous lesions in four. Before bypass epicardial imaging refined the preoperative diagnosis in five (21%) patients, influencing the surgical procedure in three patients (atrioventricular connection v directatriopulmonary anastomosis in two, Glenn shunt v atropulmonary anastomosis in one). After bypass left ventricular diastolic filling and systolic function was monitored in all patients. Colour flow mapping and pulsed wave Doppler allowed the immediate haemodynamic results to be assessed (repair integrity and pulmonary blood flow characteristics). Ventricular augmentation of pulmonary blood flow was documented by pulsed Doppler in two out of three patients with valved homograft atioventricular connections. After total cavopulmonary anastomosis (five patients) low velocity non-pulsatile flow patterns were observed. Eight important residual lesions were detected in six patients (residual intracardiac shunts in three, mitral valve regurgitation in three, restrictive ventricular septal defect in ventriculoarterial discordance in one, pulmonary artery obstruction in one. From the results after bypass an immediate revision during a second period of bypass was judged to be necessary and feasible in three (12%) patients. One patient with ambiguous results after bypass from colour flow mapping and contrast study (ultrasonic shadowing by prosthetic material) required early reoperation for residual interatrial shunting. Final studies documented optimal repair in 21 (87%) patients. No complications related to the technique were encountered.

Intraoperative Doppler ultrasonography proved to be of unique additional value to the surgical management of patients undergoing a Fontan type procedure. It permitted refinements in the preoperative diagnosis, an excellent assessment of ventricular function, and the identification of residual lesions requiring immediate revision during a second period of bypass.

**Verapamil sensitive ventricular tachycardia: effects of vagal manoeuvres and adenosine**

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Right ventricular outflow tract (RVOT) tachycardia has been shown to be sensitive to both adenosine and verapamil and is thought to be due to triggered automaticity. Fascicular tachycardia is another form of ventricular tachycardia that is sensitive to verapamil but its mechanism is unknown. We studied the effects of vagotonic manoeuvres, intravenous adenosine (up to 0.25 mg/kg in incremental doses), and intravenous verapamil (0.15 mg/kg) during tachycardia in nine patients (mean age 31 (5) years), two with incessant RVOT tachycardia and seven with inducible fascicular tachycardia. The diagnosis was made at invasive electrophysiological study in all patients. No patient had evidence of structural heart disease. Vagal manoeuvres did not have any effect on any tachycardia. Adenosine interrupted tachycardia in both patients with RVOT tachycardia, for a period proportional to the dose of adenosine (from 25–30 s) but had no effect on tachycardia in any of the seven patients with fascicular tachycardia. Verapamil produced stuttering termination of tachycardia with no change in RR interval in both patients with RVOT tachycardia. In the six patients with fascicular tachycardia who were given intravenous verapamil the arrhythmia was slowed and then terminated (from mean RR interval of 362 (58) ms to 488 (97) ms; p < 0.01). In four of these patients RR interval alternation was observed before termination.

The lack of response of fascicular tachycardia to adenosine suggests that the mechanism is different from RVOT tachycardia. The slowing of fascicular tachycardia before termination with verapamil suggests the presence of a calcium channel dependent re-entrant circuit as a basis for the arrhythmia.

Exaggerated dispersion of repolarisation provoked by premature ventricular stimulation: a mechanism for ventricular arrhythmia

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Exaggerated dispersion of ventricular repolarisation may create a substrate for ventricular arrhythmia. We compared steady state variation in monophasic action potential duration at 90% repolarisation (MAP90) between widely spaced right ventricular endocardial sites (range 7–14, mean 11) at two drive cycle lengths in two groups: group 1 (n = 10), patients with normal right ventricular myo-cardium; group 2 (n = 10), patients with disease right ven-tricular myocardium and ventricular tachycardia (VT).

Maximum difference in MAP90 at 600 ms drive cycle length in group 1 was 41.5 (7.3) ms, falling to 27.2 (7.8) ms at 430 ms drive cycle length and was not significantly (p > 0.1) different from group 2 (31.3 (5.8) ms and 30.5 (5.5) ms respectively). We next investigated the effect of perturbation of the steady state difference in MAP90 between simultaneously recorded adjacent right ventricular sites in 10 controls and six patients with right ventricular disease and ventricular tachycardia. Ventricular stimuli of increasing prematurity were introduced on a background of continuous pacing at 600 ms drive cycle length, until the effective refractory period was reached. The difference in MAP90 between adjacent endocardial sites after premature stimulation at effective refractory period +10 ms was significantly greater (p < 0.001) in those with right ventricular disease and ventricular tachycardia (45 (24–5) ms) compared with controls (5 (6–3) ms).

We therefore suggest that dynamic rather than static dispersion of MAP90 may contribute to susceptibility to ventricular arrhythmia.

Quantitative analysis of the P wave in paroxysmal atrial fibrillation

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Signal averaging of the QRS complex can identify patients at risk of ventricular arrhythmias, yet similar techniques applied to the atria have so far been disappointing. Variability in the underlying disease of the patient groups studied and difficulty in identifying late potentials because of interference by His bundle signals during the PR interval may account for these poor results. Using a template recognition system specific to the P wave, we recorded signal averaged electrocardiograms from nine patients with idiopathic paroxysmal atrial fibrillation and from 15 control subjects. From vector magnitude plots of the P wave we calculated P wave duration, area ratio and root mean square voltage above various frequencies, and peak and mean spatial velocity. Significantly greater high frequency activity and spatial velocity were observed in the group of patients with paroxysmal atrial fibrillation (root mean square voltage > 40 Hz, paroxysmal atrial fibrillation 327 (92) mV, control 235 (34) mV, p = 0.03. Peak spatial velocity, paroxysmal atrial fibrillation; 6-44 (1-76) mV/s, control 4-56 (0-16) mV/s, p = 0.03).

These observations support previous intracardiac data that implicate delay and fragmentation of intra-atrial conduction in the pathogenesis of paroxysmal atrial fibrillation.

Acceleration of pre-excited tachycardias by adenosine

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The use of intravenous adenosine has been recommended by several groups for the acute management of broad complex tachycardia. The short half life of this agent, however, has precluded assessment of its effects on refractoriness of accessory pathways and its effects on pre-excited tachycardias are not known. To assess the effects of adenosine in this condition it was administered to 26 patients with pre-excitation. Intravenous adenosine (12 mg) was administered to seven patients (group 1) during atrial pacing at a cycle length 20 ms below that required to cause stable 2:1 conduction block in the accessory pathway (mean pacing cycle length 266 (35) ms). After adenosine transient 1:1 conduction occurred through the accessory pathway in six of the seven patients, indicating a shortening of antegrade refractoriness. In two patients this effect was abolished after intravenous propranolol (10 mg). Adenosine was given to 19 patients (group 2) during induced pre-excited tachycardia at a mean dose of 0.16 mg/kg (range 0.1–0.25). Pre-excited atrial flutter was accel-
erated in four patients owing to shortening of flutter cycle length (203 (5) ms to 163 (13) ms; p < 0.05). The minimum RR interval in pre-excited atrial fibrillation decreased in seven out of eight patients (259 (50) ms to 230 (42) ms; p < 0.01). Pre-excited junctional tachycardia was terminated in five out of seven patients. In one patient anterograde tachycardia accelerated (cycle length 340 ms to 250 ms) owing to a sudden shortening of ventriculoatrial conduction time with no detectable change in atrial activation sequence.

Intravenous adenosine causes a decrease in the anterograde refractoriness of accessory pathways and a decrease in minimum RR interval during pre-excited atrial fibrillation. Adenosine may also cause an increase in the ventricular rate of pre-excited atrial flutter and antidromic tachycardia through mechanisms independent of accessory pathway anterograde refractoriness.

High fidelity right atrial pressure recording during cardiac arrhythmias

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The performance of a high resolution (33 Hz) fibreoptic pressure catheter within the right atrium was studied during cardiac arrhythmias. In 15 patients (mean age 35 years, nine females) undergoing electrophysiological study the unfiltered signal was amplified and recorded on to paper. During sinus rhythm and atrial pacing a constant amplitude deflection occurred during atrial systole (a wave). During atrioventricular re-entrant nodal (six patients) the a wave was simultaneous with ventricular systole (v wave), producing a characteristic sinusoidal pattern. In atrioventricular re-entrant tachycardia (four patients) the a wave produced a characteristic distortion of the sinusoidal pattern. In atrial fibrillation (three patients) the waveform was of varying amplitude and frequency, and during atrial flutter a waves occurred alternately with v waves. During ventricular tachycardia without ventriculoatrial conduction (two patients) there were large amplitude, irregular deflections unrelated to the ventricular electrogram.

High fidelity pressure recordings produced characteristic appearances for pattern recognition of each arrhythmia studied. It permitted determination of the temporal relation between electrical and mechanical cardiac events and may have potential in the detection and recognition of cardiac arrhythmias.

Recurrence of accessory pathways after surgery: septal pathways and the "rim effect"

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Surgery for atrioventricular accessory pathways was performed on 87 patients (53 male, mean age 31 years, range 11 to 68 years) with 91 pathways. Seventy-six patients had ventricular pre-excitation; 44 pathways were left free wall, 20 left posteroseptal, eight right posteroseptal, six right free wall, and 13 anteroseptal. Four patients had two pathways (three left free wall and left posteroseptal, one left free wall and anteroseptal). Endocardial dissection was performed in 74 patients, supplemented with cryoablation in a further four patients; seven patients had additional dissections plus cryoablation, and two patients had a combined approach. The pathways recurred in eight patients (9%), three within one week of operation and five more than one month from operation. Seven of the recurrences were in the first 50 patients. No recurrences were due to a second pathway. Twenty percent of left posteroseptal pathways and 31% of anteroseptal pathways recurred, while only 4% of free wall pathways recurred. Reoperation was successful in all patients. Two patients with recurrence of their left free wall pathways had pre-excitation of the same electrocardiographic morphology as preoperatively, but with a longer P delta interval. At reoperation the earliest atrial activation during tachycardia had changed to the left posteroseptal position. Cryoablation or incision into the mitral annulus in this position resulted in abolition of the pathways in both patients. The same phenomenon was subsequently observed intraoperatively in two further patients, and again cryoablation or incision into the mitral annulus in this area abolished the pathways. This phenomenon can be explained by the atrial insertion of the pathway being in a rim of atrial tissue left on the mitral annulus after dissection. Thus, retrograde activation of the atria is through the exit of the rim in the posteroseptal region, whereas anterograde conduction is unchanged but prolonged.

We conclude that left posteroseptal and anteroseptal pathways have a higher recurrence rate than free wall pathways (6/33 v 2/58; p < 0.05), and this should influence selection of patients for surgery. Repeat surgery is successful in abolishing these pathways. Care must be taken with left free wall pathways to prevent conduction through an atrial rim.

Cerebral metabolic autoregulation is disturbed in children undergoing cardiopulmonary bypass

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There is a high incidence of neurological morbidity after paediatric cardiopulmonary bypass surgery. Our hypothesis is that cardiopulmonary bypass surgery disturbs the autoregulation of cerebral blood flow in relation to cerebral metabolic rate, making children susceptible to ischaemic brain damage at times of low cerebral perfusion or high cerebral metabolic rate. We made 73 serial measurements of cerebral blood flow and cerebral metabolism in 17 children (aged 6 weeks–6 years) undergoing cardiopulmonary bypass surgery. A standard anaesthetic was used (enflurane 0–2%, fentanyl 30 μg/kg, membrane oxygenator). Cerebral blood flow was measured with the Kety Schmidt technique and cerebral consumption or production of oxygen, lactate, and pyruvate determined by arteriosuperior jugular venous bulb concentration differences (AJVD) × cerebral blood flow. Cerebral blood flow ranged from 0.09–1.38 ml/g/minute and cerebral oxygen consumption from 125–4658 nmol/g/minute. Metabolic autoregulation of cerebral blood flow was disturbed in all children. Before and after cardiopulmonary bypass, high cerebral metabolic rates (up to three times normal) were associated with normal cerebral blood flow. That cerebral blood flow was
insufficient for cerebral metabolic rate was indicated by AJVDO₂s up to four times normal and significant cerebral lactate production. The closest link between cerebral blood flow and cerebral metabolic rate occurred during hypothermic bypass when metabolic rates and blood flows were both lower than normal and AJVDO₂s were close to the normal range.

We conclude that children undergoing cardiopulmonary bypass have disturbed metabolic autoregulation, the effects of which are minimised during hypothermia. That this occurred before bypass suggests that the stress response to major surgery—for example, sternotomy—may have adverse effects on cerebral autoregulation.

Pulmonary autograft for aortic valve replacement: 22 years later
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The endothelium dependent vasodilator substance P dilates normal and diseased coronary vessels in humans in vivo and produces a maximal response similar to that seen with intracoronary isosorbide dinitrate (ISDN). Twelve cardiac transplant recipients underwent intracoronary infusions of substance P after their annual investigations. All patients were well with no evidence of rejection and with angiographically normal coronary arteries and no evidence of accelerated coronary sclerosis. Substance P in increasing doses was infused at 2 ml/min for two minutes into the left coronary circulation in 11 transplant recipients and into the right coronary artery in one recipient followed by 2 mg isosorbide dinitrate infused over two minutes. Coronary artery diameters were measured in 23 vessel segments in 12 transplant recipients. The following doses of substance P (pmol/l) were infused: saline, 1-4, 2-8, 5-6, 11-2, 22-4, and isosorbide dinitrate. The mean (SE) percentage increase in diameter to increasing doses of substance P were as follows: 0 (0), 6-5 (2-9), 10-9 (2-9), 12-1 (2-9), 16-5 (2-6), 19-2 (3-1), 25-8 (2-2) respectively. In 15 vessel segments the maximal response occurred at the two maximal doses of substance P and the remainder produced the maximal response at the lower doses of 2-8 and 5-6 pmol/l. The maximal response to substance P was 22% (SE 2-9%) (mean percentage change in diameter). This was not significantly different from that achieved with isosorbide dinitrate. There was preserved endothelial dependent vasodilation in transplanted coronary arteries to substance P comparable with that seen with nitrates.

We conclude that coronary endothelial function is preserved in transplant recipients and that substance P provides a useful tool for testing endothelial function in these patients.

Adenosine enhances the efficacy of hypothermic cardioplegic arrest
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We previously showed the beneficial effect of adenosine during reperfusion after ischaemic arrest. This study was designed to evaluate its potential role as an additive during hypothermic cardioplegia in a dose-response study in the isolated working rat heart. With a protocol that mimics clinical practice in the United Kingdom groups of hearts were subjected to three hours of ischaemic arrest at 20°C with multidose infusions of St Thomas’s Hospital cardioplegic solution No 1 every 30 minutes. Adenosine was added to the cardioplegic solution in concentrations of 0 (control), 0-1, 5-0, 10-0, and 20-0 mmol/l. Six hearts were studied in each group. The recovery of cardiac function was enhanced in all hearts that received adenosine, and the optimum concentration was found to be 10 mmol/l. Mean recovery of cardiac output (expressed as a percentage of its preischaemic control value) in this group was 61-8% (3-7%) in contrast with 35-4% (5-1%) in the control group (p < 0-01). Thus, in its optimal concentration, adenosine improved the efficacy of the cardioplegic solution by almost 75%. Parallel metabolic studies were performed to determine myocardial nucleotide content at various times. Adenosine significantly increased coronary flow during the ischaemic period, and its beneficial effect might have been mediated by better perfusion of the microvasculature.

These observations further support the suggestion that adenosine may have potential in surgical practice, particularly during extended periods of cardioplegic arrest.

Preserved endothelial dependent response to intracoronary substance P in cardiac transplant recipients
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Does hyperglycaemia contribute to intellectual dysfunction after cardiac surgery?

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Evidence from published work on animals and clinical evidence from published work on stroke and cardiac arrest suggests that hyperglycaemia during cerebral ischaemia can influence cerebral recovery after an ischaemic insult. If the cerebral changes that occur after cardiopulmonary bypass are caused by microemboli and are therefore ischaemic in origin then hyperglycaemia during cardiopulmonary bypass may be important.

Routine practice at this hospital has been to use either a 5% dextrose or Hartmann’s solution prime in the cardiopulmonary bypass circuit. There was no gross clinical difference between the two sets of patients. It was therefore considered ethically acceptable to study the outcome in the two groups in a prospective study. Seventy patients having elective coronary revascularisation were prospectively randomised into either of the primes. The groups were comparable in age, sex, and bypass and cross clamp times. Neuropsychological assessment was performed with a well proved test battery before and eight weeks after surgery. Blood glucose concentrations rose to a mean of 26 mmol/l in the 5% dextrose group and 6 mmol/l in the Hartmann’s group during bypass. There were no deaths in either group, there were two clinical neurological events, both occurring in the hyperglycaemic group, and both patients made good recoveries. Neuropsychological deficit was defined as a deterioration in two or more tests of 1 SD from the preoperative mean group score between preoperative and eight week testing. With this definition there was no difference between the groups; 36% of patients in each group showed significant deficits. More detailed analysis of the results did, however, show differences. When score changes between the pre-operative and eight week tests were assessed it was found that in 17 out of the 18 versions of the tests more patients in the hyperglycaemic group deteriorated than did the normoglycaemic controls. With a two tailed binomial statistic this difference was significant.

Hyperglycaemia may be a detrimental factor in the development of intellectual morbidity after cardiac surgery. We advocate the use of a non-glucose containing prime, regular monitoring of plasma glucose concentration, and the prompt correction of hyperglycaemia should it occur during cardiopulmonary bypass.

Mechanical support for acute ventricular failure

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In 1989 a total of nine adults had short to medium term ventricular assistance with the Centrimed centrifugal pump. The eight male patients and one female patient (age range 21 to 54 years) all had severe ventricular failure that could not be managed without full support for one to five days. Six patients had left ventricular assistance, one had bilateral support, and the remaining two patients had right sided support only. Complications included severe bleeding necessitating further exploration and renal failure; there were no problems from emboli or from failure of the centrifugal pump itself. Of the four survivors, two had peri-transplantation acute heart failure, one was used as a deliberate bridge to cardiac transplantation after arrhythmia surgery, and the fourth was weaned from his device after five days of support. The survivors all had their device inserted at an early phase in their decline, illustrating the importance of patient selection and timing. All survivors were New York Heart Association class I, including the one weaned patient, whose ventricle was barely contracting at the time of insertion.

The cost of the centrifugal pumps is cheap relative to the cost of sophisticated ventricular assist devices and provides encouraging results for medium term support. The use of these pumps in the context of acute cardiogenic shock may prove worth while.

Potential impact of population screening for prenatal diagnosis of congenital heart disease

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Mid-trimester screening for detection of congenital heart disease (CHD) is now advocated in the United Kingdom. To assess the potential impact we reviewed 350 consecutive neonatal admissions up to September 1989 (group A), and prospectively assessed 81 consecutive infants admitted since then (group B) at a single centre. Severe CHD was defined as lesions requiring high risk, multiple, or purely palliative surgery for survival. In group A 167 and of 350 (47%) patients, all with severe CHD, could have been detected on a screening four chamber view at 18–20 weeks gestation. In group B 55 out of 81 (68%) patients, all with severe CHD, were potentially detectable prenatally; 16 out of 26 of the remainder also had severe CHD. Only 1 out of 81 (1%) did not have CHD. All 81 had received fetal ultrasoundography, but scanning was performed only before 18 weeks’ gestation in 54 out of 81 (67%), too early to reliably detect CHD. Six out of 81 (7%) were high risk pregnancies for CHD, and 6 out of 81 (7%) had extracardiac anomalies. Third trimester diagnosis of severe CHD occurred in five cases. Reassurance to mothers that the fetal heart was normal had been provided in 37 out of 81 (46%). Forty one out of 71 (58%) mothers in group B with infants with severe CHD volunteered their preference for termination of pregnancy if mid-trimester diagnosis had been available.

Consequently, mid trimester detection of CHD rarely occurs despite almost universal fetal scanning. Major training at primary scan level and modifications of the timing of existing fetal anomaly screening is required, but the potential impact of effective screening on the incidence of severe CHD postnatally is considerable.

Use of flecainide in fetal atrial tachycardia

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Flecainide is a potent antiarrhythmic drug that has been shown to be valuable in treating atrial, junctional, and ventricular arrhythmias. After recent reports of the adverse side effects of flecainide treatment, however, it has been
advised that this drug should be confined to high-risk patients and those with life threatening arrhythmias. The intrauterine development of a fetal tachycardia and heart failure is a life threatening condition for the fetus with a mortality that is reported to be between 20% and 50%. Many drugs have been reported to be useful in the treatment of fetal tachycardias—for example, digoxin, verapamil, quinidine, procainamide, amiodarone, and propranolol—giving some indication of the difficulty of managing these cases successfully. We used flecainide in a group of 13 patients for a fetal atrial tachycardia associated with intrauterine cardiac failure. Eleven of the 13 patients responded by conversion to sinus rhythm. One fetus died in utero and one fetus the rhythm subsequently converted with alternative treatment. Of the 11 patients, nine were alive and well three months to two years after delivery and two are not yet delivered. These results compare favourably with previous forms of antiarrhythmic treatment used in the fetus.

Flecainide is a useful drug in selected cases of fetal atrial tachycardia associated with intrauterine cardiac failure, but its use should be restricted to centres experienced in the management of these cases.

R wave synchronised atrial pacing as an adjunct to the management of His bundle tachycardia after surgery

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Eleven children aged 3 days to 13 years were treated with R wave synchronised atrial pacing for His bundle tachycardia (HBT) after bypass cardiac surgery for various cardiac anomalies. All patients developed severe low cardiac output with the onset of HBT. Maximum rate of HBT was 170–250 beats/min. Eight children were treated with antiarrhythmic drugs, including amiodarone in six, flecainide in one, and digoxin in three, with some decrease in rate. Ten children were surface cooled to a core temperature of 32°C or less, which similarly resulted in a decrease in rate without restoration of sinus rhythm. Atrial pacing restored atrioventricular synchrony in each patient. The pacing stimulus was synchronised either manually or automatically to the R wave of the HBT so that atrial depolarisation preceded the next R wave by an appropriate PR interval. The blood pressure increased immediately with the onset of atrial pacing in 10 (mean 15 mm Hg). This was associated with an increase in urine output and allowed a decrease in inotropic support. One child developed atrial flutter necessitating cardioversion but no other side effects were seen. Despite these measures four children died. Of the 7 survivors, six sustained sinus rhythm which developed from 2 to 10 days after the onset of HBT. One child has severe neurological impairment as a consequence of low cardiac output, the others are alive and well.

The R wave synchronised atrial pacing is a useful adjunct to the management of life threatening HBT after surgery.

Effect of balloon dilatation of right ventricular outflow tract on size of pulmonary valve annulus and arteries in tetralogy of Fallot

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The effect of balloon dilatation of right ventricular outflow tract on the pulmonary valve annulus and arteries was evaluated in six children with tetralogy of Fallot who required palliation for increasing cyanosis. A total of 13 procedures were performed. The age at the first balloon dilatation ranged from 0·6 to 12·7 months (mean 7·2 months). The diameters of the pulmonary valve annulus and right and left pulmonary arteries were measured angiographically before the balloon dilatation and a mean of 4·8 months (range 1·5–9·6 months) later at the next procedure. Pulmonary valve annulus diameter increased from 7·1 (2·2) mm to 9·8 (2·4) mm after balloon dilatation (p = 0·01); diameter of the pulmonary arteries increased from 6·9 (1·9) mm to 8·9 (1·7) mm on the right (p < 0·01) and 6·7 (2·6) mm to 8·0 (2·6) mm on the left (p < 0·04). Predicted right ventricular to left ventricular systolic pressure ratio after surgical correction without a transannular patch based on these measurements decreased from 0·8 (0·22) before to 0·58 (0·10) after balloon dilatation. No surgical shunts were required for palliation. Three of the patients had surgical correction at a mean age of 18 months.

In conclusion, these results show that there is an increase in size of the pulmonary valve annulus and pulmonary arteries after balloon dilatation in tetralogy of Fallot.

Continuous wave Doppler after surgical repair of coarctation of the aorta

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High flow velocities in the descending aorta may sometimes be detected by continuous wave Doppler after satisfactory repair of coarctation. To investigate this phenomenon the pressure gradient across the aortic arch and flow velocities in the descending aorta were measured simultaneously in 20 patients aged 4·7 to 33 years undergoing cardiac catheterisation. Peak to peak instantaneous peak pressure drop across the arch were measured with a double lumen catheter. Velocity in the descending aorta was recorded with a continuous wave transducer from the suprasternal notch and peak pressure drop was calculated with the modified Bernoulli equation. Catheter instantaneous peak gradient was higher than peak to peak in all but one case with variable differences (−2 to +31 (mean 12·4) mm Hg) between the two measurements. Similarly, Doppler instantaneous peak gradient was higher than catheter peak to peak with differences of −3 to +28 (mean 11·5) mm Hg. Comparison of Doppler and catheter instantaneous peak gradient showed a mean difference of only 0·9 mm Hg, but individual differences ranged from −17 mm Hg to +22 mm Hg. These errors may be due to poor alignment with flow, inability to measure and correct for proximal flow velocity with continuous wave Doppler, and complex flow dynamics in the aortic arch.
Continuous wave Doppler gradient after repair of coarctation must be interpreted with caution. It is almost always higher than peak to peak pressure drop at catheter and even when compared to instantaneous peak gradient, measured invasively it may importantly overestimate or underestimate pressure drop.

**Primary balloon coarctation aortoplasty in neonates**

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Primary balloon coarctation aortoplasty was attempted in 10 consecutive neonates (age range 2–23 days) with coarctation of the aorta. Associated abnormalities included transposition of great arteries (one), ventricular septal defect (five) and ductus arteriosus (five, including three receiving alprostadil). It was not possible to cross the coarctation site in one patient. In two patients with severe isthmal hypoplasia there was no change in the gradient after dilatation. In the remainder the residual gradients were trivial (gradient before dilatation, 33 (13), after 7 (8) mm Hg, p < 0.001) and angiography showed complete relief of coarctation. Two patients subsequently had no evidence of recoarctation 22 and 37 weeks after dilatation. Five developed severe recoarctation between 5 and 12 weeks after dilatation. Recoarctation was rapidly progressive in three, there having been no appreciable gradient on Doppler as recently as two weeks before its development, and more slowly progressive in two. Three patients underwent a second dilatation procedure. One patient subsequently remained well with no residual gradient 18 weeks later. Restenosis occurred within eight weeks in the other two. All failures have undergone successful surgical repair.

Primary balloon aortoplasty can be performed in most neonates with excellent immediate results. Severe isthmal hypoplasia is, however, a contraindication to balloon dilatation and early restenosis is an important problem. These results do not support the continued use of primary balloon coarctation aortoplasty in neonates.

**Standardised exponential exercise protocol**

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The development of a standardised exercise protocol has been hindered by the use of different exercise modes. On a treadmill work at each stage is dependent on body weight, but during bicycle exercise work is weight independent. We have designed a new treadmill protocol with one minute stages, beginning at a low workload (predicted oxygen consumption (VO₂) 7 ml/kg/min) and increasing exponentially to a predicted VO₂ of 50 ml/kg/min after 15 minutes (standardised exponential exercise protocol (STEEP) test). After adjustment for body weight this protocol is also suitable for a bicycle ergometer. The STEEP test was initially validated in 30 normal male subjects (aged 29–55), each of whom performed the two protocols in random order. The mean VO₂ rose exponentially, and close agreement was observed between the treadmill and the bicycle protocols. A higher proportion of subjects completed the treadmill protocol (27 ν 15; p < 0.005). Sub-maximal heart rates were slightly higher during the bicycle test. Twenty subjects with mild to moderate heart failure (VO₂max, 12–25) were then exercised to symptom limited maximum with the STEEP tests. The mean VO₂ was similar for each stage of the treadmill and the bicycle protocols, as in the normal subjects. Exercise time and VO₂max were, however, significantly higher with the treadmill test.

This protocol is the first to use an exponential rise in workload. By adjusting for body weight similar mean VO₂ was obtained for each stage of the bicycle protocol as the treadmill protocol in both normal subjects and patients with heart failure. As VO₂max is higher with treadmill testing, however, the exercise time is also significantly longer.

**Role of intraoperative epicardial ultrasonography in surgery for congenital heart disease**

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In a prospective study we used intraoperative epicardial echocardiography (cross sectional imaging (epi-2D)), colour flow mapping (CFM), and pulsed and continuous wave Doppler (PW, CW) in 308 patients both before and after cardiopulmonary bypass for total correction of congenital heart disease to determine the potential value of this technique in surgical management. Lesions studied were isolated ventricular septal defect (76), atrial septal defect (eight), atriointerventricular septal defect (31), Ebstein's malformation (nine), Fontan procedures (24), transposition of great arteries (45), Fallot (19), double outlet right ventricle (11), left ventricular outflow tract obstruction (15), aortic or mitral disease (16), miscellaneous (36), and reoperations (18). Studies before repair (epi-2D, CFM, PW) refined the pre-operative diagnosis in 87 (28%) patients; this influenced surgical management in 36 (12%) and altered the preoperative diagnosis in 10 (3%). Studies before bypass were, however, incomplete (11 patients) or misleading (seven patients) in 6% of the patients.

Studies after repair permitted the immediate assessment of the surgical repair, and the monitoring of volaemia and ventricular function and aimed at excluding any significant residual lesion. Based on the results of these studies immediate revision during a second period of bypass was performed in 10 (3.3%) patients. The haemodynamic information obtained was valuable for postoperative management in about a quarter of the patients. Only two patients required early reoperation (one because of missed lesions, one because of misinterpretation). Problems inherent in the interpretation of the epicardial studies were (a) flow masking behind prosthetic material used for the repair; (b) limited access (large transducers relative to sternotomy); (c) multiple transducers being required for complete investigations; and (d) difficulty in measuring residual lesions. On line interpretation is a problem. Relevant complications were not encountered.

The major contributions of intraoperative Doppler ultrasonography to surgery for congenital heart disease are
Ambulatory haemodynamic monitoring: a new method for simultaneous recording of pulmonary and systemic arterial pressures and ST segment

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A modified (digital) Oxford system for recording intrarterial blood pressure and frequency modulated electrocardiogram has been combined with a new method for long term pulmonary artery pressure monitoring. A catheter tip manometer is inserted into the pulmonary artery in a specially profiled sheath which allows isolation of the sensor for in vivo gain and zero drift calibration. All signals are recorded on to a modified MR10 recorder, pressure waveforms being in digital format, sampled at 40 Hz with 0·3 mm Hg resolution. The frequency response of the sheath or sensor was flat from 1 to 20 Hz with negligible phase distortion or square wave overhoot. The recording reply system has a band width of 20 Hz and was linear within 0·6 mm Hg from 0 to 70 mm Hg. Beat by beat pulmonary artery pressures obtained by this system simultaneously with an on line statham P50 transducer showed preserved waveforms and pressures within 0·3 mm Hg (systolic) and 2·0 mm Hg (diastolic) during pacing tests. Recordings in 24 subjects over 24-58 hours gave a pulmonary artery pressure range of 17·2-57·34 mm Hg. Each recording had 5-10 calibrations showing start end zero drift of -2 to +2 mm Hg, with some intermediate calibrations giving -3·5 to +7·5 mm Hg drift; in the latter case the transducer failed. Reproducibility between days 1 and 2 of the recording (n = 20) was 1·8/0·9 mm Hg.

This system provides accurate long term pressure recordings combined with ST segment analysis for the study of myocardial ischaemia and function and for the assessment of interventions.

Angiographic and ischaemia correlates of transient dilatation of the left ventricle on dipyridamole stress thallium-201 testing

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The occurrence and significance of myocardial ischaemia dilatation of the left ventricle (TID) during dipyridamole thallium-201 scintigraphy was studied in 73 patients undergoing coronary angiography. The TID ratio was calculated by dividing the computer derived left ventricular area on the initial anterior planar image by the image at four hours. The extent of ischaemia was assessed by using the Thallium 201 reversibility score (initial—four hour score) and a score of > 7 used to represent extensive ischaemia. In 11 patients with non-significant (< 50%) stenosis the TID ratio was 0·98 (0·046). An abnormal TID (> 3 SD) was defined as ≥ 1·12. The 15 patients with abnormal TID had a higher incidence of critical (≥ 90%) stenosis (93%), collateral (67%), and extensive ischaemia (54%) and a lower incidence of myocardial infarction (33%) than the 58 patients with a normal ratio (55%, 24%, 12·5%, and 72% respectively; p < 0·05). The incidence of dipyridamole induced positive electrocardiograms, increased lung uptake and chest pain was not significantly different. An abnormal TID ratio was a sensitive (63%) and specific (85%) marker of triple vessel critical coronary disease.

Thus, TID may be observed during dipyridamole thallium-201 testing and implies extensive myocardial ischaemia caused by underlying critical coronary stenosis.

Adverse respiratory reactions to intravenous dipyridamole for myocardial stress thallium studies

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To assess whether the use of dipyridamole stress in myocardial thallium studies is associated with adverse respiratory effects 22 consecutive adults (12 subjects with chronic airflow obstruction and 10 with no history or signs of respiratory disease) referred for imaging were studied with serial spirometry before and during the stress imaging procedure. Triplicate measures of forced expiratory volume in one second (FEV1) were taken at baseline, at subsequent spirometry repeated 10 minutes after starting dipyridamole infusion (0·57 mg/kg), and again at 25 minutes after initial cardiac imaging. Analysis of variance was used to assess the effect of the drug on respiratory function. Individual responses were varied, but overall there was a significant decline in FEV1 from baseline, with a mean (SE) reduction of 42·9 ml (p < 0·0001) at 10 minutes and of 48·9 ml (p < 0·0001) at 25 minutes; in most cases the change was asymptomatic. In those with chronic reversible airflow obstruction resting FEV1, fell by 4·5% (58·11 ml; p < 0·0001) at 10 minutes, and by 4·7% (61·11 ml; p < 0·0001) at 25 minutes compared with falls of 1·0% (22·15 ml; NS) and 1·4% (33·15 ml; p < 0·05) at 10 and 25 minutes in those without respiratory disease. In two subjects, both with chronic reversible airflow obstruction, symptomatic worsening breathlessness developed associated with falls in FEV1, of 12% (196 ml) and 23% (125 ml) respectively. In one, breathlessness and change in FEV1 abated spontaneously by 35 minutes. The other subject and another subject with a fall of 11% (160 ml) without breathlessness were given intravenous aminophylline with prompt alleviation of symptoms and changes in FEV1. In none did examination or lung uptake support a diagnosis of pulmonary congestion. Changes in FEV1 were unrelated to presence or absence of reversible myocardial thallium defect.

The use of intravenous dipyridamole for cardiac studies can cause reduction in FEV1 sufficient to be clinically important for those subjects with known chronic reversible airflow obstruction and can induce clinical asthma. Aminophylline seems rapidly to reverse these effects and should be available for immediate intravenous use should this occur.
Role of transoesophageal echocardiography in evaluation of atrial baffle function

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Abnormalities of atrial baffle function can develop early or late postoperatively after an atrial correction procedure and may occur in patients with and without symptoms. Methods previously used to assess atrial baffle function have included precordial echocardiography and cardiac catheterisation. Single plane transoesophageal echo-cardiography (TOE) can provide an optimal assessment of the atrial morphology and flow patterns within both atrial chambers. To evaluate whether TOE offers an alternative investigative approach to the spectrum of atrial baffle abnormalities we investigated 15 patients (14 Mustard, one Senning; mean age 16·3 years) on an outpatient basis (eight adults) or under heavy sedation or during general anaesthesia for cardiac catheterisation (seven children). TOE findings were compared with those derived from precordial echocardiography and cardiac catheterisation in every case. Furthermore, the transoesophageal scan planes that must be recorded for evaluation of the whole systemic and pulmonary venous pathways were correlated with anatomical specimens. As precordial ultrasonography permitted the visualisation only of the supraventricular portion of the systemic venous pathway it failed to identify the wide range of systemic venous baffle abnormalities present (3/15). TOE studies using cross sectional imaging, colour flow mapping, and pulsed Doppler showed superior limb obstruction in six patients (three severe, three mild), mid-baffle obstruction in two, and inferior limb obstruction in two. The entire pulmonary venous pathway could be scanned by both TOE and precordial echo-cardiography. Both techniques identified three cases of mid-pulmonary venous obstruction (two mild, one moderate). Individual pulmonary vein velocity profiles however, could be recorded only with TOE pulsed Doppler. Precordial studies detected residual baffle leaks (one large, two small), in only three patients whereas TOE flow mapping identified 11 such baffle leaks (one large, 10 small), which in two patients were multiple.

We conclude from these findings that TOE was of great additional value in the definition of a range of often clinically unsuspected baffle abnormalities. In our opinion it is likely to become the investigative method of choice for baffle malfunction.

Residual ductal tissue in aorta: histological study in resected specimens of coarctation

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Subclavian flap aortoplasty for coarctation repair in the first three months of life has been associated with a significant incidence of recurrence. Having had such an experience, we extended the use of resection and end to end anastomosis to this age group. The histological findings in 23 specimens resected between 1985 and 1987 are reported and the implications for recurrent coarctation are discussed. In 22 of the 23 specimens there was a circum-ferential sling of ductal tissue around the aorta at its junction with the ductus. In all 22 cases projections of ductal tissue extended distally for a variable length from the sling. These projections were on the side of the aorta opposite the ductus and on the aorta below its junction with the ductus. The most distal part of the projections were not completely excised in 11 patients. The aortic incision in subclavian flap aortoplasty is likely to be within the projection of ductal tissue opposite the ductus and may or may not extend beyond it into normal aortic tissue. There would then be a residual oblique circumferential sling of ductal tissue passing beyond the apex of the flap, the maturation of which could lead to recurrence coarctation. In conclusion, these findings suggest a histopathological basis for recurrence of coarctation after subclavian flap aortoplasty and support the view that the flap should extend far down the descending aorta.

Magnetic resonance imaging: evaluation of the pulmonary arteries in right heart obstruction

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Since November 1987 the pulmonary arteries of 30 patients (age range 0-03 to 12·8 years, mean 3·0 years) with obstruction of the outflow of the right ventricle have been studied with a 1·5 T magnetic resonance imaging system. Fifteen had tetralogy of Fallot, two double outlet right ventricle with pulmonary stenosis, and 13 pulmonary atresia. Nineteen of the studies used a head coil (32 cm) and two another in the older age group used the standard body coil. All 30 children had echocardiography before magnetic resonance imaging and 27 had angiography. Multiple slices (5-7 mm thick) were acquired in straight or oblique transverse and coronal planes, depending on individual anatomy. The images obtained were subsequently reviewed to evaluate our ability to show pulmonary artery anatomy. In two patients presence of central pulmonary arteries was excluded. In 27 of the patients the pulmonary trunk, the bifurcation, and right pulmonary artery up to the first hilar branch were well demonstrated. The left pulmonary artery was more difficult to image successfully. It was imaged in its entirety in 12, these patients being predominantly in the most recent part of the series. Only the proximal portion was imaged in another 13 patients. In three patients the imaging of the left pulmonary artery was unsuccessful. The best images of the left pulmonary artery were obtained in various planes in different patients. The most consistently successful plane was oblique coronal planned from the initial transverse images. Magnetic resonance imaging of the pulmonary arteries in patients with congenital heart disease is a valuable additional technique, but successful imaging requires careful selection of appropriate oblique imaging planes.

Comparative roles of epicardial and precordial echocardiography in the assessment of surgical repair for congenital heart defects

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In 94 consecutive patients (age range 3 days–68 years; mean 7 years) undergoing surgical repair of a congenital heart defect via a median sternotomy the results of epicardial cross sectional (epi-2DE) and Doppler colour flow imaging after bypass were compared with those of sequential precordial echocardiography (a) within 24 hours of surgery and (b) after hospital discharge. There were two intraoperative deaths and two early deaths (within 10 days of surgery) associated with poor systemic ventricular function on epi-2DE. In the remainder during subsequent precordial echocardiography the systolic blood pressure was greater than at epi-2DE by a mean of 24 mm Hg (range -15 to +40 mm Hg). In six out of seven patients with significant residual defects, epi-2DE and Doppler colour flow imaging correctly identified the defect, enabling surgical revision during a second period of bypass. In one patient a residual shunt at atrial level after a total cavopulmonary anastomosis was identified by contrast precordial echocardiography 24 hours later and required immediate reoperation. Minor degrees of peri-patch shunting was a common finding, and persisted at the time of hospital discharge in 17 out of 46 patients who had undergone patch closure of a ventricular septal defect as part of the surgical procedure. Additional trabecular ventricular septal defects were missed on epicardial colour flow imaging in three patients, one of whom required subsequent reoperation. Epi-2DE with spectral Doppler underestimated residual outflow tract gradients in five patients who had calculated instantaneous systolic gradients on follow up precordial echocardiography of between 50 and 70 mm Hg. Residual left atrioventricular valve regurgitation after repair of complete atrioventricular septal defect was also underestimated by epicardial colour flow imaging in three patients.

Epi-2DE and Doppler colour flow imaging permits the recognition of the majority of residual defects requiring immediate reoperation. Documentation of poor ventricular function after bypass was associated with a higher mortality. Assessment of residual outflow tract gradients or valve regurgitation by epicardial echocardiography is, however, inaccurate in view of the rapidly changing haemodynamics.

Ventricular septal defect in Yucatan miniature pigs

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In an effort to associate morphological features of ventricular septal defect with patterns of inheritance we studied the hearts from a colony of Yucatan miniature pigs with spontaneously occurring congenital heart defects. Ventricular septal defect was encountered in 57 out of 81 neonates from 15 consecutive litters. Of 73 hearts preserved for morphological assessment, 52 were found to have defects within the ventricular septum, noticeably similar to those observed in humans with deficient ventricular septum. Three of these hearts showed evidence of spontaneous closure of pre-existing defects. The defects were perimembranous in 34, being characterised by fibrous continuity between the leaflets of the tricuspid and aortic valves. These defects extended so as to open across the apical trabecular septum in six cases and toward the subpulmonary outlet in 28, though involvement of septal musculature was usually slight. Defects surrounded by muscle and opening to the subpulmonary outlet were found in 12 pigs. Defects characterised by absence of the outlet septum and fibrous continuity between the leaflets of the aortic and pulmonary valves (doubly committed juxta-arterial defects) were found in a further six hearts, two of which had fibrous continuity between the aortic and tricuspid valves, whereas the remaining four had muscular posteroinferior rims. Prolapse of the right coronary leaflet of the aortic valve was found in 14 hearts, eight with perimembranous, two with muscular, and four with doubly committed defects. Atrial septal defects were found in 12 of the 52 hearts with deficient ventricular septation; only one

Intraoperative ultrasound assessment of the arterial switch operation

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The arterial switch operation induces acute changes in both ventricular function and geometry. The time course and nature of these changes immediately after bypass and their relation to the final outcome has not previously been documented. Final outcome is also determined by other factors such as successful coronary reimplantation and unobstructed great vessel anastomosis. Intraoperative ultrasound studies might be able to monitor the changes in both global and segmental left ventricular function and define any significant residual anatomic lesion. Therefore 37 consecutive patients (31 neonates) undergoing a switch operation were studied prospectively by epicardial ultrasonography using cross sectional and M mode echo cardiology, colour flow mapping, and spectral Doppler. Echocardiography before bypass documented the relative size and function of the left and right ventricles and septal geometry and motion. Ventricular septal defect morphology was confirmed in 13 patients. Unsuspected morphological findings were documented in four patients (11%). Adequate visualisation of coronary morphology was difficult and two out of three intramural coronaries were missed. Studies after bypass showed that the increase in left ventricular size and changes in the geometry of both ventricles were immediate. There was wide variation in early left ventricular function as assessed by M mode echocardiography and computer assisted cross sectional wall motion analysis, which did not relate to final outcome (no deaths intraoperatively and only one postoperatively). On line left ventricular function assessment was valuable in optimising volume loading and inotropic treatment. Septal dyskinesia was a common finding. Discrete segmental dyskinesia of the posterior left ventricular wall was seen in one patient, leading to the diagnosis of a circumflex artery compression; immediate surgical revision (Lecompte manoeuvre) resulted in rapid normalisation of posterior wall motion. Further residual lesions documented but not required surgical revision included mild neoaoartic (two patients) or neopulmonary (five patients) incompetence and three tiny ventricular septal defects. Immediate aortic or pulmonary anastomotic gradients were excluded in all.

We have confirmed that intraoperative ultrasonography provides unique information on the acute changes in left ventricular geometry and function after a switch procedure, and that it is a sensitive method for the exclusion or diagnosis of any significant residual morphological lesion.
atrial septal defect was seen among 21 hearts with an intact ventricular septum. Anomalies of the aortic arch were associated with ventricular septal defect in two cases, one with a solitary arterial trunk and one with hypoplasia of the aorta and patency of the arterial duct. All of these findings are replicated in human hearts.

This strain of pig, therefore, provides an ideal large animal model for morphologic and genetic investigations concerning the details of ventricular septation, including potential mechanisms of late spontaneous closure.

**Effect of a new class III antiarrhythmic agent (UK 68 798) on QT interval and heart rate**

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UK 68 798 (Pfizer) is a new class III antiarrhythmic agent that is devoid of subsidiary class I and II properties in animals. A study of the electrophysiologic effects of UK 68 798 at a range of intravenous doses was performed in 18 patients (mean age 55, range 42–65 years) admitted for diagnostic coronary arteriography. Three groups of four patients each received infusions of 1, 5, 3, and 4.5 μg/kg over 10 minutes. UK 69 798 had no significant effect on heart rate, PR interval, or QRS duration. The mean QT interval increased by a maximum of 36 ms (9–4%), 52 ms (13–1%), and 83 ms (21–7%) at the three doses. Equivalent increases in QT were 9.7%, 9.6%, and 20.1%. Mean plasma concentrations at the end of infusion for the three doses were 1.74, 3.35, and 5.11 ng/ml. There was a linear correlation between the area under the plasma concentration/time curve and dose and between plasma concentration and change in QT. Mean plasma elimination half life was 8.7 h. The increase in QT interval had fallen to 4–6%, 2–4%, and 9.7% at 60 minutes after infusion. In a further six patients, however, a divided dose regimen giving two thirds over 15 minutes and the remainder over 45 minutes maintained stable QT prolongation over one hour. No adverse effects were noted in any patient.

UK 68 798 seems to be a specific class III antiarrhythmic agent that warrants further invasive electrophysiological evaluation.

**Enhanced safety of a low energy non-arcing ventricular catheter ablation system compared with high energy defibrillator discharges**

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A new system for low energy direct current (DC) cardiac ablation has recently been described. The effects of DC catheter ablation were compared in 22 pigs with two systems, a standard 7F electrode with defibrillator high energy (HE) shocks (100–150 J) and a capacitive waveform low energy (LE) system (25–30 J) with a 7F contoured tip electrode. Baseline haemodynamic measurements, left ventricular angiography, 12 lead electrocardiography, and electrophysiological stimulation studies were undertaken before delivery of single (HE, n = 5 pigs; LE, n = 5) or five (HE, n = 7; LE, n = 5) shocks to the left ventricle. Voltage and current were recorded. Survivors were restudied at four weeks, after which hearts were excised for histological examination. No chronic differences in left ventricular ejection fraction (LE 54.9% to 54.3%; HE 54.4% to 55.5%) or electrocardiographic findings were found. Mean (SD) values for HE were 2035 (298) V, 135 (26) J, 65 (33) A, and 35 (14) Ω and for LE were 2460 (302) V, 29 (4) J, 45 (17) A, 60 (19) Ω (differences significant, each at p < 0.001). The HE group sustained more postshock arrhythmias and more severe hypotensive episodes. No deaths occurred in the LE group, compared with five in the HE group (one perforation, one electromechanical dissociation, one astyole, two intractable ventricular fibrillation; p < 0.01, χ² test). One animal died at 24 hours. No sudden deaths occurred during follow up. Chronic lesions in the multiple shock groups, characterised by transmural fibrosis and wall thinning, were comparable in size for both systems (HE 6.5–3 cm², LE 6.3–3 cm²). No significant mural lesions were observed in animals receiving single shocks.

The contoured tip electrode with a low energy capacitive shock produces similar myocardial lesions to conventional shocks, but with less trauma. This non-arcing system should enhance the safety margin for ventricular catheter ablation using DC shocks.

**Time to termination of paroxysmal junctional tachycardia as a predictor of tachycardia suppression with antiarrhythmic treatment**

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Prophylactic antiarrhythmic drugs for paroxysmal junctional tachycardia are usually selected empirically, and oral treatment is frequently unsuccessful as a result. Suppression of tachycardia at electrophysiological study is predictive of long term efficacy but is invasive and expensive. The aim of this study was to determine if the time to termination of tachycardia after intravenous drug treatment could predict the results of invasive antiarrhythmic suppression studies. Tachycardia termination and subsequent reinduction was attempted on 54 occasions in 35 patients with inducible sustained junctional tachycardia with one of three antiarrhythmic drugs (flecainide 2 mg/kg, sotalol 1.5 mg/kg, disopyramide 2 mg/kg). All infusions were given over 10 minutes and restimulation was attempted 10 minutes after completion of the infusion. Tachycardia terminations were classified as early (<5 minutes) or late (>5 minutes). Tachycardias that did not terminate with drug treatment were terminated by ventricular pacing. Nineteen of the 54 tachycardias were terminated early (13/20 with flecainide, 5/20 with sotalol, and 1/14 with disopyramide). These arrhythmias were all successfully suppressed during subsequent attempts at reinduction. Nineteen tachycardias were terminated late: successful suppression was achieved in only 12 of these (2/5 with flecainide, 5/8 with sotalol, and 5/6 with disopyramide). Sixteen episodes of tachycardia were not terminated by drugs (2/20 flecainide, 7/20 sotalol, 7/14 disopyramide), and none of these arrhythmias were suppressed during subsequent reinduction attempts.

Early termination of paroxysmal junctional tachycardia by an antiarrhythmic drug is more likely to be followed by arrhythmia suppression than is late termination (p < 0.05) or failure of termination (p < 0.001).
Two forms of back up defibrillation for antitachycardia pacing in ventricular tachycardia

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The risk of fatal acceleration has limited the use of antitachycardia pacemakers in the treatment of ventricular tachycardia (VT). We report our experience with two forms of back up defibrillation in seven patients (mean age 57 (12) years, all men, five with ischaemic heart disease and two with dilated cardiomyopathy) with recurrent VT despite drug treatment that could be terminated by ventricular pacing. The mean VT rate was 168 (26) beats/min. Three patients, each with a single configuration of haemodynamically stable VT, had an antitachycardia pacemaker implanted with a single ventricular wire. Both detection and response modes were activated only by a magnet in a local accident and emergency department where external defibrillation was available. The patients were followed up for a mean of 16 (range 13–18) months and had a mean of six (range 0–9) episodes pace terminated. The mean time from onset of tachycardia to treatment is 25 minutes, and one patient's tachycardias did not last sufficient time (10–15 minutes) to present to hospital. Acceleration occurred once, requiring external defibrillation. Four patients had a device implanted via a thoracotomy capable of both antitachycardia pacing and internal defibrillation. Two had more than one configuration of VT and two had a previous cardiac arrest. The devices were programmed to detect and treat either slow VT with pacing or low energy direct current (DC) shock or ventricular fibrillation and fast VT with maximum energy DC shock. After a mean follow up of four (range 1–7) months, spontaneous VT was terminated by burst pacing a mean of nine (range 0–32) times. In one patient a one joule shock accelerated a spontaneous tachycardia and in two patients pacing accelerated an induced tachycardia. The accelerated rhythm was detected and terminated automatically by a full energy shock in all patients. One patient had spontaneous VF automatically defibrillated.

To conclude, these data further show that pacing termination of ventricular tachycardia by a device requires back up defibrillation. A casualty activated device had a lower capital cost and was simpler to implant, but the long delay to treatment means that it should not be used for haemodynamically unstable arrhythmias. Antitachycardia pacing for VT should therefore be combined in a device offering internal defibrillation.

Textured surface left ventricular assist devices continue to consume platelets after intermediate term implantation in the calf model

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Textured surface left ventricular assist devices (TSLVADs) have been developed with a view to permanent clinical implantation but have already been used as a short term bridge to transplantation. An essential requirement of such devices is a non-thromboembolic and haematologically stable blood contacting surface. In textured surface devices this occurs, to some extent, as blood constituents are attracted to form a strongly adherent coagulum with subsequent neointimal formation, thus avoiding the thromboembolic complications commonly associated with smooth surfaced devices. The haematological consequences of TSLVAD implantation were evaluated in 17 calves for up to four months. Attraction and deposition of blood cellular elements on to the device surfaces after implantation resulted in an increased plasma haemoglobin concentration immediately after the operation, a fall in platelet count to 25% of preoperative values by day 2, and a fall in red cell count to 65% after one week. Plasma haemoglobin values returned rapidly to normal and red cell numbers were normal within one month. Red cell survival measured at one month (n = 10) and three months (n = 3) after implantation were similar to preimplantation values. After the initial thrombocytopenia there was a rebound thrombocytosis which peaked after one week. Platelet concentrations then fell, reaching a plateau at about 65% of preimplantation values, where they remained. Platelet life-span measured at one month (n = 10) was significantly decreased (mean (SE) days 3·01 (0·11) v 1·76 (0·15); p < 0·001) and, although there was some improvement, remained so after three months (n = 4, 2·06 (0·47); p < 0·01).

These longer term results have shown that the developing neointima, while remaining strongly attached to the TSLVAD surfaces, continues to be highly consumptive of platelets three months after implantation and that longer term evaluation is needed before these devices can be considered for permanent use.

Coronary reactivity to ergometrine: possible relation to accelerated coronary sclerosis in cardiac transplant recipients

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Severe coronary artery spasm can occur in orthotopic cardiac transplant recipients. To investigate the possible mechanisms and the relevance of coronary spasm to the subsequent development of coronary disease the responses of the coronary arteries to intracoronary ergometrine maleate were studied in 10 patients who had undergone orthotopic cardiac transplantation and were shown to have normal coronary arteries at angiography. Ergometrine in doses of 1, 5, and 10 μg was injected into the left coronary artery followed by 2 mg of isosorbide dinitrate. Proximal coronary artery luminal diameters were measured by automated computed quantitative angiography of the left anterior descending (LAD) and circumflex (LCX) vessels. Five patients (responders) showed a dose-response curve to intracoronary ergometrine which was similar to that previously seen in non-transplant recipients (mean percentage diameter change (SE) −24·68 (1·93) for LAD, −24·06 (3·91) for LCX). The remaining five patients (non-responders) showed a virtually flat dose-response curve significantly different from that of the responders (p = 0·001 for LAD, p = 0·013 for LCX). Angiography after two years showed significant coronary disease in four of the five responders to ergometrine. In contrast, the five non-responders to ergometrine continued to have no detectable disease by angiography.
Fall in epicardial evoked T wave amplitude in cardiac allograft rejection

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The repolarisation phase of the surface electrocardiogram is usually a sensitive indicator of myocardial damage but has proved disappointing in the diagnosis of cardiac allograft rejection. To enhance sensitivity we have serially measured epicardial evoked T wave amplitude with an externalised Rhythmix pacemaker system telemetered to a TP2 analyser in 13 patients (12 men, one woman, median age 49 (range 34–57) years) followed for 19 (14–26) days after transplantation. A total of 228 records were analysed. Rejection was defined on endomyocardial biopsy. During the study 18 of the 31 biopsy specimens showed evidence of rejection. One patient had no biopsy specimens showing rejection, seven had one, four had two, and one patient had three. After rejection was diagnosed patients received intravenous methylprednisolone for three days. In 11 patients the initial rejection episode was associated with a significant fall in the evoked T wave amplitude (from 1-3 (0-7–2-3) mV to 0-6 (0-5–1-8) mV; p < 0-005) which began 2 (1–4) days earlier. One patient with uncontrolled diabetes had no change in T wave amplitude during the rejection episode. No fall in T wave amplitude occurred in the absence of rejection. In the patients with a negative subsequent biopsy specimen there was an increase in T wave amplitude to approach baseline (1-0 (0-7–1-8) mV). Patients with more than one positive biopsy specimen had no further significant change in T wave amplitude, which may be due to the ongoing rejection.

These results suggest a potential non-invasive method of detecting cardiac rejection which is both sensitive and specific for first rejection episodes.

Does transmitral pulsed wave Doppler reliably diagnose acute rejection in heart transplant recipients?

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Recent studies suggest that changes in pulsed wave transmitral Doppler (PTD) indices of diastolic function are early markers of acute rejection after orthotopic heart transplantation. We prospectively studied 30 patients (23 men, seven women) between 1–40 (median 5) months after transplantation with serial PTD studies using a simultaneous phonocardiogram. The 250 consecutive ultrasound studies were related to the concurrent biopsy results (Billingham classification). On each occasion the average values of 20 consecutive beats were determined for peak early diastolic velocity (E, ms/s), peak late diastolic velocity at atrial contraction (A, ms/s), E/A ratio, isovolumic relaxation period (IVR, ms), IVR% (percentage change in IVR from previous value), IVR/rr (heart rate corrected IVR), time velocity integral (TVI, cm), diastolic filling period (DFP, ms). For every Billingham classification the pooled average values (SD) of each parameter are presented. In addition intraobserver and interobserver variability were analysed over 200 individual beats in 10 different patients. Thus for each Doppler parameter the threshold for individual physiological change (beyond measurement variability) was calculated: E 5.6%; A/A 16.6%; IVR 8%; TVI 4.6%; DFP 3%. With these criteria we could assess in individual patients whether there was a true physiological change during an episode of acute rejection. Of the 250 observations, 42 were Billingham classification 0; the corresponding values were E 0.85 (0.24); E/A 2.12 (0.87); IVR 61 (17); IVR% 11 (50); IVR/rr 0.09 (0.03); TVI 14 (4); DFP 321 (84). In Billingham classification 1 there were 179 observations and their corresponding values were E 0.83 (0.24); E/A 1.96 (0.87); IVR 69 (17); IVR%, 5 (29); IVR/rr 0.10 (0.03); TVI 15 (4); DFP 324 (118). In Billingham classification 2 there were 29 observations and their corresponding values were E 0.89 (0.22); E/A 2.09 (1.03); IVR 68 (18); IVR 5 (26); IVR/rr 0.10 (0.03); TVI 15 (4); DFP 302 (88).

Despite a low measurement variability, there is considerable overlap among patients without acute rejection (Billingham classification 0), those with infiltrates (Billingham classification 1, mild acute rejection), and those with infiltrates and myocytolysis (Billingham classification 2, moderate acute rejection). PTD could not distinguish between patients requiring specific rejection treatment (Billingham classification 2) and others, either at group level or in individual patients, and therefore could not diagnose acute rejection. This suggests that haemodynamic factors other than acute rejection alter diastolic function in these patients early after heart transplantation, obscuring the development of Doppler changes, formerly described as diagnostic of acute rejection.

Influence of donor heart ischaemic time on left ventricular contractility in heart transplantation: assessment by the conductance catheter

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Donor ischaemic time (from explantation to implantation) may have an important impact on left ventricular (LV) systolic performance after orthotopic cardiac transplantation. Accordingly, we studied 14 transplant recipients (mean 25 months after transplantation) divided into two groups according to ischaemic time (group 1 <140 min, n = 7, mean (SD) 128 (10) min; group 2 >150 min, n = 7, 178 (15) min) (p <0.01). LV contractility was assessed with a conductance catheter to generate LV end systolic pressure volume relations (Ees) over a wide range of loads generated by inferior vena cava balloon occlusion. Data were acquired under control conditions and during dobutamine infusion (3 mg/kg/min). No patient had angiographic coronary artery disease or rejection by right ventricular biopsy. No intergroup differences were noted for age, sex of donor and recipient, time since transplantation, and body surface area. Heart rates were similar in both groups (baseline: group 1 84 (5), group 2 85 (2) beats/min; dobutamine: group 1 100 (17), group 2 102 (13) beats/minute. Patients in group 1 had higher baseline LV contractility (group 1 Ees 2.5 (1.0), group 2 Ees 1.1 (0.4); p <0.01) and a greater response to dobutamine compared with patients in group 2 (4.7 (1.9), 2.2 (0.9): P <0.01).

Thus, there is a direct relation between donor ischaemic time and long term LV systolic performance under baseline conditions and during β1 adrenoceptor challenge.
In vivo imaging of low density lipoprotein

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The non-invasive identification of atheroma would have important therapeutic implications. The biodistribution of low density lipoprotein (LDL) is important in identifying patients with lipid abnormalities. LDL plasma kinetics have been studied with radiolabelling, which is a standard technique. It has been found possible in animal models to image atherosclerotic plaques that have taken up the radiolabel. Initially standard iodine labels were used but more recently a method of labelling with technetium-99m has been described, which provides better imaging characteristics. Initial work in rabbits has shown in vivo images of rabbit aorta, with increased uptake in hypercholesterolaemic (Watanabe) rabbits compared with controls. In 10 human volunteers biodistribution of iodine-123 and technetium-99m labelled LDL was similar, with uptake initially in the blood pool then predominantly in liver and spleen and subsequent excretion in intestine. Blood clearance of technetium labelled LDL was faster than that of the iodine labelled LDL (55 (25) v 308 (158) at 80%, of 5 minute sample, 285 (204) v 1328 (138) at 60%). In six patients with peripheral vascular disease asymmetrical femoral uptake was seen in five of them at the site of their angiographically shown obstruction.

This suggests that technetium labelled LDL is a suitable tracer to provide non-invasive quantitative biodistribution of LDL and may accumulate sufficiently in peripheral atheromatous plaque to allow in vivo imaging.

Application of magnetic resonance velocity mapping to mitral and pulmonary flow of healthy volunteers

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Transmitral and pulmonary venous flow are important indices in evaluating left ventricular diastolic function. Magnetic resonance velocity mapping was used to measure transmitral blood flow and pulmonary venous flow velocity in 20 healthy volunteers. Velocity measurement was acquired in an oblique plane parallel to the horizontal long axis of the heart. By the same technique quantitative blood flow was measured in planes perpendicular to the right and left lower pulmonary veins (RLPV, LLPV). Flow (ml/s) was calculated from cross sectional area (cm²) and mean velocity (cm/s). Transmitral flow showed two positive peaks, one during early ventricular diastole and the other during atrial systole. Peak mitral flow velocity in early diastole was 68 (12) cm/s and in atrial systole 39 (10) cm/s and the ratio between the two was 1.9 (0.6). Pulmonary venous flow showed two positive peaks, one during ventricular systole and another in diastole. A small backflow during atrial systole was noticed. Peak systolic velocity in the right lower pulmonary vein was 41-3 (11) cm/s, peak diastolic velocity 36-0 (10) cm/s, and peak back flow velocity 12 (2) cm/s. The mean flow indices were 13-0 (3-8) ml/s/m² and 11-9 (2-6) ml/s/m² in the RLPV and LLPV respectively.

Magnetic resonance flow imaging provides a non invasive measurement of transmitral and pulmonary venous flow which is of clinical importance in evaluating various cardiac diseases.

Combined three dimensional intravascular ultrasound imaging and three dimensional flow presentation

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The clinical use of intra-arterial ultrasonic imaging in conjunction with angioplasty is rapidly approaching. We have developed a computer based imaging system for reconstructing three dimensional models from ultrasonic data acquired intraluminally with an 8F catheter mounted probe. We report an assessment of the accuracy of the system and present preliminary data on the combined presentation of three dimensional flow fields and three dimensional arterial images. Measurements made directly and from the computer reconstructions of multiple diameters in 10 hollow metallic and plastic phantoms (internal diameter 6–48 mm) were compared. After calibration, the direct and computed measurements correlated extremely highly (r = 0.98). For 10 in vitro arterial specimens direct measurement at known levels of histological section prepared without “pressure fixxing” were made with an estimated error of 10%, Discrepancy between the direct and computed measurements of up to 12% was observed, again consistent with accurate ultrasonic measurement.

Knowledge of the three dimensional morphology of a vessel has enabled us to calculate theoretical three dimensional flow velocities based on calculations of the Navier-Stokes equation. The resultant flow fields are represented by colour mapping on the computer screen. Combining accurate three dimensional computer visualisation of the arterial wall and three dimensional flow information produces a powerful diagnostic tool.

Magnetic resonance imaging of pericardial disease

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Complete examination of the pericardium by established methods (computed tomography and echocardiography) can be difficult. Diagnosis of pericardial constriction often depends on invasive pressure measurements and malignant involvement may be only fully shown at operation or necropsy. We evaluated the use of magnetic resonance imaging in detecting pericardial disease, particularly in diagnosing pericardial constriction and malignant invasion. A total of 108 adults were examined in a 0.5 Tesla magnetic resonance scanner by electrocardiographic gated spin echo sequences.Appearances of the pericardium were defined in 16 normal volunteers, 59 patients with heart disease unlikely to involve pericardium (including 25 patients after
operation), eight patients with catheter proved pericardial constriction, and 15 patients with pericardial effusions. In normal volunteers and patients with miscellaneous heart disease the pericardium was up to 3 mm thick and in the postoperative group it was up to 3-3 mm. The cardiac cycle did not affect these measurements. Patients with pericardial constriction had pericardial thicknesses of at least 3-3 mm. In patients with pericardial effusions magnetic resonance imaging showed malignant involvement of the pericardium better than alternative methods.

Magnetic resonance imaging accurately shows pericardial thickening and is a good predictor of pericardial constriction. It shows malignant involvement of the pericardium more clearly than alternative non-invasive methods.

Dobutamine magnetic resonance imaging in patients with coronary artery disease

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Magnetic resonance imaging is difficult during dynamic exercise, and this has limited its value in patients with coronary artery disease. With intravenous dipyridamole and cine magnetic resonance imaging we previously showed wall motion abnormalities in two thirds of patients in whom thallium defects were seen. To increase this sensitivity we have now used intravenous dobutamine, which increases myocardial oxygen demand and has the advantages of being administered by peripheral infusion, a short half life, and low arrhythmogenicity. Twenty two patients with stable angina underwent coronary angiography, thallium tomography, and cine magnetic resonance imaging. Images were acquired in three perpendicular planes before and after dobutamine, allowing direct comparison of perfusion and wall motion, which were graded in nine segments as normal, reduced, or absent. Twenty patients had coronary artery disease, of whom 19 (95%) had reversible perfusion defects after dobutamine. All 19 also had reversible wall motion abnormalities. The perfusion and wall motion defects corresponded closely in site and extent. The two patients with normal epicardial arteries also had corresponding wall motion and perfusion abnormalities. Chest pain occurred in 18 patients but was easily controlled by decreasing the infusion rate. Transitory arrhythmias were seen in eight patients but were insignificant. The average increase in double product with dobutamine was 34%, 57%, 87%, and 104% with 5, 10, 15 and 20 μg/kg/minute respectively.

We conclude that magnetic resonance imaging during dobutamine stress is safe, feasible, and well tolerated and that it may be possible to extend the clinical role of magnetic resonance in patients with coronary artery disease.

Assessment of regional myocardial ischaemia by a combination of nuclear imaging (99mTc-methoxyisobutylisonitrile) and monophasic action potential recordings

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Monophasic action potentials recorded from the surface of the myocardium provide a sensitive measure of early and localised myocardial ischaemia. The duration of the action potential shortens in response to ischaemia. The slow monophasic membrane characteristics of 99mTc-methoxyisobutylisonitrile (MIBI) permits injection of the isotope at a time and site distant from the imaging process. We combined 99mTc-MIBI myocardial perfusion imaging with recordings of left ventricular endocardial monophasic action potential to detect myocardial ischaemia induced by incremental atrial pacing. Sixteen patients (age range 40–73; 10 women) undergoing investigation for chest pain were studied. After routine coronary angiography a monophasic action potential recording catheter was inserted into the left ventricle and its position documented by biplane cinematography. Recordings were made during incremental right atrial pacing. Each pacing train was maintained for two minutes, thereby establishing steady state conditions. At peak paced heart rate 400 MBq 99mTc-MIBI was injected intravenously. Myocardial perfusion single photon emission computed tomography (SPECT) was performed one hour later with rest SPECT obtained the following day (two day, two doses protocol). Thirteen patients had significant coronary artery lesions. Abnormal perfusion was identified in 45 out of 117 myocardial segments (sensitivity 83% and specificity 80%). Monophasic action potential recordings were obtained from areas with reversible perfusion defects in six patients and from areas of normal perfusion in another six. The extent of action potential shortening was significantly greater (p < 0.05) for the recordings from the myocardial areas with reversible perfusion defects (28.6 ms per 100 ms decrease in cycle length) compared with normally perfused areas (23.5 ms). 99mTc-MIBI while proving an ideal agent for use in conjunction with cardiac catheterisation procedures, is effective in identifying perfusion defects with atrial pacing stress. In addition, electrical changes of ischaemia have been shown in areas of myocardium where perfusion defects exist.

Transcoronary alcohol ablation of the atrioventricular node

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Catheter ablation of atrioventricular conduction is accepted treatment for intractable atrial arrhythmias but disadvantages include modest success rates, right ventricular damage, and the need for general anaesthesia. A new technique of selective catheterisation of the atrioventricular nodal artery (AVNA) and embolisation with absolute alcohol was attempted in six patients. In two patients the AVNA was not clearly identified and could not be catheterised; these patients subsequently underwent electrical ablation. In four patients the AVNA was clearly visualised and all four patients underwent successful transcatheter ablation. The AVNA was entered with a steerable 0.013 inch wire and a 2.2F infusion catheter manipulated down a conventional 9F angioplasty guiding catheter. A His bundle electrode provides an excellent visual target.
when engaging the AVNA. Position within the AVNA was confirmed radiographically, and infusion of ice cold saline produced temporary A-H block in all four patients. Immediate and to date persistent block then occurred after injection of 0.5 ml absolute alcohol in three patients who both had an expected minor rise in cardiac enzyme activities (peak creatine kinase (heart type) < 50 IU, normal 0-20). One patient who had 1 ml alcohol injected developed a significant increase in enzyme activity (creatinine kinase (heart type) 146 IU). Subsequent echocardiography showed normal systolic function. Three out of four patients had escape rhythms, which were all narrow complex, mean cycle length 1130 ms. Coronary artery spasm developed in three out of six patients before injection of alcohol and resolved immediately with intracoronary nitrate treatment.

Ablation of the atrioventricular node by alcohol embolisation is an attractive and feasible alternative in patients who would otherwise require conventional ablation.

Use of automatic implantable defibrillators in the United Kingdom

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Implanted defibrillators represent an important option in the treatment of ventricular arrhythmias. Such devices implanted in the United Kingdom up to January 1990 were surveyed. Forty-nine devices have been implanted in 40 patients, data being complete in 34 patients (mean age 53 (13), 28 men) with a mean follow up of 9 (10) months. Twenty-one patients had ischaemic heart disease, nine patients dilated cardiomyopathy, and four patients other disease. The arrhythmia was ventricular tachycardia in 21 (6%) patients, ventricular fibrillation in six (18%) patients and both in seven (21%), and 25 of the 34 (74%) patients had had a preimplant cardiac arrest. Drug treatment had failed in all patients and ablation had failed in four (transvenous in four patients and surgical in two of these). Mean ejection fraction was 31% (16%), median 25%. In the past 12 months 18 of the 34 (53%) patients had their first device implanted and the number of implanting centres increased from five to 10. All have been implanted via a thoracotomy with two epicardial patches. Seventeen out of 40 (43%) patients had devices implanted with defibrillator only function, 14 (35%) had devices with back up pacing implanted, and nine (22%) had devices with combined antitachycardia pacing implanted in the past seven months. Successful termination of spontaneous arrhythmias occurred in 17 of the 34 (50%) patients with no failures. No patients have died.

Although the overall numbers are small, there has been a dramatic increase in both the number of devices and centres implanting in the past 12 months. This is probably due to the expanding capabilities of the devices increasing the proportion of patients with ventricular arrhythmias in whom such a device is the treatment of choice. In this high risk group (74% with previous cardiac arrest, mean ejection fraction 31%) it is encouraging that there have been no deaths.

Acute and chronic histological appearances in catheter mediated ventricular ablation by low energy and conventional defibrillator systems

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The histological effects of lower energy direct current ablation are not well described. This study compares the acute and chronic (four weeks) histological appearances of two DC catheter ablation systems in the pig. A standard 7F electrode with defibrillator high energy (HE) (100–150 J) shocks and a capacitive waveform low energy (LE) (25–30 J) source with a contoured tip 7F electrode were used to deliver endocardial left ventricular shocks in 22 pigs. The catheter electrode was placed on the left ventricular free wall. Single (HE, n = 5 pigs; LE, n = 5) or five (HE, n = 7; LE, n = 5) unipolar cathodal shocks were delivered. Surviving animals were restudied after four weeks, when the hearts were excised, fixed, and stained for detailed studies. Fifteen chronic lesions and six hearts with acute lesions were examined. One specimen was obtained at 24 hours. Transmural and endocardial fibrosis without chronic inflammatory cell infiltrates were seen with HE and LE lesions. No significant long term electrocardiographic or left ventricular angiographic correlates with extent and type of lesion were observed. Cartilage type and carbon deposits were absent in chronic lesions. A mitral leaflet haematoma and left ventricular aneurysm was observed after four weeks after multiple LE shocks in one animal. Macroscopically, acute lesions were poorly defined. Microscopically, acute lesions produced contraction band coagulation, interstitial haemorrhage, and haemosiderin pigment deposits. Pronounced nuclear alignment was observed after acute shocks without cellular disruption. A fivefold reduction in ablation energy with a non-arcing capacitive waveform system produces comparable acute and chronic myocardial lesions with a conventional system in vivo. Differences in voltage, current, or energy may account for differing clinical but not histological effects.

Funding for implantable defibrillators in the United Kingdom: a comprehensive study

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In the past decade the use of implantable defibrillators has increased considerably throughout the world. All implanting centres in the United Kingdom have been surveyed, and though roughly 8000 devices have been implanted worldwide, only 40 patients have received implantable defibrillators in the United Kingdom. Each device, including patches and sensing leads, costs about £13,000 plus the cost of implantation, and funding difficulties have been one factor limiting their use. The source of funding has been examined in all cases. None of the centres has been allocated a specific defibrillator budget either centrally or locally. Twenty patients had their devices funded from pacing budgets, nine were funded by the referring health district, three were funded from “one off” regional funds, three were paid for privately, two were funded out of hospital contingency budgets and two by
and has risen from five to 10. All 25 of the 40 patients (62\%) have received their implants in the past 12 months, and the number of implanting centres has risen from five to 10. All patients are currently alive and well, and treatment has been effective in all.

Implantable defibrillators have been shown to be cost effective by others, and the treatment is now well established. Specific budgets should be established to allow this treatment to be offered to appropriate patients, most of whom have life threatening arrhythmias.

Low energy ablation of accessory pathways: use of test shocks and non-arcing shocks

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Catheter ablation has potential as an alternative treatment to surgery for the Wolff-Parkinson-White syndrome, avoiding sternotomy and cardiopulmonary bypass. It remains experimental because of uncertainty about success rates and the risk of cardiac rupture due to the high pressures produced from arcing and gas expansion at the catheter tip. We have devised a system that delivers shocks of low energy without arcing. Catheter ablation was considered in patients with accessory pathways undergoing electrophysiological study before planned surgery. Ablation was attempted in 12 patients (age range 11–78). The site of the accessory pathway was posteroseptal (PS) in six, left free wall (LF) in four, and right free wall (RF) in two. Test shocks of 2–15 J were delivered to the site of earliest atrial activation during tachycardia. There was no effect on accessory pathway conduction in five patients (two PS, two RF, one LF) and catheter ablation was abandoned. These patients went on to planned surgery. Further shocks of 15–25 J were delivered to the remaining seven patients in whom transient loss of accessory pathway conduction followed test shock delivery. Shocks were delivered outside the coronary sinus or in four (PS), inside the coronary sinus in one, from the mitral annulus in one, and between the mitral annulus and the coronary sinus in one, four to 24 shocks (mean five, mean shock energy 19 J) were delivered. There were no episodes of coronary sinus rupture, tamponade, or coronary artery spasm. The only complications were transient episodes of atrial fibrillation and secondary atrioventricular block. At follow up (mean 13 months) in the seven patients who underwent ablation there was no accessory pathway conduction in five and modified conduction in two. Five patients remain free of tachycardia and are not taking any drugs and two are symptom free taking previously ineffective medication.

Low energy test shocks may be useful in selecting successful sites for ablation. Repeated non-arcing shocks are effective and safe for the ablation of accessory pathways at low energies and without barotrauma. Initial clinical experience suggests that this method may be an alternative to surgery in some patients.

Surgery for medically refractory ventricular tachycardias: resection, implantable defibrillators, or transplantation?

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Since October 1984, 33 consecutive patients (mean age 56.5 years) have undergone elective surgery for ventricular tachycardias. Thirty were males. Twenty-three had map guided extensive endocardial resection (EER), seven had implantable cardioverter defibrillators (ICDs), and four underwent cardiac transplantation. In the EER group four had additional localised exclusion cryoablation to scarred papillary muscle and the septum was crossed by a right ventricular scar in four. Twenty-two out of 23 had concomitant aneurysmectomy or coronary artery bypass grafting, or both. There was one operative death (4.3\%) in a patient who required additional mitral valve replacement and aneurysmectomy. There were three late non-sudden cardiac deaths with no recurrence of ventricular tachycardia. Of 18 long term survivors, one developed recurrence shortly after EER and had an ICD implanted; one developed a new arrhythmia at one year which was controlled by drug treatment; 16 had no recurrence of ventricular tachycardia at a mean follow up of 35 months. All seven with ICDs are alive. The four transplant recipients are well at short term follow up (mean five months).

EER is the treatment of choice if the ventricular tachycardia is reproducible and not polymorphic. Although a low ejection fraction in itself is not a contraindication for EER, ICDs are generally reserved for those with poor ventricular function and relatively infrequent tachycardia who do not meet the constraints for EER. Transplantation is primarily indicated in those within accepted age limits if poor ventricular function is associated with frequent tachycardia.

Suprapulmonary stenosis in transposition of the great arteries after arterial switch operation

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The arterial switch procedure has been the operation of choice for transposition of the great arteries at our institution since 1977. This procedure was chosen to prevent postoperative complications such as arrhythmias and venous obstruction. Instead pulmonary trunk (PT) narrowing has become the main medium term complication for this condition. To assess this problem we studied 39 consecutive patients who underwent the arterial switch procedure (1977–89). Follow up included yearly echocardiographic evaluation, cardiac catheterisation (n = 8) when indicated, and magnetic resonance imaging (n = 12). Some degree of suprapulmonary stenosis developed in 39 patients (52\%), of whom four had a direct anastomosis after an initial banding of the PT, six had a direct anastomosis alone, eight a “French technique” after initial banding of the PT, and 21 “French technique” alone. This narrowing varied from mild in 4 patients (1–4.2 m/s) to moderate in 20 patients (2–3 m/s) and severe in 15 patients (3–4.5 m/s), of whom 12 (30\%) required reoperation to enlarge the PT. The location of the narrowing was supravalvar in 20 (51\%), at the bifurcation in 13 (33\%), and at the pulmonary branches in one (3\%). In five (13\%) the precise location could not be determined.

We conclude that suprapulmonary stenosis was a frequent postoperative complication (52\%) in our population. Most of these were mild or moderate, and only a small...
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Options for surgical repair in hearts with univentricular atrioventricular connection and subaortic stenosis

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Thirteen patients underwent surgical treatment because of subaortic obstruction in hearts with a univentricular atrioventricular connection. Nine patients underwent surgical enlargement of the ventricular septal defect and four patients had construction of an aortopulmonary anastomosis and closure of the pulmonary trunk (The Damus-Kaye-Stansel procedure). Two patients underwent enlargement of the septal defect and two having the Damus-Kaye-Stansel procedure also had a modified Fontan procedure. One patient had complete atrioventricular dissociation after direct enlargement of the ventricular septal defect that necessitated insertion of an epicardial pacemaker. One patient died within 30 days of the operation after enlargement of the defect and two patients after the Damus-Kaye-Stansel procedure. There was one late death, occurring in a patient who underwent enlargement of the ventricular septal defect. Ten patients subsequently underwent conventional cardiac catheterisation and angiography or transcutaneous Doppler flow studies, or both, to assess the relief of the subaortic obstruction. The result was satisfactory in all.

In the light of this experience, we now recommend direct surgical enlargement of the restrictive ventricular septal defect for relief of subaortic stenosis occurring with a univentricular atrioventricular connection to a dominant left ventricle as it seems to be haemodynamically effective with a low operative mortality and morbidity.

Determinants of long term growth after surgical repair of a large ventricular septal defect in infancy

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The ultimate growth potential of infants undergoing early corrective cardiac surgery is as yet unknown. This study examined the long term growth patterns of 46 otherwise normal infants who survived primary surgical repair of large ventricular septal defect before 7 months of age. All available patients and their families were asked to return for follow up measurement of weight, length, and head circumference. Each measurement was expressed in SDs from the mean for age based on established local values. At a mean of 60 years after operation the mean weight, length, and head circumference of 35 infants of normal birth weight were only marginally abnormal in comparison with the reference population (−0·4 SD, −0·1 SD, and +0·5 SD; p > 0·02, p > 0·05 and p = 0·008 respectively) and did not differ in any parameter from those of 44 normal siblings. Among 11 low birthweight infants, however, all three parameters remained highly abnormal at long term follow up, both in comparison with the reference population (−1·7 SD, −1·7 SD, and −0·9 SD; p < 0·001 for each) and in comparison with 22 normal siblings. Other than birth weight, only the severity of the preoperative growth disturbance for each parameter had an influence on late postoperative growth. Weight, length, and head circumference scores at six months after operation correlated significantly with those at latest follow up, and a significant correlation also existed between patient and mid-parental height scores.

Early repair of large ventricular septal defect results in near normal long term growth in normal birthweight infants. These results support a policy of early surgery in infants with large ventricular septal defect and poor growth due to congestive heart failure.

Continued treatment with prostaglandins after pulmonary valvotomy for pulmonary atresia with intact ventricular septum

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Pulmonary atresia with intact ventricular septum (PA) is widely treated by stabilising with E type prostaglandin (PGE), then performing pulmonary valvotomy with modified Blalock-Taussig shunt. We elected to perform pulmonary valvotomy alone while continuing PGE postoperatively in 11 neonates with tripartite right ventricle and good size pulmonary arteries. All received PGE2 preoperatively, intravenously or orally, for one to 56 days (median 3 days). The median age at operation was four days. In six the diagnosis was made on echocardiographic criteria alone; five also had cardiac catheterisation. Open pulmonary valvotomy was performed by cardiopulmonary bypass in eight, inflow occlusion in three. PGE2 was continued postoperatively. One infant died 18 hours postoperatively with low cardiac output and high right atrial pressure probably related to inadequate atrial communication. In two infants the oxygen saturation fell severely and a Blalock-Taussig shunt was performed within 18 hours. The eight others were given PGE2 for 3-44 days (mean 19 days). Balloon valvuloplasty was performed in two and infundibulotomy in one during the first three weeks postoperatively. Ten survived and have been followed up for six to 36 months postoperatively; one had an outflow patch at 22 months, three others atrial septal defect closure at 18 to 24 months. Infants with PA and tripartite right ventricle respond well to pulmonary valvotomy alone with continued postoperative PGE treatment. Avoiding a shunt simplifies postoperative management.

Late arrhythmias after the Fontan procedure

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Arrhythmias are a problem in managing aging patients who have undergone the Fontan procedure. Between 1972 and 1989, 58 patients have had this operation performed at this hospital. Of these patients, 31 have had postoperative arrhythmia documented, although most of these arrhythmic episodes were transient or fatal (11 cases) immediately...
after operation. The incidence of arrhythmia was greater in patients operated on for double inlet single ventricle (14 out of 20 (70%)) than for tricuspid atresia (16 out of 35 (46%).) Twelve patients developed late arrhythmias three months to 17 years (mean onset 4·7 years) after operation; 12 developed atrial arrhythmias, three nodal rhythm, two ventricular tachycardia, and one complete heart block. Age, right atrial pressure, pulmonary artery pressure, and previous shunt surgery were not preoperative determinants of tendency to early or late arrhythmia. At cardiac catheterisation 1 to 8 years postoperatively, however, there were significantly higher mean right atrial pressures in those that developed late arrhythmias (16·1 mm Hg, compared with 11·0; p < 0·01) and high pulmonary artery pressures (13·1 mm Hg, compared with 8·8 mm Hg; p < 0·01). Eighty-four percent of cases of atrial arrhythmia in particular occurred in the context of significant right atrial to pulmonary artery obstruction, and of the 16 patients in the series requiring reoperation for such obstruction, 63% had documented atrial arrhythmia. The occurrence of junctional and ventricular arrhythmias did not correlate with any variable measured preoperatively or postoperatively.

Rhythm disturbance, in particular atrial arrhythmia, is encountered increasingly in survivors of the Fontan procedure, compromising cardiac function. In this context right atrial to pulmonary artery obstruction should be sought even if not clinically apparent.

Is a subpulmonary ventricle in a Fontan circulation a Trojan horse?

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The optimal Fontan circuit is still controversial. We measured cardiac output by Doppler echocardiography during graded submaximal (up to 1·5 W/kg) supine bicycle exercise in seven patients (mean age 12·8 (2·8) years) 6·8 (2·1) years after a Fontan with a valved right atrium to right ventricle connection and in 29 patients (age 12·8 (6·0) years) 4·7 (3·6) (years after a right atrium to pulmonary artery connection. Results were compared to age matched controls. Patients with a right atrium to pulmonary artery connection had a normal cardiac index at rest, but increased with exercise were smaller than normal (p < 0·05). In contrast, patients with a right atrium to right ventricle had a lower cardiac index both at rest (p < 0·05) and during exercise (p < 0·01). Controls and patients with a right atrium to pulmonary artery connection increased their stroke volume (+ 19% (nine percent and (15%) (12%) respectively) with exercise but all patients with a right atrium to pulmonary artery Fontan had a fixed or decreasing stroke volume presumably due to the small, poorly compliant right ventricle incorporated in the circuit. Even the three patients with a right atrium to right ventricle Fontan who functioned as a biventricular heart (no antegrade pulmonary flow during ventricular diastole) were unable to increase their stroke volume with exercise. Age, time of follow up, or ventricular contractility (except when severely impaired) had no predictive value in a multivariate analysis.

The right atrium to right ventricle circuit is thus rate dependent and more vulnerable to the effects of tachycardia. This, together with the high incidence of conduit dysfunction-reoperation, argues against incorporation of a right ventricle in the Fontan circuit.