THE 70TH ANNUAL GENERAL MEETING of the British Cardiac Society was held at the Scottish Exhibition and Conference Centre, Glasgow on 30 April to 3 May 1991.

The President, D Chamberlain, took the Chair during private business. A McLeod and D Ward (on the retirement of S Hunter and J Hutton) and R Hall (on the retirement of A Henderson) were elected to Council.

Deaths during the year:
T E Lowe, J Kempson Maddox, J H Wright.

New Members 1991:
M Baig (Leeds); N Banner (Harefield); P Barnes (Salford); H Bethell (Hants); M Buchalter (Cambridge); N Buller (London); V Challenor (Southampton); J Chambers (London); A Coats (Oxford); T Cripps (Oxford); P Cummins (Birmingham); S Davies (London); K Evans (Swansea); A Fairfax (Stafford); A Fitzpatrick (Southampton); D Hackett (London); M Heber (Telford); K Hogg (Glasgow); S Holmberg (London); A Jones (Salisbury); C Jones (Cardiff); N Джоветт (Pembridge); C Kirk (Cardiff); S Large (Cambridge); R Levy (Manchester); N Lewis (Cardiff); P Lewis (Stockport); R Lewis (Yorkshire); J Lyons (Surrey); A McCance (Leicester); J McEwan (London); J McMurray (Glasgow); J Martin (London); R Maxwell (Gwynedd); W Morrison (Liverpool); D Mulcahy (London); M Papouchado (Bristol); J Parsons (Leeds); C Pattison (London); S Pocock (London); W Pugsley (London); P Quigley (Dublin); A Redington (London); S Richardson (Belfast); M Rigby (London); D Sandler (Derbyshire); D Smith (London); J Smith (London); T Spyt (Leicester); N Sreeram (Liverpool); P Sutton (London); P Thomas (London); P Wilmshurst (London); K Woods (Leicester).

New Corresponding Members:
R Falk (USA); H Madiera (Portugal); S Mody (India).

The following are abstracts of the papers that were presented.

Medical audit in the coronary care unit
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Systematic medical audit to assess and improve the quality of care has become an established part of routine clinical practice. In many departments this has relied on the examination of case records drawn at random from those of recent inpatients. The incomplete nature of this system gives no information on overall patient management strategies in an acute specialty such as cardiology. To monitor aspects of patient management within a coronary care unit (CCU) a tailor made, computerised system has been introduced, allowing the rapid collation of information for monthly, quarterly, and yearly audit. All patients admitted to the CCU have a form attached to their records on which details of their age, sex, diagnosis, drug treatment and other management, investigations, complications, and outcome are recorded. Forms are updated on the daily CCU ward round and on discharge from the unit. Information is coded and entered into a specially constructed computer database. Statistics are compiled by an audit program, written in dBASE programming language, to produce monthly and quarterly reports. These provide a breakdown of age distribution, length of stay, drug treatment, and outcome within diagnostic categories. The data are automatically formulated to produce an output that can be directly displayed at monthly clinical audit meetings without the need for further intervention or modification. Case notes relating to any deaths or complications are retained for discussion. During the first nine months of operation 492 patients were treated in the CCU and their details entered into the database. The resulting output provided an accurate picture of our acute cardiac management and led to a number of changes in management policy.

This system represents a straightforward and inexpensive approach to a more complete medical audit without imposing a large time burden on medical staff. It would be applicable to any unit and could be extended to cover any other areas of inpatient care.

Is the time saved by thrombolysis in accident and emergency departments significant?
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Royal Victoria Infirmary and Freeman Hospital, Newcastle upon Tyne

The earlier thrombolysis is administered after myocardial infarction the greater the reduction in mortality. From July 1989 to November 1990 thrombolysis was administered to 264 patients with prehospital onset of acute myocardial infarction, 160 at the Royal Victoria Infirmary (RVI), where patients are admitted to the coronary care unit (CCU) from an accident and emergency department, and 104 at Freeman Hospital (FH), where patients are admitted directly to the CCU as there is no accident and emergency department. The catchment areas of these hospitals are similar. Time (minutes) from onset of pain to arrival in hospital was shorter in the RVI than in FH (145 ± 193; p < 0.0001). Time from arrival to thrombolysis was longer in the RVI than in FH (84 ± 52; p = 0.0001). Thus the time from onset of pain to thrombolysis in each hospital (RVI = 228, FH = 243; p = 0.09) was similar. In the RVI thrombolysis was given in the accident and emergency department to 39 patients and in the CCU to 121 patients. In the accident and emergency department thrombolysis was given earlier after the onset of pain (176 ± 245; p = 0.0008) and earlier after arrival in hospital (49 ± 96; p < 0.0001) than in the CCU. Patients treated at the RVI’s accident and emergency department were compared with...
patients treated at FH. After arrival in hospital the delay in receiving thrombolysis was the same in both groups, but administration of thrombolysis was sooner after the onset of pain in the RVI's accident and emergency department (176 ± 243; p = 0.0004).

Provision of thrombolysis in an accident and emergency department can allow a subgroup of patients to receive thrombolysis almost 50 minutes sooner than after transfer to a CCU. Even direct admissions by a general practitioner to a CCU are associated with delay in receiving thrombolysis, which might be avoided by direct patient access to an accident and emergency department with facility for thrombolytic administration.

Thrombolysis at home: a dream became reality in the south of Italy

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We describe a programme of thrombolysis at home that is running in the south of Italy. The programme started in March 1990 with the purpose of treating patients with suspected acute myocardial infarction at home with thrombolytic treatment. The organisation consists of 364 local doctors trained in thrombolysis who administer the drugs at home; 25 cardiologists from our coronary care unit; a system of on line electrocardiographic transmission; and two ambulances equipped with resuscitation equipment. The doctors administer the thrombolytic agent after transmission of the electrocardiogram and consultation with the coronary care unit team. If the diagnosis of suspected acute myocardial infarction is confirmed by the cardiologists from the coronary care unit the ambulance leaves the hospital with an emergency team composed of two paramedical staff and a cardiologist. The programme aims at treating patients from a general population of 400,000 people. The thrombolytic drug administered is recombinant tissue-type plasminogen activator. Fifty three patients with suspected acute myocardial infarction have been treated so far. The diagnosis of acute myocardial infarction was confirmed in 21 of the 53 patients by electrocardiographic and enzymatic changes. The average time elapsed from the onset of symptoms and thrombolysis was 33-8 (25) minutes, and the average time from thrombolysis to admission to the coronary care unit was 75-6 (21-7) minutes. No deaths and no major bleeding complications were registered in the 53 patients treated. Twenty three patients had non-Q wave myocardial infarction and three required emergency coronary artery surgery. Although we have treated a small number of patients, we found the administration of the thrombolytic drug safe enough to continue giving it at home.

Clinical audit increases thrombolysis prescription rates to elderly patients with suspected acute myocardial infarction

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Derriford Hospital, Plymouth

Fears of haemorrhagic complications, and doubts about efficacy, may limit thrombolysis prescription to elderly patients with suspected acute myocardial infarction. Retrospective five month audit of 264 patients aged > 64 admitted to the coronary care unit (CCU) found that 110 (42%) had acute myocardial infarction, of whom 13 (12%) received streptokinase, and 32 (35%) had such treatment withheld either because of dyspepsia or for unsatisfactory reasons. CCU staff were informed of this low thrombolysis uptake rate and nursing staff were instructed to question senior house officers when thrombolytic treatment was prescribed for patients with chest pain. One year later a second, prospective five month audit was performed without the knowledge of CCU staff. During the second audit 55 out of 119 (46%) patients with acute myocardial infarction received either streptokinase or recombinant tissue-type plasminogen activator (p < 0.01 compared with first audit) and 13 out of 79 (16%) patients with unstable angina also received thrombolytic treatment. Reasons for omitting treatment were significantly different between the two studies (p < 0.02 by χ² test). Similar numbers of patients in both the first and second audits were excluded because of specific contraindications (20 (22%) < 17 (26%), delay in presentation after onset of chest pain (14 (15%) v 18 (28%)), and delay in diagnosing acute myocardial infarction (25 (28%) v 23 (36%)). More patients were excluded because of dyspepsia (10 (11%) v 1 (2%)) or for unstated reasons (22 (24%) v 5 (8%)) in the first compared with the second audit.

The audit process has identified an easily remediable deficiency in the clinical management of elderly patients with acute myocardial infarction and has resulted in an improved thrombolysis uptake rate which is now similar to that reported in younger patients.

Audit of extended ambulance aid in management of cardiac arrest

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Ambulance crews receiving extended training learn the skills of vein cannulation, endotracheal intubation, drug administration, arrhythmia recognition, and defibrillation. We present a retrospective analysis of 274 report forms and electrocardiograph rhythm strips related to the management of out of hospital cardiac arrest by ambulance staff with these skills. Seven (2.5%) patients were managed for primary respiratory arrest; three were later discharged from hospital alive. In 98 (35.8%) patients the initial resuscitation protocol was for ventricular fibrillation (VF); 26 were admitted and 17 discharged. In 169 (61.7%) patients the initial resuscitation protocol was for asystole or electromechanical dissociation (EMD); 11 were admitted and one was discharged. Endotracheal intubation was attempted in 226 cases and was successful in 214 (94.7%). Vein cannulation was attempted in 219 cases and was successful in 192 (87.7%). Drugs were administered to 71 patients presenting in VF and to 145 patients in asystole or EMD. We judged that drugs were important in restoring cardiac output in four of the 17 survivors of VF and in the patient who survived EMD. Ninety seven per cent of drug administrations were non-contributory. There were deviations from the VF protocol in 27 (27.5%) cases: 11 related to incorrect energy of the first shock, 13 to incorrect timing of drug administration, and three to inappropriate drug usage. There were 27 (16.0%) deviations from the asystole protocol. The majority related to failure to complete the protocol and there were four cases of inappropriate drug use.

This study shows the need for continuing medical audit of paramedical practice.
Financial audit of antitachycardia pacing in patients with supraventricular tachycardia

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This study assessed the financial implications of antitachycardia pacing in patients with frequent supraventricular tachycardia. Intertach pacemakers were implanted in 24 patients (mean age 46 years, five males): 21 had atrioventricular nodal re-entry tachycardia. A mean of 4.9 (range 0-8) drugs had failed and patients had been admitted to hospital a mean of 3:29 (0-31) times over a mean symptomatic period of 12.3 years (2 months to 25 years). The mean admission time for implantation was 2.8 (2-7) days. One patient with the Wolff-Parkinson-White syndrome underwent surgery. Over a mean follow up period of 21 (2-42) months all patients had their symptoms well controlled. Infection occurred in two patients and pain over the pacemaker required resiting in two. Two patients were admitted for supraventricular tachycardia. Six patients continue to take antiarrhythmic drugs. Costs were calculated, including value added tax, capital charges, and allocated overheads. The cost per year before pacing was £605 including drug costs (£163), clinic visits (£139), and hospital admissions (£303). The mean cost of pacemaker implantation was £3579, including the pacemaker and lead (£2839), admission and procedure (£269), readmissions (£136), and first pacing check (£35). Subsequent annual follow up cost was £74, including annual clinic visits (£35) and drug costs (£39). The cost of pacing is £3823 while medical management costs £3630, assuming pacemaker life of six years: with a 10 year life the cost is £4219 compared with £6050.

To conclude, the excess cost of implantation of an antitachycardia pacemaker is minimal in patients with frequent supraventricular tachycardia despite drug treatment and is justified by excellent control of symptoms and reduction of drug usage and hospital admissions.

Balloon dilatation of pulmonary valve for palliation of tetralogy of Fallot

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We attempted balloon dilatation of the pulmonary valve (BV) for palliation of recurrent cyanotic spells or severe persistent cyanosis in 67 patients with tetralogy of Fallot. Eight patients had associated complete atioventricular septal defects. The median age at BV was 5 months (range 0-03-52 months) and the balloon to annulus ratio 1.5 (range 0.86-3.44). There were no deaths resulting from BV. In three patients the pulmonary valve could not be crossed and an aortopulmonary shunt was performed at the same hospital admission. In the remaining 64 patients the systemic arterial oxygen saturation (SaO₂) after BV increased from 74% (range 44-99%) to 90-5% (range 45-100%); p < 0.01. Follow up catheterisation and angiography were performed in 35 patients 12 months (range 3-30 months) after BV. Of these, the condition of 24 had been adequately palliated by BV (group A), while 11 had required an aortopulmonary shunt 1 month (range 0-3 months) after BV (group B). The two groups were similar (p > 0.1) with respect to age at BV, pulmonary annulus diameter (AD), ratio of combined pulmonary artery to descending aortic diameter (PA:DAO) before BV, and the interval to follow up investigation. Patients in group A, however, had an immediate improvement in SaO₂ from 74% (range 56-99%) to 91% (range 69-100%) (p < 0.01). The change in SaO₂ in group B was non-significant from a median of 67% (range 47-83%) to 76% (range 45-97%). The AD in group A had increased from 6.75 mm (range 3.64-14 mm) to 10.55 mm (range 6.0-26.8 mm) (p < 0.01) and was greater than that expected from growth alone (p < 0.01) over the same period. The change in AD in group B was similar (p > 0.1) to that expected from growth alone over the period of follow up. The increase in PA:DAO was similar in both groups from a median of 1.85 to 2.21 in group A and from 1.67 to 2.26 in group B (p > 0.1). Of 42 patients who had corrective surgery, 27 required a transannul patch for reconstruction of the right ventricular outflow tract. The use of a transannul patch was similar in groups A and B.

BV is safe, provides adequate palliation, and promotes growth of the annulus and pulmonary arteries in tetralogy of Fallot. Failure to improve SaO₂ immediately after BV is an indication for an aortopulmonary shunt.

Mechanisms of relief of right ventricular outflow obstruction by percutaneous balloon dilatation in tetralogy of Fallot

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Twelve children with tetralogy of Fallot and increasing cyanosis underwent balloon dilatation of the right ventricular outflow tract (RVOT) as their only palliative procedure. Mean age at the time of the first dilatation was 10.5 months (range 5.5 to 20 months). Four children subsequently underwent a second balloon dilatation 3-5 to 10 months (mean 3 months) after the first procedure. There were no major complications during any of the dilatation procedures, and all the children experienced an improvement in arterial oxygen saturations. The time interval between the first dilatation and total correction was 3 to 19 months (mean 9.4 months). At the time of surgery tearing of a pulmonary valve cusp was noted in five patients—but in none was there any evidence of annular disruption. In eight children there was extensive scarring of the infundibulum consistent with muscular disruption at the time of RVOT dilatation, with subsequent fibrosis and contracture of the RVOT. This may have contributed to later recurrence of the RVOT obstruction but did not preclude a satisfactory surgical repair. Signs of balloon dilatation were absent in only one child.

Balloon dilatation of the RVOT relieves symptoms for a variable length of time and is a suitable alternative primary palliative procedure in children with symptoms of tetralogy of Fallot.

Five year follow up after balloon dilatation of pulmonary valve: is obstruction completely relieved at the expense of pulmonary incompetence?

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No long term data exist after balloon dilatation of the
pulmonary valve (BPV). We reviewed 34 of our first 40 consecutive patients a mean of 5-2 (SD 0-8) years after BPV. Twenty seven had isolated pulmonary stenosis, five Noonan’s syndrome, and two previous surgical valvotomy. Six patients were excluded because of death (two), residence abroad (two), pulmonary artery stenoses (one), and Ebstein’s anomaly (one). The transpulmonary gradient was 73 (34) mm Hg before BPV, 34 (26) immediately after, 22 (9) at catheterisation 6 (0-6) months later (29 patients), and 19 (10) by Doppler ultrasonography at five years. Repeat BPV had been performed in eight patients (three with Noonan’s syndrome), which was the index procedure for analysis. All had symptoms. At five years eight patients (four with Noonan’s syndrome) had a residual transpulmonary gradient >20 mm Hg (group A) whereas in the remaining 26 the transpulmonary gradient was <20 mm Hg (group B). In the seven patients with Noonan’s syndrome and in patients with previous surgical valvotomy transpulmonary gradient was reduced from 74 (24) before BPV to 23 (12) at five years, with the highest residual gradient being 41 mm Hg. The balloon to annulus ratio was larger for patients with pulmonary stenosis in group B than in group A (1-2 (0-1) v 1-0 (0-07), \( p = 0-005 \)), whereas large balloons were used in patients with Noonan’s syndrome in group A (1-3 (0-1)). Patients in group B were more likely to have significant pulmonary incompetence (6/24 v 0/8) and had a greater right ventricular to left ventricular long axis diastolic dimension ratio (0-47 (0-1) v 0-35 (0-04), \( p = 0-05 \)). Pansystolic tricuspid regurgitation on Doppler ultrasonography was found in only two patients. Relief of transpulmonary gradient persisted at five years especially when “oversized” balloons were used. Acceptable results can still be obtained for dysplastic valves. More complete relief of transpulmonary gradient was associated with increased RV dimension probably because more pulmonary incompetence is induced. This is well tolerated at five years but may be important in the longer term.

Early results of transcatheter laser assisted balloon dilatation of pulmonary valve atresia
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Transcatheter laser assisted balloon dilatation for pulmonary valve atresia was attempted in seven children aged 1 day to 2 years (weight 2-1-9-1 kg). In five the ventricular septum was intact but in two there was also a ventricular septal defect. Blalock-Taussig shunts had been performed in three, while in four the arterial duct was still patent. A 0-018 inch “hot tip” laser guide wire, powered by a 3-5 Watt Nd-YAG laser, successfully crossed the atretic valve in six patients: in four antegrade from the right ventricle and in two retrogradely from the pulmonary artery. Balloon dilatation of the pulmonary valve was then performed with 5-8 mm balloons. In one patient with additional infundibular atresia the laser wire perforated the right ventricle during antegrade advancement; the resulting cardiac tamponade responded to needle pericardiocentesis and the leak had sealed at operation for a shunt three hours later. During follow up at 2-8 months oxygen saturations >85% were maintained in all but one (72%) and none required surgery. Doppler pulmonary valve gradients ranged from 18 to 75 mm Hg, and of those with an intact septum, the arterial duct had closed in two and the septal defect had either closed or become restrictive in all.

Laser assisted pulmonary valve dilatation is a promising new treatment strategy in patients with pulmonary valve atresia. Its potential role in avoiding palliative surgical shunting and right ventricular outflow tract reconstruction will be determined during longer term follow up.

Balloon dilatation of aortic recoarctation: determinants of haemodynamic results
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Balloon dilatation of recoarctation of the aorta was performed in 26 patients who underwent 30 procedures over eight years. Age at first dilatation ranged from 2-6 months to 18:3 years (median 8 months). After dilatation the systolic gradient decreased from 49 (17) mm Hg to 20 (17) mm Hg (\( p < 0-001 \)). The gradient was <20 mm Hg after the first dilatation in 17/26 (65%) patients. In the remaining nine patients gradients of 25-80 mm Hg remained. During follow up of 2 months to 6-7 years (mean 1-8 years) five of the 17 patients with good initial results developed further restenosis needing repeat dilatation or surgery (one for an aneurysm). Of the nine patients with gradients >20 mm Hg, one had repeat dilatation and three reoperation; five were managed conservatively. After follow up of 2 months to 6-7 years (mean 1-8 years) 15 (58%) patients had a good and 11 (42%) a poor late result. Two (8%) patients developed aneurysms, one early and one 2 months after balloon dilatation. The aortic diameters at different levels of aortic arch and isthmus, normalised to aortic diameter at diaphragm level, in patients with good results were significantly larger than those in patients with poor results. A balloon to aortic diameter ratio at diaphragm level close to 1-0:1:0 had a significantly favourable influence on late results; ratios of <0-8:1-0 were associated with a poor outcome, both early and late.

Balloon dilatation, though a preferable alternative to surgery, occasionally fails to produce a good result. This is influenced both by the anatomy of the aortic arch and by the balloon to aortic ratio at diaphragm level.

Assessment of suitability of atrial septal defects for transcatheter closure in children: role for transoesophageal echocardiography?
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The ability of transoesophageal echocardiography to identify the features of oval fossa atrial septal defects that determine suitability for transcatheter closure was assessed in a prospective study. The features considered were size, fenestration, adequacy of margin for anchorage of the device, and clearance from right pulmonary veins, coronary sinus, inferior caval vein, and mitral valve. Findings were compared with operative anatomy and precardial echocardiography. Transoesophageal echocardiography with a 5 MHz, 13 mm single plane oesophageal transducer was performed in 12 anaesthetised children before surgery.
Age and weight at study ranged from 3 to 9 years (median 5) and from 13 to 23 kg (median 17). All studies took less than 10 minutes and were uncomplicated. One defect had multiple fenestrations, not identified on precardial echocardiography. Direct measurement of the horizontal size of the defect was possible and estimation of vertical size was attempted by noting movement of the endoscope at the teeth while the defect was scanned from its superior to inferior margins. In all cases distances from the defect to the posterior atrial wall and to the mitral valve could be measured. The coronary sinus was seen in four patients. The caval veins and pulmonary venous inflow were identified in all patients but not in the same echo plane as the defect. In one case proximity to the inferior caval vein, which would have precluded clam shell closure was not appreciated. The exact site of entry of the right upper pulmonary vein was rarely established.

Transoesophageal echocardiography provides some anatomical detail not readily available from precardial echocardiography, estimation of adequacy of margin around the defect for anchorage of an occluding device and clearance from the mitral valve. It cannot, however, reliably identify all the features which determine suitability for transcatheter closure such as vertical size and the proximity of the right pulmonary veins, coronary sinus, and inferior caval vein, which are not imaged in the same plane as the defect.

Angioplasty of total occlusions by the MagnaRail system

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Percutaneous transluminal angioplasty (PTCA) of coronary occlusions has produced disappointing results, with a reported primary success rate of between 42% and 66% compared with over 95% in non-occlusive stenoses. The MagnaRail system (Schneider) may possess advantages to improve results. The 0.021 inch guide wire has a steel shaft over which balloons of differing diameters may be passed. At the tip of the wire is a flexible tungsten spring and a 1 mm olive. This arrangement maximises “pushability” and minimises intimal trauma. We investigated the success rate in 54 patients with coronary occlusions (left anterior descending in 12, right coronary artery in 25, circumflex in 14, vein grafts in three). The index vessel was considered to be occluded in all cases. There was angiographic evidence of bridging collaterals in 14 patients, retrograde collaterals in 33, and both in five. Twelve vessels had no distal flow. There were no deaths and no patients required surgery. The primary success rate (a residual stenosis of less than 50% and disappearance of collaterals when present) was 83-0%. The age of the occlusion could be estimated from a change in anginal severity or myocardial infarction. In 32 patients it was estimated to be less than three months (group A) and in 22 greater than three months (group B). The primary success rate in group A was 84-0% and in group B 82-0% (NS). The commonest reason for failure was intraprocedural occlusion in group A (5/5 failures) whereas in group B failure was either due to inability to cross the lesion (2/4 failures) or due to the wire tracking preferentially into a proximate side branch (2/4 failures). In 14 patients it was necessary to redilate the lesion with a different sized balloon. This was easily performed over the guide wire. A disadvantage of the system was the guide wire opacity which necessitated withdrawal before angiography. It was often possible to recross the lesion even if a dissection was present.

Thus the MagnaRail system is highly successful in PTCA of coronary occlusions and has a primary success rate that approaches that of PTCA of non-occlusive stenoses. Comparisons with other equipment are required but it should be considered the system of first choice in angioplasty of total occlusions.

Treatment of chronic coronary artery occlusions with the Terumo glide wire

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Seventeen patients (12 male, five female) with coronary occlusions of more than three weeks duration (range 3 weeks–2 years) and lesions that could not be crossed with conventional or olive tipped wires (Magnum wire—three cases) were operated on with either the 0-35 (eight cases) or the 0-18 (nine cases) Radiofocus Terumo glide wire. The 0-35 wire was introduced into the coronary artery without a balloon catheter. If this wire crossed a lesion it was withdrawn and a conventional wire was introduced along the track made by the larger wire. The 0-18 wire was introduced via a large lumen coronary balloon. Coronary arteries treated were the right coronary in nine patients, the circumflex in three, and the left anterior descending in four. The 0-35 wire crossed in five out of eight cases. The 0-18 wire crossed in six out of nine cases. Angiography after angioplasty with the use of these wires showed some degree of dissection in all cases. The overall success in our institution in crossing occlusions with conventional wires is 41% in 80 cases, the use of hydrophilic wires in chronic coronary occlusions has increased the primary success rate of our procedures.

Further investigations of this technology may reduce the need for expensive devices for the treatment of coronary occlusions.

Myth of the “safe procedure”: disobliteration of chronically occluded coronary arteries

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The risk of myocardial infarction and its complications should be lower in coronary angioplasty (PTCA) of chronically occluded vessels than it is in PTCA of non-occluded vessels. We reviewed the results of disobliteration of chronic coronary occlusions at our institution between 1987 and 1990. An attempt was made to recanalise 98 occluded vessels in 93 patients (left anterior descending artery in 46, left circumflex artery in 14, right coronary artery in 38). Primary success (defined as antegrade flow of contrast at the end of the procedure) was achieved in 47 vessels (47-9%). Failure to cross the occlusion, without adverse consequences, occurred in 41 lesions (41-8%). Local dissection of the vessel was observed in two cases (2%) and thrombus formation was seen in another two (2%). An extensive dissection of the target vessel (the right coronary artery in all cases) occurred in six patients (6-1%) and was associated with chest pain and the electrocardio-
graphic changes of acute myocardial ischaemia in five (83-3%). In all cases chest pain was controlled medically (including laser balloon angioplasty in one and stent implantation in two), but there was myocardial necrosis in three. There was no change in symptom class in three patients, but the condition of three deteriorated by at least one class and all three patients underwent coronary artery bypass grafting, two during the same hospital admission.

PTCA of chronically occluded coronary arteries is associated with a low primary success rate. The risk of myocardial ischaemia and infarction is similar to that of PTCA in other settings, despite "support" for the distal vessel via collateral channels from the contralateral coronary artery. Disobliteration of the right coronary artery in particular carries a high risk of dissection (15-8%), for reasons which are not yet clear.

Impact of late restenosis in long term outcome of percutaneous transluminal coronary angioplasty for chronic total occlusions

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Though percutaneous transluminal coronary angioplasty (PTCA) can often recanalise chronically occluded vessels, controversy remains as to the clinical benefit of the procedure in the long term. We report on the follow up over a period of 20 (16) months of 72 patients who underwent PTCA for chronic total or functional occlusion. The primary success rate was 65%. The groups in whom PTCA was successful and unsuccessful were similar in terms of age, sex, cardiovascular history, and number of diseased vessels and vessels dilated. Of the 25 patients in whom PTCA was unsuccessful, eight (32%) were referred for coronary artery surgery (CAS) and 17 (68%) were treated medically. Of the group in whom the procedure was successful, 27 (57%) remained free of symptoms or had minimal symptoms throughout the follow up and 17 (36%) had recurrence of symptoms and underwent repeat angioplasty. All had restenosis of the previously occluded artery. Three patients were referred for CAS, 11 underwent repeat PTCA, and three continued with medical treatment. Repeat PTCA failed in four patients (success rate 73%). Three of them were referred for surgery. In addition, there were one cardiac and two non-cardiac deaths, all in the group in whom PTCA was successful. During the first six months of follow up CAS was indicated in eight (32%) patients in the group in whom PTCA failed while only three (6%) patients in the same group referred for surgery because of symptomatic restenosis with or without failed repeat PTCA (p < 0.005). Symptomatic restenosis occurred, however, in six patients after the first six months of follow up (35% of all symptomatic restenosis), resulting in three additional referrals for surgery and making the total figure of referrals for CAS in the successful group six (12%). At the end of follow up a significant difference in the number of patients without symptoms or with minimal symptoms in the successful and failed groups was found among survivors who did not undergo CAS (32/35 vs. 9/16 respectively, p < 0.03).

We conclude that patients with successful PTCA of chronically occluded arteries benefit in the long term from a significant reduction in their anginal symptoms. Late symptomatic restenosis seems to be common, however, and is a cause of late referral for CAS, reducing the early advantage of successful over failed cases in terms of need for surgery.

Emergency treatment of acute coronary dissection during angioplasty

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Coronary artery dissection causing acute myocardial ischaemia complicates 5% of coronary angioplasty (PTCA) procedures. The outcome of emergency coronary artery bypass grafting (CABG) in this situation is frequently unsatisfactory because of delay in re-establishing coronary perfusion. To provide more immediate reperfusion we have used, in a non-randomised fashion, laser balloon angioplasty (LBA) or self expanding intracoronary stents in 44 patients in whom PTCA was complicated by coronary artery dissection. LBA was performed in 13 patients and stent implantation performed in 31. A satisfactory immediate result, with resolution of antegrade blood flow and resolution of clinical and electrocardiographic evidence of myocardial ischaemia, was obtained in 41 patients. In one patient stent implantation was undertaken after an unsatisfactory result on LBA. Emergency CABG was performed in one patient after stent implantation. Seven patients (23%) receiving stent implantation had acute myocardial infarcts (one Q wave, six non-Q wave), one of whom died 24 hours after the procedure (3% mortality), and one patient receiving LBA had a Q wave myocardial infarct. Stent occlusion requiring disobliteration within the first week of implantation occurred in two patients (one received thrombolysis, the other repeat PTCA) and was associated with non-Q wave infarction in one patient. During six months of follow up restenosis occurred in four patients in the LBA group (29%) and was managed by repeat PTCA in two and CABG in two. In the group receiving stent implantation there was one clinically silent permanent occlusion and two deaths (1 week and 3 months after the procedure). Restenosis was seen in two patients (6-4%) in this group, one of whom underwent PTCA and the other CABG.

Both LBA and coronary stent implantation can ensure rapid coronary reperfusion with myocardial salvage in acute coronary dissection after PTCA and are acceptable alternatives to emergency CABG. LBA has fewer early complications, but stent implantation is associated with lower rates of restenosis.

Coronary angioplasty in 1990: experience of 100 procedures in a centre without on site surgical cover

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The debate on the need for on site surgical standby for coronary angioplasty is based on the currently accepted success rates of 90% and the need for emergency surgery of between 2% and 5%. Increased operator experience and technical advances might be expected to result in an
improvement in these figures. We present the data on the first 100 procedures since 1 January 1990 performed in a centre without on site surgical cover. Coronary angioplasty was performed in 90 patients (71 male, age 58-5 years). The clinical indication was stable angina in 60 patients, unstable angina in 25, postinfarction unstable angina in 13, and acute myocardial infarction in two. Single vessel angioplasty was performed in 61 patients, two vessel in 38, and three vessel in one and 13 patients had total occlusions. The overall success rate was 91%, and 98-9% when total occlusions were excluded. There were no deaths or need for emergency bypass surgery. One patient sustained a Q wave myocardial infarction and one patient had an abrupt occlusion successfully redilated. Two patients were cardioverted for ventricular tachycardia during the procedure, one patient required ventilation for a pulmonary embolus 24 hours after the procedure, and three patients had complications related to arterial access. Restenosis requiring repeat angioplasty was required in nine patients.

These results in a patient population with a higher than average risk profile due to the high percentage with unstable and postinfarction angina suggest that the trend towards improved success in coronary angioplasty persist. None of the patients required emergency surgery, which questions the requirement for immediate on site surgical standby for all patients undergoing coronary angioplasty.

Edinburgh randomised trial comparing Björk-Shiley and porcine valve replacements: results at 12 years

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Patients undergoing heart valve replacement may receive a mechanical prosthesis necessitating lifelong anticoagulant treatment or a porcine bioprosthesis without an absolute need for anticoagulants. We carried out a randomised prospective trial to compare the durability and incidence of valve related complications of the Björk-Shiley mechanical prosthesis with the Hancock and Carpentier-Edwards porcine prostheses. The mitral valve was replaced in 261 patients, the aortic in 211, and both in 61; survivors were followed up for a mean of 12 years. We found a trend towards improved actuarial patient survival with the Björk-Shiley prosthesis, but this was not statistically different (Björk-Shiley 51-5% (3-2%), porcine 44-4% (3-2%) alive at 12 years; \( p = 0.08 \), log rank test). There was no significant difference in the actuarial incidence of reoperation at five years, but at 12 years significantly more patients with a porcine prosthesis had undergone reoperation (Björk-Shiley 8-5% (2-0%), porcine 37-1% (4-1%); \( p < 0.001 \)). An analysis combining death and reoperation as end points for an actuarial assessment of survival with the original prosthesis intact confirmed improved valve survival in patients with Björk-Shiley prostheses (Björk-Shiley 48-6% (3-2%), porcine 30-0% (3-0%) at 12 years; \( p < 0.001 \)). Bleeding requiring admission to hospital or blood transfusion occurred significantly more frequently in those with Björk-Shiley prostheses (Björk-Shiley 18-6% (3-2%), porcine 7-1% (2-3%) at 12 years; \( p < 0.01 \)). There was no significant difference at 12 years in the actuarial occurrence of embolism (Björk-Shiley 21-1% (3-1%), porcine 26-4% (3-5%) or endocarditis (Björk-Shiley 3-7% (1-4%), porcine 4-6% (1-6%)).

We conclude that there is improved valve survival with the Björk-Shiley prosthesis but with an attendant increased risk of bleeding associated with the need for anticoagulant treatment.

Late functional results after surgical closure of acquired ventricular septal defect

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Between 1973 and 1988, 101 patients (mean age 69 years, range 53-88) underwent surgical treatment for acquired ventricular septal defect (VSD) in this unit, with an early mortality of 20-8%. Of the 60 current survivors, 58 (97%) were followed up for 38-8 (34) months and form the study population. Clinical examination, radionuclide multigated acquisition ventriculography, and colour flow mapping was undertaken in 46 patients, 42 of them having additional 24 hour Holter monitoring; the remaining 12 were interviewed by telephone. Subjective exercise tolerance was adequate for daily living in 47 patients (81%) (New York Heart Association class I, 29 patients; class II, 18 patients).

Assessment of cardiac valves by endovascular ultrasonography: a new approach

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Current methods of valve assessment are still not infrequently prone to interpretative error and a “gold standard” has yet to be found. We assessed intravascular ultrasonography in seven explanted bioprostheses mounted in a prototype valve rig approximating “normal” cardiac conditions and studied them with a 20 MHz mechanically rotating probe. This was compared with simultaneous video optical images. In five cases good correlation was obtained, including orifice area (with a calibrated grid), commissural anatomy, leaflet pliability, and tissue characterisation (calcification v fibrosis v normal). In all five cases the mode of valve failure was accurately assessed (critical stenosis, two cases; leaflet perforation or tear, or both, two; and subacute bacterial endocarditis, one). The maximum depth of field in our system was 10-12 mm. This resulted in fair field attenuation with poor image quality in the remaining two valves, which were both large with peripheral tears.

We conclude that intravascular ultrasonography seems to provide definition of anatomy superior to conventional imaging systems. The prime use of the present system would be in evaluating valve stenosis, or small valves, because of its reduced depth of field. The ideal intravascular ultrasonography imaging system should utilise a lower frequency (10-15 MHz) or a larger aperture to extend the range and depth of field such that both large and small valves, whether incompetent or stenotic, could be usefully and accurately studied.
Left ventricular ejection fraction was reduced at 39\% (15\%) for the group. Colour flow mapping identified a small, haemodynamically insignificant residual VSD in eight patients (17\%). Important, but asymptomatic arrhythmias were noted on a 24 hour tape in 28 patients (67\%), including frequent monomorphic or polymorphic ventricular premature beats (17\%), ventricular tachycardia (two), paroxysmal atrial fibrillation (two), paroxysmal atrial tachycardia and supraventricular tachycardia, or both (seven). Exercise testing failed to provoke arrhythmias in any patient.

Despite significant impairment of ventricular function, the majority of survivors of surgical repair of acquired VSD can expect a good quality of life. Asymptomatic arrhythmias are common in the survivors of acquired VSD repair and may account for the late mortality in this group.

**Overcoming peroperative spasm of the internal mammary artery: which is the best vasodilator?**

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After mobilisation, vasospasm often reduces flow through the internal mammary artery. An established method of relaxing the artery and increasing flow is to wrap it in a papaverine soaked swab. To our knowledge, the ability of other topical vasodilators to overcome spasm of the internal mammary artery has not been studied clinically. We have investigated the effect of five agents: normal saline, papaverine, nifedipine, glyceryl trinitrate, and sodium nitroprusside on free flow in the artery in 50 patients undergoing myocardial revascularisation. Under controlled haemodynamic conditions free flow was measured before any pharmacological intervention and a median of 18-5 minutes after the pedicle had been sprayed with one of five agents. Normal saline produced a small increase in flow from a median of 23 (range 17-88) to 38 (20-84) ml/min (NS), whereas a significant increase occurred with papaverine from 25 (16-78) to 43 (34-112) ml/min (p < 0.01). Nifedipine and glyceryl trinitrate raised free flow almost threefold, from 23 (14-66) to 71 (45-118) ml/min and from 23 (14-58) to 62 (46-126) ml/min respectively (both p < 0.001). Sodium nitroprusside, however, with an increase in flow from 26 (10-58) to 108 (46-196) ml/min, 250\% above control values, proved to be more effective than nifedipine and glyceryl trinitrate (p < 0.05).

We therefore recommend the topical use of sodium nitroprusside to relieve peroperative spasm of the internal mammary artery.

**Mechanisms underlying intimal thickening in arteriovenous bypass grafts**

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In pig saphenous vein to carotid artery bypass grafts the time course of changes in the following variables were related: (a) medial and intimal size by morphometry of transverse sections, (b) cell number and density by DNA concentration and by counting nuclei in transverse sections, (c) endothelial morphology by scanning electron microscopy, and (d) tissue cholesterol concentration. In the first week after grafting medial and intimal thickening were associated with an increase in cell number. Between one and four weeks after grafting further rapid medial and intimal thickening occurred without a further increase in cell number but with a reduction in cell density, which suggested that cell migration, hypertrophy, and the laying down of extracellular matrix were responsible. Between four and 39 weeks after grafting a slower rate of medial and intimal thickening was associated with a parallel increase in cell number and no further change in cell density. A largely intact endothelium was observed in grafts recovered either one or four weeks after grafting. Cholesterol concentration was slightly raised one week after grafting but it declined to values similar to those in veins by 27 weeks after grafting.

We conclude that three processes contribute to medial and intimal thickening—namely, (a) an initial phase of rapid smooth muscle cell proliferation, (b) smooth muscle cell migration, hypertrophy, and synthesis of extracellular matrix, and (c) a late phase of slower smooth muscle cell proliferation. Late smooth muscle cell proliferation occurs under a morphologically intact endothelium and without progressive cholesterol accumulation.

**Cardiac surgery: breaking with intensive care**

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The need for intensive care units for the recovery of patients undergoing cardiac surgery is questionable on clinical and economic grounds. Between January and December 1990, 705 adult patients underwent open heart surgery at the Oxford Heart Centre. Six hundred and twenty five of these patients were managed postoperatively through a recovery area. This practice is based on a prospective study of 245 consecutive patients over the first four month period. The mean age of the patients was 63-2 years, and they underwent a wide variety of operative procedures. Ninety per cent of them underwent recovery in a dedicated three bedded recovery area where the management protocol led to rapid extubation and step down in dependency care. The median time for ventilatory support was 90 minutes after transfer to the area, with only five patients being subsequently admitted to the general intensive care unit for prolonged respiratory and cardiac support. During the same period only 10 patients were electively admitted to the general intensive care. Two patients (0-8\%) in this group died in hospital.

Our study confirms that nearly 90\% of patients undergoing cardiac surgery today may undergo recovery safely and effectively in a more economical area.

**Contribution of systolic compression to impaired coronary reserve in cardiac hypertrophy**

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The impaired coronary reserve associated with left ventric-
cular hypertrophy may be due to a structural change in the coronary vasculature or to a functional impairment of flow secondary to increased extravascular forces. Left ventricular hypertrophy was induced in guinea pigs by aortic constriction. The vascular effects of hypertrophy were studied in isolated buffer perfused hearts 72 (6) days after aortic constriction (n = 15) and compared with sham operated controls (n = 12). Maximal dilatation and heart block were induced by adenosine infusion, allowing systolic effects to be abolished by brief cessation of pacing. Coronary reserve was defined as (vasodilated flow)/(basal flow) × 100%. Coronary resistance was computed from the pressure flow relation over the perfusion range 30–70 mm Hg. To examine the effects of systole on minimal coronary resistance an extravascular index was defined as the percentage increase in mean flow when systolic effects were eliminated. Basal flow, coronary reserve, and the extravascular index were measured at a perfusion pressure of 50 mm Hg. Heart weight was increased in the hypertrophied group (4.8 (0.2) g) compared with controls (3.3 (0.1) g) (p < 0.001). Basal coronary flow was equal in both groups (3.2 (0.2) × 3.0 (0.2) ml/min/g), but minimal coronary resistance was increased in the hypertrophied group (4.5 (0.44) × 3.70 (0.37) mm Hg/ml/min/g) (p < 0.05), giving rise to a decreased coronary reserve (141% (5.5) × 231% (24.1)) (p < 0.01). The minimal coronary resistance of the whole heart was equal in both groups (0.95 (0.1) × 1.06 (0.1) mm Hg/ml/min). The extravascular index was increased in the hypertrophied hearts (59.2% (3.5) × 45.7% (5.0)) (p < 0.05), despite there being no difference in left ventricular systolic or diastolic pressure at a constant heart rate (200 beats/min). Analysis of the pressure flow relation in the beating heart showed a greater increase in minimal coronary resistance induced by systole in the hypertrophied hearts (1.6 (0.2) × 0.9 (0.1) mm Hg/ml/min/g) (p < 0.05).

These findings indicate that coronary reserve is impaired in hypertrophied guinea pig hearts because of inadequate vascular development. In addition, systolic compression reduces coronary flow to a significantly greater extent in hypertrophied than normal hearts.

**Diltiazem reduces left ventricle mass without increasing myocardial collagen concentration in deoxycorticosterone acetate-salt hypertension**

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Some antihypertensive drugs reverse left ventricular hypertrophy but may increase the degree of myocardial fibrosis if concurrent collagen regression does not occur. Laboratory and clinical reports suggest that diltiazem can reverse left ventricular hypertrophy but little is known about its effects on collagen metabolism. This study examined the effects of short term diltiazem treatment on left ventricular mass and collagen content in a hypertensive rat model. Stable deoxycorticosterone acetate (DOCA)-salt hypertension was induced in male rats over 12 weeks. They were then divided into two groups. One group (n = 5) received diltiazem in distilled water as drinking fluid (0.3 mg/ml increased over two weeks to 0.7 mg/ml and maintained at 0.7 mg/ml for a further five weeks). The other group (n = 6) received distilled water. Normotensive controls received tap water throughout. After seven weeks hearts were removed and the dry mass of the left ventricle free wall plus interventricular septum was determined. Collagen content was estimated by spectrophotometric assay of hydroxyproline in the hydrolysed samples. There was an 18% reduction in systolic pressure in the diltiazem treated group (164 (5) mm Hg compared with 200 (5) mm Hg; p < 0.01). Although left ventricle mass was significantly higher in both hypertensive groups when compared with normotensive controls, absolute left ventricle mass was 18.5% lower in the treated group (p < 0.05). There was no significant difference between the hydroxyproline concentration in the hypertensive groups but total content of hydroxyproline in the treated group was 18.8% lower than in the untreated hypertensive group (p < 0.05).

Collagen regression appeared to parallel left ventricle mass reduction and there was no increase in the ratio of fibrotic tissue within the myocardium after regression of left ventricular hypertrophy with diltiazem. Thus it is likely that left ventricle mass reduction with diltiazem would not be associated with an unfavourable increase in myocardial stiffness.

**Membrane current changes as basis for arrhythmogenesis in hypertrophied myocardium**

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In hypertrophied myocardium action potential duration (APD) is prolonged, and this may be a key to the substantially increased risk of arrhythmias in this condition. Using the voltage clamp technique we have investigated membrane currents in a model of chronic, stable left ventricular hypertrophy to find out which current mechanisms are involved in APD prolongation. Systemic pressure overload was induced by subrenal aortic coarctation in the guinea pig. Single cardiac myocytes were isolated by enzymatic perfusion, and on stimulation at 0.2 Hz the mean APD at 90% repolarisation (APD<sub>90</sub>) was 310 (SEM 17) ms in cells from sham operated animals (n = 22) and 358 (13) ms in hypertrophied cells (n = 34, p < 0.05, unpaired t test). The density of the L type calcium current was significantly increased in hypertrophy (−11.1 (0-7) pA/pF, n = 34), compared with −8.6 (0-4) pA/pF in control myocytes, n = 25, p < 0.02). The current generated by sodium-calcium exchange was elicited by interrupting action potentials at different times and clamping to the resting potential. This current, which is also the principal component of the arrhythmogenic "transient inward" current, was greatly increased and prolonged in hypertrophied cells (current density −1.6 (0-2) pA/pF in controls, n = 7, −2.8 (0-2) pA/pF in hypertrophy, n = 23, p < 0.01). The time dependent potassium current, i<sub>K</sub>, is not significantly different in hypertrophied cells. Increases in calcium and sodium-calcium exchange current therefore account for APD prolongation in hypertrophy.

In this model of hypertrophy not associated with heart failure we found an increase in cell contractility. Mean cell shortening on depolarisation was 8-4 (1-2) µm in control myocytes n = 15, 20-0 (1-8) µm in hypertrophied myocytes, n = 25, p < 0.001. The time to peak contraction is unchanged but the duration of contraction is prolonged in hypertrophy.
Identification of \( x \) and \( \beta \) cardiac myosin heavy chain isoforms as major autoantigens in idiopathic dilated cardiomyopathy

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Immunisation with the cardiac myosin isoform induces experimental autoimmune heart disease in genetically predisposed mice. These mice produce heart specific autoantibodies, some of which are directed against the cardiac myosin isoform. We have reported the presence of circulating heart specific autoantibodies in a subgroup (25%) of patients with dilated cardiomyopathy (DCM) by indirect immunofluorescence. To identify the autoantigen(s) recognised by heart specific autoantibodies in human disease we tested by western blotting serum samples from 14 patients with DCM who were positive for cardiac antibody and 25 controls who were negative for such antibodies (six DCM, six ischaemic or valvular heart failure, 13 normal subjects). Crude myofibrillar proteins, extracted from fresh frozen human atrial or ventricular specimens with alkaline pyrophosphate buffer, were used as antigens. Sodium dodecyl sulphatepolyacrylamide gel electrophoresis (SDS-PAGE) of myofibrillar proteins (5 \( \mu l \)/lane) was performed (Laemmli's method) with 10% and 4% polyacrylamide gels. The proteins were electrophoretically transferred to nitrocellulose sheets (Towbin's method); the paper strips were then incubated in serum samples at 1/100 dilution for two hours. The reaction was revealed with a peroxidase labelled second antibody against human immunoglobulin.

On western blotting 12 of the 14 (86%) DCM serum samples containing heart specific antibodies reacted with both the \( x \) and \( \beta \) isoforms of myosin heavy chains; none of the 13 normals (\( p = 0.0001 \)) and one of the 12 heart failure negative control serum samples (8%, \( p = 0.0002 \)) contained antibodies against myosin heavy chains. In contrast, controls and patients had antibodies to ventricular myosin light chain isoform 1 (MLC-1v): DCM serum samples (8/14, 57%), heart failure negative control serum samples (4/12, 33%), and normal samples (2/13, 15%, \( p = NS \)).

These findings indicate that \( x \) and \( \beta \) cardiac myosin heavy chain isoforms are major autoantigens in patients with dilated cardiomyopathy.

Diversity of myosin heavy chain mutations that cause familial hypertrophic cardiomyopathy

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Familial hypertrophic cardiomyopathy has been defined as a heart muscle disorder of unknown aetiology. Recently we showed that mutations in the \( x \) and \( \beta \) cardiac myosin heavy chain genes cause familial hypertrophic cardiomyopathy in some but not all families. Two myosin heavy chain gene mutations have been characterised to date: affected individuals from one family have an \( x/\beta \) hybrid gene while affected individuals from an unrelated family have a \( \beta \) missense mutation. To determine the proportion of familial hypertrophic cardiomyopathy that is attributable to mutations in the myosin heavy chain locus we have begun a systematic screening of the peptide encoding sequences in the \( x \) and \( \beta \) cardiac myosin heavy chain genes. Single exons, derived from DNA obtained from affected individuals in 40 unrelated families with familial hypertrophic cardiomyopathy, were amplified by the polymerase chain reaction and examined by a combination of denaturing gradient gel, single stranded conformational polymorphism, and ribonuclease protection analysis. To date, new missense mutations have been identified that alter highly conserved amino acids in four families. The sites of these mutations suggest a clustering effect in a region of the globular head of the myosin heavy chain molecule.

Assessment of the diversity of the mutations causing familial hypertrophic cardiomyopathy will provide new insights into the myosin heavy chain functional domains and may suggest additional candidate proteins for causing the disease in families not linked to chromosome 14q11-12. In addition, identification and localisation of myosin heavy chain mutations will facilitate development of diagnostic probes for familial hypertrophic cardiomyopathy.

Changes in expression of \( \beta \) myosin heavy chain and \( c\text{-}myc \) genes in left and right ventricles of spontaneously hypertensive rats

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It is proposed that processes that stimulate cardiac hypertrophy are coupled to control of cardiac mass through signal transduction pathways mediated by proto-oncogene products such as \( c\text{-}myc \). To examine the role of \( c\text{-}myc \) in the development of hypertrophy and its association with expression of "fetal" contractile proteins we compared concentrations of \( \beta \) myosin heavy chain (MHC) and \( c\text{-}myc \) mRNAs in spontaneously hypertensive rats with those in Wistar Kyoto controls at 1-84 days after birth (n = 8-10 in each group). \( \beta \) MHC and \( c\text{-}myc \) mRNAs were measured in left and right ventricles by northern and dot hybridisation to specific oligonucleotides and cDNAs respectively. An increase in heart weight was evident in spontaneously hypertensive rats by three days (52-9 (SE 1·5)mg v 33-5 (1·1)mg, \( p < 0·05 \)), with similar differences in weight maintained up to 84 days. Transient stimulation of left ventricular \( c\text{-}myc \) mRNA was seen at one and three days with no difference from controls at later points (day 1, 0-84 (0-07) optical density units/total mRNA \( v 0-5 \) (0-11) (\( p < 0·01 \)); day 3, 0-12 (0-06) v 0-11 (0-21) (\( p < 0·05 \))); this preceded an increase in left ventricular \( \beta \) MHC mRNA at 9, 14, and 35 days (day 9, 0-95 (0-14) v 0-53 (0-11) (\( p < 0·05 \)); day 14, 1-99 (0-29) v 1-26 (0-22) (\( p < 0·05 \)); day 35, 1-98 (0-31) v 1-33 (0-23) (\( p < 0·05 \))). In the right ventricle there were reductions in \( \beta \) MHC and \( c\text{-}myc \) mRNAs in spontaneously hypertensive rats between 14 and 85 days, changes not seen earlier (\( \beta \) MHC: day 14, 0-36 (0-12) v 3-66 (0-82) (\( p < 0·01 \)); day 35, 0-24 (0-09) v 0-98 (0-43) (\( p < 0·005 \)); day 84, 0-14 (0-03) v 0-30 (0-08) (\( p < 0·005 \)); \( c\text{-}myc \): day 14, 3-25 (5·83) v 5-83 (0-85) (\( p < 0·05 \)); day 35, 3-04 (0-9) v 8-54 (1·2) (\( p < 0·005 \)); day 84, 0-23 (0-07) v 0-25 (0-05) (\( p < 0·005 \))).

Transient stimulation of \( c\text{-}myc \) in the left ventricle is in...
accord with a role in cardiac growth as well as maintenance of β MHC expression; later hypertrophic growth in spontaneously hypertensive rats in the absence of myc stimulation indicates that myc is not an essential signal for increases in cardiac mass. Reductions in right ventricular β MHC and c-myc mRNAs are compatible with a reduction in right ventricular load in this model of hypertrophy.

Assessment of atrial morphology by paediatric transoesophageal echocardiography

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Atrial morphology was prospectively evaluated in 86 unoperated children with congenital heart disease (age 0.2-14.8 years, mean 3.8 years) by both transoesophageal (TOE) and transthoracic echocardiography (TTE) to determine the diagnostic accuracy of both techniques and to define the potential contribution of TOE in patients with atrial septal defects. The information derived from these studies was correlated with one another and with that obtained by subsequent surgical inspection (53 patients) or by cardiac catheterisation, or both (78 patients). TOE allowed the visualisation of both atrial appendages and thus the direct diagnosis of atrial situs in every case. This was not possible in any patient by TTE. Right and left atrial isomerism was defined in two patients each. In one patient TTE suggested left atrial isomerism, but she was diagnosed as having situs solitus by TOE. Left juxtaposition was defined in four patients by TOE but in only one by TTE. All four had subsequent confirmation. Patency of the oval fossa was shown in 21 patients by TOE and in only 10 by TTE. Left heart catheterisation could be performed through the oval fossa in 17 of these patients. In two children secundum atrial septal defects were identified by TOE that had been missed by previous TTE. In the remaining 26 children with secundum defects TOE allowed a better definition of the relation of the defect to the pulmonary veins, the tricuspid valve, and the coronary sinus. In particular the anterosuperior rim of the defect was consistently better visualised by TOE. Redundant oval fossa flap valves were readily identified by TOE. In three children sinus venosus defects were identified by TOE that had been missed by TTE. All five had subsequent confirmation. Multiple atrial septal defects were documented in four patients by TOE and in only one by TTE. Primum defects were equally well documented by either technique (nine patients). A subtot al cor triatriatum was diagnosed in one child only by TOE and was subsequently confirmed on surgical inspection.

TOE provides an improved evaluation of atrial morphology when compared with transthoracic echocardiography. It provides the direct diagnosis of atrial situs and juxtaposition of the atrial appendages. The atrial septum is documented in much more detail by TOE than by TTE. Thus TOE may be expected to have a major impact on patient selection for transcatheter closure of atrial septal defects.

Monitoring interventional cardiac catheterisation by paediatric transoesophageal echocardiography

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Paediatric single plane transoesophageal echocardiography was used in 17 children scheduled for interventional cardiac catheterisation (six balloon dilatation of the pulmonary valve, four balloon dilatation of the aortic valve, one pulmonary angioplasty, two aortic angioplasty, two duct occlusion, and two Mustard baffle dilatation) to determine its potential value as a dedicated monitoring technique. The age at investigation ranged from 0-9 to 14-6 years (mean 6-0 years), the weight from 9-5 to 49-2 kg (mean 22.8 kg). The transoesophageal studies were completed in all patients without complications being encountered. Procedure time was not prolonged in any case. Preintervention studies provided important new information in two patients, which led to the cancellation of the procedure. The technique allowed real time assessment of catheter placement across the aortic valve and the relation of the catheter to the atrioventricular valves during balloon dilatation of valves and duct occlusion. Chordal rupture of the tricuspid valve was documented in one child. In a further two patients balloon position with respect to the atrioventricular valves was modified according to the transoesophageal findings. Immediate changes in aortic valve morphology and function during balloon dilatation of the aortic valve were able to be closely monitored and aortic regurgitation could be excluded before each balloon inflation. In contrast, only little information on pulmonary valve morphology and function could be obtained. Localised dissection of the descending aorta or the branch pulmonary artery could be excluded during angioplasty procedures. Transcatheter occlusion of a ductus arteriosus was not enhanced by single plane transoesophageal monitoring. Valuable morphological and haemodynamic information on systemic venous pathway obstructions and enhanced guidance of catheter position was provided during Mustard baffle dilatations.

Paediatric transoesophageal echocardiography is a new important guidance and monitoring technique during interventional cardiac catheterisation in children. It provides additional important morphological information, the immediate identification or exclusion of complications, and the assessment of haemodynamic changes.

Hypoplastic left heart syndrome: increasing antenatal detection is associated with diminishing prevalence postnatally

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During the past 10 years over 600 cases of congenital heart disease have been detected prenatally, of which 101 cases were the hypoplastic left heart syndrome. Seventy three of these cases were seen in the last three years, the rise in detection rate being related to the introduction of four
chamber view screening on routine obstetric scans. Of the 101 cases, 83 (82%) were referred because the four chamber view was thought to be abnormal. Of 74 cases diagnosed before 24 weeks’ gestation, the majority of parents (85%) elected to terminate the pregnancy when counselled about the prognosis. There were three intrauterine deaths so that of a possible 101 infants, only 35 reached postnatal care. None of these 35 infants survived. Although the Norwood procedure or cardiac transplantation are potentially available to treat these infants, the results are still poor. The majority of infants are not treated and die in the neonatal period. Two mothers in our series elected for transplantation but in neither infant was the procedure successful.

Simultaneously with the increase in the numbers detected prenatally has occurred a fall in the number of cases seen in a regional paediatric cardiology centre from 14 to 16 cases in 1986 and 1987 respectively to eight, seven, and six cases in 1988, 1989, and 1990 respectively. If the four chamber screening programme is extended nationwide this condition could almost disappear from postnatal practice.

Hypoplastic left heart syndrome: is transplantation the answer?

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The hypoplastic left heart syndrome (HLHS) is the commonest cause of neonatal death from congenital heart disease. Cardiac transplantation now offers the prospect of a medium term survival of up to 80% but will only become a reality if suitable infant donors are available. We performed a retrospective survey of deaths from HLHS to assess the potential need for neonatal cardiac transplantation and of deaths from anencephaly and head injury to try to identify potential donors. Data for the Northern region, 1982–9 were obtained from the Regional Surveys of Perinatal Death and Fetal Abnormality, the Office of Population Censuses and Surveys, hospital records, and coroners’ reports. Forty one cases of HLHS were identified (median six per year; 1:6700 live births). Nine out of 41 (22%) were unsuitable for transplantation because of prematurity (seven) or multiple congenital abnormalities (two), leaving 32 potential recipients. Since November 1986 nine out of 20 cases of HLHS (45%) were diagnosed in utero and in seven the pregnancy was terminated. In 1982–9 there were no liveborn fetuses with anencephaly > 2500 g birth weight and > 35 weeks’ gestation. From 1979–86, 30 infants died of head injury but 29 out of 30 (97%) would have been unsuitable as cardiac donors because of size > 8 kg (nine), early death (12), non-accidental injury (seven), or cardiac injury (one).

We conclude that the numbers of infants dying of anencephaly or head injury will not be sufficient for neonatal transplantation. If cardiac transplantation is to be used in HLHS an alternative source of donors will have to be identified. The introduction of widespread fetal echocardiographic screening may drastically reduce the number of liveborn children with HLHS.

Does altitude accelerate the progression of pulmonary vascular disease in children with left to right shunts? A quantitative morphometric lung biopsy study

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The chronic hypoxia of altitude has been shown to raise pulmonary vascular resistance in inhabitants of the high Andes and the Himalayas. The effect of altitude on pulmonary vascular resistance in children with congenital heart defects is unknown. We studied 19 children, aged 4 months to 15 years (median 11 months), with left to right shunts (ventricular septal defect (VSD) eight, ductus arteriosus (DA) seven, both VSD and DA four) from Johannesburg, South Africa (1800 m). All patients had equal systemic and pulmonary artery systolic pressures at cardiac catheterisation. Ratio of pulmonary to systemic flow ranged from 0.44 to 3.1 (mean 1.6) and pulmonary arteriolar resistance index (PARI) from 4.2 to 25.5 μm² (mean 9.7) in air. Pulmonary vascular resistance was reactive as shown by a fall of PARI > 2 μm² in seven out of 11 patients with administration of oxygen. Lung biopsy specimens taken at the same admission were studied with quantitative morphometric techniques. Results were compared with normal values at sea level and with those in patients with VSD at sea level. All patients showed increased muscularity of arteries with extension of muscle to peripheral intra-acinar arteries. All had "arterialised" veins. Intimal change was present in 10 patients (mild in seven, severe in three). Percentage wall thickness of pre-acinar arteries was 14–39 (normal, sea level 5.8–6.4 (p < 0.001); VSD, sea level 8.0–13.3 (p < 0.001)). Mean percentage wall thickness of 51–100 μm arteries was 22.7 (normal, sea level 7.4 (p < 0.001); VSD, sea level 16.2 (p < 0.001)) and of < 50 μm arteries was 26.4 (normal, sea level 9.6 (p < 0.001); VSD, sea level 21.9 (p < 0.05)). Arterial size (external diameter of arteries accompanying respiratory bronchioli) and arterial numbers (alveolar-arterial ratio) were both within normal limits. In cases of VSD at sea level structural changes in the pulmonary arteries were related to age and pulmonary vascular resistance. In our series no such relation was seen.

Children with left to right shunts who live at moderate altitude have increased muscularisation of pulmonary arteries compared with that in their counterparts at sea level. Interestingly, however, they show no reduction in arterial size or numbers unlike those at sea level.

Advanced pulmonary vascular disease: 24 hour urinary excretion of vasoactive eicosanoids

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Prostacyclin (PGI₂) and thromboxane (TXA₂) have opposing actions on pulmonary vascular smooth muscle and platelets and PGI₂ is used in the treatment of pulmonary hypertension. We have, therefore, investigated
eicosanoid biosynthesis in 18 patients with advanced pulmonary vascular disease (age 11–24 years, median 17.5 years; mean pulmonary vascular resistance (PVR) 17.5 Um⁻²) and in seven controls (age 11–40 years, median 20). We also studied 18 patients (age 0.2–2.25 years, median 0.9 years) with a left to right shunt and a high pulmonary blood flow but reversible pulmonary vascular changes (mean PVR 2.5 Um⁻²) and seven controls (age 0.9–2.25 years, median 1.3 years). Twenty four hour urinary concentrations of the PG1₂ metabolite 2,3-DN-6-oxo-PGF₁α and the TXA₂ metabolite 2,3-DN-TXB₂ were measured by immunoaffinity chromatography and gas chromatography electron capture mass spectrometry. In patients with advanced pulmonary vascular disease the mean urinary concentration of 2,3-DN-6-oxo-PGF₁α was 139 (SEM 19) ng/g creatinine, significantly lower than that in the controls (184 (13)) (p < 0.05), and the 2,3-DN-TXB₂ was 376 (54), significantly higher compared with the controls (272 (19)) (p < 0.05). In the younger patients with high pulmonary blood flow the 2,3-DN-6-oxo-PGF₁α concentration was 437 (43) (control 514 (113)) and 2,3-DN-TXB₂ concentration was 1287 (148) (control 858 (213)).

PG1₂ and TXA₂ biosynthesis may be higher in younger children when the pulmonary vascular bed is more labile than later. In advanced pulmonary vascular disease there may be an imbalance in eicosanoid biosynthesis which favours vasoconstriction and platelet aggregation and this trend may exist before the development of irreversible pulmonary vascular changes.

Study of low dosage prostaglandin: usage and complications

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Low dosage intravenous (<0.01 μg/kg/minute) and oral prostaglandin E have been reported to produce fewer complications than higher intravenous doses (0.02–0.1 μg/kg/minute) in the manipulation of the arterial duct for congenital heart disease. Over a three year period 34 neonates (aged 30 weeks gestation to three weeks; weight 1.45–3.86 kg) were treated with low dosage intravenous or oral prostaglandin for cyanotic (29) and acyanotic (six) lesions. Eighteen (53%) had complications associated with this treatment, with 14 having more than one complication. Major complications occurred in nine (26%) patients—necrotising enterocolitis (seven), apnoea or bradycardia, or both (five), convulsions (one), haemorrhage (one) and required a change of management. The factors common to all neonates who developed necrotising enterocolitis were cyanotic congenital heart disease, prostaglandin administration, and enteral feeding. All four premature infants in this study developed necrotising enterocolitis. Other complications included feeding intolerance (seven), pyrexia (four), clinical heart failure (three), tachypnoea (two), thrombocytopenia (two), and jitteriness (one).

In contrast to other studies, we report a similar high incidence of complications with low dose intravenous and oral prostaglandin as has been reported in the use of high intravenous dosage. Prostaglandin usage in any form deserves caution.

Comparative aortic root measurement in controls and in children and adolescents with Marfan’s syndrome

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Functional aortic root involvement is well recognised in adult patients with Marfan’s syndrome, but less is known about aortic root involvement in younger patients. Furthermore, confusion about which regions of the aortic root to measure serially and the absence of suitable normal centiles for comparison make interpretation of such measurements difficult. By retrospectively reassessing the aortic root dimensions from stored images (obtained by cross sectional echocardiography) in 378 children and adolescents with innocent murmurs normal centiles for four separately recognisable regions of the root were obtained. These regions included (a) valve annulus, (b) sinuses of Valsalva, (c) sinotubular junction, and (d) proximal ascending aorta. Corresponding retrospective measurements from follow up data in 41 patients with Marfan’s syndrome aged up to 21 years were obtained for comparison. In patients with Marfan’s syndrome the earliest change observed was in the sinus of Valsalva region, which dilated progressively postpubertally to above the 90th centile for age and body surface area but which was not accompanied by aortic incompetence. It preceded postpubertal dilatation of the annulus, the latter heralding the onset of valve incompetence.

We conclude that in Marfan’s syndrome the four regions within the aortic root should be sequentially measured from cross sectional echocardiography, with particular attention being paid to the valve annulus.

Absent pulmonary valve syndrome: surgery in infants with airway obstruction

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From 1979 to 1989, 17 infants with the absent pulmonary valve syndrome and severe airway obstruction underwent extensive pulmonary aneursmorrhaphy utilisingcardiopulmonary bypass (age range 4 days–14 months, mean 5.4 months; weight range 1.7–9.3 kg, mean 4.8 kg). Twelve of these patients underwent associated transternal ventricular septal defect (VSD) closure and infundibular resection and a short transannular patch. Two underwent transventricular VSD closure and infundibular resection and no transannular patch; one underwent transventricular VSD closure and transannular patch. Two patients underwent pulmonary aneursmorrhaphy alone. All 17 infants left the operating theatre with good haemodynamic function. Three patients (two premature, weighing 1.7–2.3 kg) died (hospital mortality 17.6%) postoperatively (12 days–5 months) because of severe airway obstruction that could not be relieved despite further tracheobronchopexy procedures in two of the three patients. One of the 14 patients discharged from hospital died subsequently after reoperation. This patient, the first in the series, was found to have an undetected, obstructed right pulmonary artery from redundant wall at necropsy. Four other patients successfully underwent reoperation—pulmonary artery branch stenosis in two, closure of a previously un repaired VSD in one, and branch pulmonary artery stenosis with significant pulmonary incompetence (PI) in one. In the remaining
nine survivors PI was present but currently well tolerated. In two the right ventricle was dilated but contracting well. In seven right ventricular size was within normal limits. There were 13 long term survivors (range of follow up 3 months–7 years, mean 52.3 months). Eight of the 13 had episodic wheeze of mild to moderate severity that was responsive to sympathomimetic bronchodilator aerosols. The remaining five were free of symptoms.

The insertion of a pulmonary valve at operation may well not be necessary for a successful outcome. It may, however, need to be inserted at a later date because of free PI and right ventricular dilatation, as has occurred in one patient to date.

Pulmonary atresia, ventricular septal defect, and hypoplastic pulmonary arteries with major aortopulmonary collaterals: use of central end to side shunt as staging procedure

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Twenty-eight patients with pulmonary atresia, ventricular septal defect, hypoplastic pulmonary arteries with major aortopulmonary collaterals (MAPCAs), and very small pulmonary arteries underwent a direct central end to side shunt as a staging procedure between 1980 and 1989. Age range was 2 months–32 years, with 22 patients under 1 year of age. Two patients had an absent left pulmonary artery and 26 a confluent main pulmonary artery, right pulmonary artery, left pulmonary artery system. Pulmonary artery diameter was 1–1.9 mm in seven patients, 2–2.9 mm in 17, and 3–3.9 mm in four. The central shunt was the initial staging procedure in 27 patients. There were three hospital deaths (10.7%) (70% confidence interval 5% to 20%), including one patient who went through the unifocalisation and correction in the one hospital admission. Major complications in the 25 survivors included congestive cardiac failure from over shunting in 10 (mild to moderate with no haemodynamic instability in eight and severe ventilator dependent in two, both of whom then successfully proceeded through unifocalisation to correction within one month), endocarditis in one, and tamponade associated with pericardial closure in one. There were 25 survivors of the first hospital admission and, of these, 13 proceeded through unifocalisation to correction (ventricular septal defect patch fenestration, one patient) with no deaths, including two patients who underwent shunting, unifocalisation, and correction successfully during the first hospital admission (overall 14 corrections with one death). Seven patients await further surgical staging. In four patients further staging has been suspended because criteria for correction (pRV/LV < 0.7, no remaining sizable hypoplastic pulmonary arteries with major aortopulmonary collaterals, two out of three lung segments connected to native pulmonary arteries) have not been achieved in three patients, and one adult patient, much improved by the central shunt, has currently withdrawn from the programme. There was one late death four months after a fourth preparatory operation (open mitral valvotomy for mitral stenosis). Proximal right pulmonary artery stenoses occurred in 75% of patients (70% confidence interval 63% to 85%) and left pulmonary artery stenoses in 50% (70% confidence interval 38% to 62%), but overall satisfactory pulmonary artery growth was achieved in 75% of hospital survivors (70% confidence interval 63% to 85%) investigated postoperatively (n = 24). A philosophy of early entry into a staged programme has evolved.

Aorta-pulmonary window: an echocardiographic “blind spot”

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Though case reports indicate that cross sectional echocardiography (2DE) can diagnose isolated aortopulmonary window (APW), the accuracy of diagnosis is unknown. We therefore reviewed all 16 patients (age 1 day–2 years, median 3 months) with APW seen since 1982, when routine 2DE became available at our institution. When APW was an isolated lesion (seven patients) initial 2DE diagnosed the lesion in all but one. The exception was a cyanosed, dysmorphic neonate with persistent fetal circulation. The APW was identified on the second 2DE examination when she next presented aged 4 months with heart failure. In nine patients APW was associated with other cardiac abnormalities (ventricular septal defect (VSD) in three, coarctation of the aorta (COA) in three, tetralogy of Fallot in two, right aortic arch (RAA) in one). The APW was diagnosed on the initial 2DE in only three of these. APW was diagnosed at the second 2DE examination in three patients (two after repair of COA and one with RAA in whom the initial study was technically inadequate in an unmedicated infant). In the remaining three patients, all with VSD, the APW was detected at angiography. On review of the initial 2DE videotapes in the seven patients in whom APW had been “missed” the lesion could be seen in all six of those with technically adequate studies, suggesting that the APW had been overlooked. The APW was best imaged by subcostal paracoronal and parasternal short axis views. Colour flow Doppler ultrasonography helped to confirm the diagnosis in the three patients seen since this technique became available. No false positive diagnosis of APW occurred.

Though 2DE can reliably diagnose APW when it is an isolated lesion, APW can be overlooked when other cardiac abnormalities are present. In patients with VSD or aortic arch abnormalities APW must be specifically excluded.

What happens to neonates with Ebstein’s anomaly?

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Little is written about the natural and postsurgical history of Ebstein’s anomaly (EA) in neonates. The only report (on 11 neonates) showed high early mortality but good outcome in those who survived the first three months. We reviewed 48 neonates with EA seen from 1960–89, presenting at a median age of 2 days. Over half of the cases (31/48 (64%)) had been diagnosed since 1980 by echocardiography. Twenty six had cardiac catheterisation at some time, with a high procedure related complication rate (11/26 (42%), including two deaths). Associated defects (other than atrial septal defect) included pulmonary stenosis (in nine) and atresia (in seven). Eighteen patients had surgery (aged 1 day to 18 years; palliative in 12 and intra-cardiac in six). Nine patients died as neonates (18%)—six of heart failure whose condition was thought to be inoperable, two suddenly, and one perioperatively. In the 39 patients surviving the first month there were 15 late deaths (38%)—five sudden (one of these late after surgery), four perioperatively, three with heart failure, two at cardiac
Pulmonary blood flow after right heart bypass surgery: role of the lungs

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With pulsed wave, transthoracic and transoesophageal Doppler echocardiography and simultaneous respirometry the effect of changes in intrathoracic pressure on pulmonary blood flow was studied in 12 patients after the Fontan procedure (FP) and in three patients after total cavopulmonary anastomosis (TCPA). In patients after FP a biphasic pattern of pulmonary blood flow was observed, coincident with atrial and ventricular systole. Normal inspiration caused a significant increase in forward flow in the pulmonary artery by a factor of 1.8 compared with expiration (p = 0.004). In patients after TCPA blood flow into the pulmonary artery was synchronous with inspiration, while the development of a larger negative intrathoracic pressure of −25 cm H₂O during a Mueller manoeuvre markedly augmented pulmonary blood flow. During a brief Valsalva manoeuvre (25 cm H₂O) there was flow reversal in the pulmonary artery. In both groups of patients large increases in pulmonary blood flow occurred when the chest was expanded by using a negative extrathoracic pressure cuirasse, while the development of a positive pressure in the cuirasse caused flow reversal.

After right heart bypass intrathoracic pressure is an important determinant of pulmonary blood flow, which may be increased when negative extrathoracic pressure is used as a means of respiratory support.

Myocardial infarction in childhood: clinical analysis of 17 patients and medium term follow up of survivors

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Myocardial infarction is rare in infancy and childhood. Between 1979 and 1989, 17 patients aged 2 months to 12 years with acute myocardial infarction of any cause (other than after cardiac surgery) were seen. Eight died from three days to three years after diagnosis (overall mortality 47%). The nine survivors, now aged 2–17 years, were followed up for 1 to 10 years (mean follow up 5 years) after infarction. The commonest causes of myocardial infarction were anomalous origin of left coronary artery from the pulmonary artery (six patients (35%)) and Kawasaki disease (five patients (27%)). The main symptoms of acute myocardial infarction were dyspnoea, vomiting, and difficulty in feeding. Diagnosis was made in all cases by electrocardiography and confirmed by echocardiography, by cardiac catheterisation, or at operation. All survivors were free of symptoms and had excellent exercise capacity. Left ventricular ejection fraction in survivors ranged from 21% to 66%, and only one child took regular cardiac drug treatment. There were no cases of late sudden death. Twenty four hour Holter monitor performed on survivors gave normal results (seven cases) or showed only minor abnormalities (one case), suggesting that serious arrhythmia is rare after paediatric myocardial infarction.

Myocardial infarction in children has a high early mortality. However, survivors have a low incidence of serious arrhythmia and have good exercise tolerance even in the presence of a low left ventricular ejection fraction.

Activation of ATP sensitive potassium channels is involved in endothelium dependent relaxation induced by acetylcholine in rabbit coronary arteries

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Hyperpolarisation may contribute partially to endothelium dependent vascular relaxation. This study assessed the possible inhibitory effects of glibenclamide and barium, inhibitors of ATP sensitive potassium (K⁺) channels, on endothelium dependent relaxation. Coronary artery rings (n = 6 in each group, mean (SEM)) were harvested from adult male New Zealand white rabbits and suspended in individual organ baths containing modified Krebs solution at 37 C and bubbled with 95% oxygen and 5% carbon dioxide. Changes of tension were recorded at a resting tension of 1 g. Rings were equilibrated for 90 minutes before K⁺ (30 mM) or prostaglandin F₂α (PGF₂α, 3 μM) was added. Acetylcholine (0.1 μM) induced relaxation by 47% (4%) of K⁺ evoked contraction (0.8 (0.1) g) and by 82% (7%) of PGF₂α evoked contraction (0.7 (0.2) g) in rings with endothelium. Glibenclamide (3 μM) had no constrictor effect on resting and precontracted endothelium intact rings. Barium (1 mM) induced slight but non-significant contraction in precontracted rings. Glibenclamide and barium partially inhibited the relaxation induced by acetylcholine. Glibenclamide (dissolved in ethanol, 3 μM) reduced relaxation induced by acetylcholine (0.1 μM) in K⁺ (30 mM) and PGF₂α (3 μM) precontracted endothelium intact rings to 41% (5%) (p < 0.05) and 71% (6%) (p < 0.05) respectively. Likewise barium (1 mM) reduced the relaxation induced by acetylcholine (0.1 μM) in K⁺ and PGF₂α precontracted rings to 39% (5%) (p < 0.02) and 69% (5%) (p < 0.01) respectively. Acetylcholine (0.1 μM) induced no significant relaxation in rings without endothelium.

These results suggest that activation of ATP sensitive K⁺ channels is part of the mechanism of the endothelium dependent relaxation induced by acetylcholine in isolated rabbit coronary artery preparations.
Cyclic guanosine monophosphate inhibits cardiac α1 adrenergic induced positive inotropy and phosphatidylinositol hydrolysis

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α1 Adrenergic induced positive inotropic effects are associated with and may be due to phosphatidylinositol (PI) hydrolysis and generation of the intracellular second messenger inositol trisphosphate (IP3). In vascular smooth muscle cyclic guanosine monophosphate (cGMP) inhibits noradrenaline induced IP3 production, but its role in myocardium is not established. We studied the effects of four different cGMP increasing interventions on phenylephrine (PE) induced inotropic effects and IP3 concentrations (measured by a selective protein binding assay) in isolated ferret papillary muscle preparations (with 1 μM acetylcholine and 10 mM lithium chloride). PE (1 nM to 10 μM) had a concentration dependent positive inotropic effect, at 10 μM increasing isometric force by 22% (4%) and unloaded shortening velocity (Vmax) by 25% (4%) (n = 14) and IP3 content by 59% (n = 10). In muscle preparations stimulated by 10 μM PE (n ≥ 8) a threefold to sixfold increase in cGMP concentration by 1 μM 8-bromo cGMP, 1 μM sodium nitroprusside, or 1 μM atrial natriuretic peptide (stimulators of soluble and particulate guanylate cyclase respectively) or 0-1 μM substance P (which releases endothelium derived relaxing factor from endocardium) significantly (p < 0.05, analysis of variance) reduced the inotropic response (for example, Vmax decreased by 46%, 59%, 78%, and 86% respectively) and the IP3 response (by 128%, 161%, 142%, and 140% respectively).

These results show that cGMP elevation inhibits both inotropic and IP3 responses to cardiac α1 adrenergic stimulation and are consistent with a role for PI hydrolysis in mediating α1 positive inotropic effects.

Platelet mediated alterations in cardiac cellular electrophysiology during normal perfusion and myocardial ischaemia

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Recent clinical and experimental evidence indicates that platelet activation contributes to the arrhythmogenic effects of myocardial ischaemia. To investigate the mechanisms responsible we studied the changes in cellular electrophysiology and arrhythmogenesis during infusion of platelets (10^9/ml) in isolated, perfused guinea pig hearts during normal perfusion and global myocardial ischaemia. Hearts were studied in four groups: A (n = 9) buffer only; B (n = 9) buffer and platelets pretreated with 1 μM forskolin; C (n = 8) buffer and platelets pretreated with 10 μM forskolin; D (n = 3) as in group B but with frozen and thawed (activated) platelets. Infusion of platelets (groups B and C) had no effects during normal perfusion, but activated platelets (group D) decreased action potential duration (APD) from 164 (1) ms to 134 (4) ms at 15 minutes of normal perfusion (p < 0.05) and produced ventricular fibrillation in all three at 21 (1) minutes. During ischaemia platelets (group B) increased the incidence of ventricular fibrillation (100% v 56% group A, p < 0.05) but this was prevented by 10 μM forskolin (group C 50% v 100% group B, p < 0.02). Platelets in group B enhanced the ischaemia induced reductions in APD (126 (2) ms v 139 (3) ms (group A), p < 0.01 at 5 minutes), but these were attenuated with platelets pretreated with 10 μM forskolin (group C 147 (5) ms v 126 (2) ms group B, p < 0.01 at 5 minutes). Hearts in group C took longer to develop arrhythmias during ischaemia than those in group B (21 (2) min v 15 (1) min, p < 0.02) and recovered more rapidly during reperfusion.

These studies show (a) that infusion of activated platelets produces deleterious electrophysiological and arrhythmogenic effects in normally perfused hearts and (b) that myocardial ischaemia causes platelet activation, which contributes to the electrophysiological and arrhythmogenic effects observed.

Fractionation of paced right ventricular electrograms in hypertrophic cardiomyopathy

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Patients with hypertrophic cardiomyopathy who have developed clinical ventricular tachycardia (VT) or fibrillation (VF) or who have died suddenly have no specific electrophysiological abnormality. We have developed a test to quantify the likely electrophysiological features of disarray that may predict which patients with hypertrophic cardiomyopathy are at risk of VT or VF. Variation in fibre calibre may cause changes in local conduction velocities and refractory periods. Disarray may lead to multiple conduction paths between two ventricular sites that may be blocked or recruited with different refractoriness of the intervening tissues. To reveal this effect the right ventricle is paced with two sequences at one site and high pass filtered electrograms are recorded from three other sites. The first sequence of 800 stimuli is a regular drive cycle with an interpolated extrastimulus every third beat with a coupling interval that decreases by 1 ms on each occasion, which generates a set of electrograms that correspond to particular interstimulus intervals. The second sequence of 1600 stimuli has a random interstimulus interval to alter the refractory state of tissue between the pacing and recording electrodes. With one path between the electrodes no change in the electrogram configuration in regular and random pacing would be expected. With multiple paths the electrograms would be expected to fragment as the activation of myocardium within the electrode receptive field changes. Each electrogram is correlated with a set of templates and the number of templates required to fit all the complexes is determined. The variability of a record corresponds to the number of templates that are generated from it. The ratio of the number of the randomly paced templates to the number of regularly paced templates (Trand/Treg) measures the recruitment of paths between electrodes. Of 12 patients with hypertrophic cardiomyopathy, three had no recorded arrhythmias or family history of sudden death, five had such a history, and four had recorded VT or VF. Trand/Treg values were 1–6–3–6, 2–0–6–5, and 2–7–5–8 respectively. The difference between the no arrhythmia, no family history of sudden death, and the pooled family history of sudden death and VT or VF groups was significant by a sign test at p < 0.01.

These results suggest that this new method of electrophysiological quantification of disarray may help predict the risk of VT and VF in hypertrophic cardiomyopathy.
Assessment of ventricular volumes by single breath nitrogen washout test

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As yet there is no simple, accurate, non-invasive technique for measuring cardiac volumes that would be suitable for routine screening of patients. We describe a new method whereby cardiogenic oscillations observed during the course of a single breath nitrogen washout test are analysed to provide an estimate of cardiac displacement volume. This test is a simple procedure for both patient and operator and can be performed rapidly without resort to sophisticated equipment. Pulsatile changes in partial pressure of nitrogen are transformed to effect a ventricular volume-time curve and yield estimates of the systolic ejection fraction (SEF), mean velocity of circumferential fibre shortening (MVCFS), end diastolic volume (EDV), end systolic volume (ESV), and other indices. A comparison with echocardiographic measurements of left ventricular dimensions in the same group of 20 normal subjects and 12 patients with ventricular disease showed significant linear correlations for SEF (r = 0.76, p < 0.001) and MVCFS (r = 0.61, p < 0.001). Echocardiographic values of left ventricular volumes likewise indicated significant correlations in respect of EDV (r = 0.54, p < 0.01) and ESV (r = 0.72, p < 0.001).

Thus, the single breath nitrogen washout test gives an accurate assessment of ventricular volume and could be a useful tool for repeated measurements to map patients' progress in units where sophisticated equipment is not available.

Does hyperinsulinaemia cause microvascular angina?

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Coronary microvascular dysfunction may underlie syndrome X—angina and supportive evidence of myocardial ischaemia but normal coronary arteriograms. Hyperinsulinaemia is implicated in the microvascular abnormalities of diabetes and hypertension. We therefore compared oral glucose (75 g) tolerance tests in 11 patients with previously characterised syndrome X (none with overt diabetes or hypertension) and 11 age, sex, and body weight matched controls. Fasting glucose concentration was normal in all subjects, but glucose tolerance was impaired (2 hour glucose concentration > 7.8 mmol/l) in six patients with syndrome X compared with two controls (p < 0.05). Fasting insulin concentrations were similar, but peak and 2 hour insulin concentrations and the area under the insulin-curve were higher in patients with syndrome X (median 116 (range 60–226) v 84 (34–110) mU/l x 10³, 100 (35–187) v 50 (15–110) mU/l x 10³, and 10.4 (5.9–19.2) v 6.7 (2.3–11.3) min x mU/l x 10³ respectively; all p < 0.01). Total and low density lipoprotein cholesterol concentrations and total triglyceride concentration were similar in the two groups, but high density lipoprotein cholesterol concentration was lower in patients with syndrome X (mean 0.93 (SD 0.19) v 1.32 (0.30) mmol/l; p < 0.01).

These findings suggest that hyperinsulinaemia occurs in patients with syndrome X and may thus contribute to the pathogenesis of microvascular angina.

Aging, autonomic function, and perception of angina

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Coronary artery disease is common in the elderly but little is known about the effects of aging on the perception of angina. We studied 90 non-diabetic men aged 35–82 years, all of whom had typical angina, to determine whether age related changes in blood pressure and autonomic function are associated with changes in anginal perceptual threshold—the time from onset of 1 mV ST depression to angina during treadmill exercise. The effects of aging on somatic pain threshold (measured by calf sphygmomanometry) were also assessed in a subgroup of 35 patients. Age showed the predicted correlations with blood pressure (r = 0.3, p < 0.001) and autonomic function as reflected by heart rate responses to Valsalva manoeuvres (r = −0.4, p < 0.001). Age also showed highly significant correlations with anginal perceptual threshold (r = 0.3, p < 0.005) and somatic pain threshold (r = 0.4, p < 0.02), older patients having longer latency between ST depression and angina and tolerating higher cuff inflation pressures. Subgroup analysis confirmed that patients over 65 had higher thresholds for angina (67 (80) v 14 (76) s, p < 0.005) and somatic pain (228 (66) v 156 (74) mmHg, p < 0.02) than the younger group. Neither variable, however, correlated significantly with blood pressure or autonomic function.

In conclusion, this study has shown that the perception of angina diminishes with advancing age. Although the mechanism is unclear, it seems to reflect a generalised hyposensitivity to pain in the elderly and is not solely attributable to age related changes in blood pressure and autonomic function.

Monophasic action potential and detection of myocardial ischaemia in humans: an appraisal using endocardial recordings

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The monophasic action potential (MAP) recorded from the surface of the myocardium provides a sensitive measure of localised myocardial ischaemia. The duration of the MAP shortens in response to ischaemia and commonly registers changes before they appear in an ECG. Although the MAP has been used to document ischaemia on the epicardial surface in both animal and human studies, it has yet to be fully appraised in this context in human endocardial recordings. In a study designed to do so, we compared changes in steady state MAP duration in endocardial recordings between normal and ischaemic areas in patients undergoing routine coronary angiography. Single site
MAPs were obtained from the left or right ventricular endocardium, or both, in 26 patients (32 recording sites) during atrial pacing to angina threshold. Each pacing rate was maintained for two minutes to allow for steady state adaptation. At peak paced heart rate technetium-99m was administered intravenously for subsequent myocardial perfusion scintigraphic imaging and documentation of ischaemia. Eighteen MAP recordings were from areas of myocardium with a normal perfusion pattern and 14 from areas with abnormal perfusion characteristics. MAP duration at 90% repolarisation for every 100 ms change in cycle length shortened by a mean (SD) of 22 ± 4 (8-2) ms in the non-ischaemic regions. The extent of shortening was significantly greater for ischaemic areas, being 33 ± 8 (9-7) ms (p < 0.01) and indicating the additional effect of ischaemia. As both shortened cycle length and ischaemia abbreviate the MAP duration, a range of values of MAP shortening in unit time was analysed for sensitivity and specificity for detection of ischaemia. A value in excess of 26.5 ms per 100 ms change in cycle length provided the optimum compromise with 88% sensitivity and specificity.

Our results provide validation for the use of endocardial MAP recordings for the detection of ischaemia. The technique would be suited to the evaluation of interventions designed to alter ischaemic responses during catheter directed therapeutic procedures such as coronary angioplasty.

Prognosis after recovery from myocardial infarction: relative importance of cardiac dilatation and coronary stenoses

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We showed previously that long term survival after infarction was best predicted by left ventricular end systolic volume measured after recovery. Surprisingly, the severity of coronary stenoses did not contribute independently to survival, and the present study was done to discover whether a longer follow up would give further information. Male survivors (n = 616, age 50 (7) years) of a first (n = 455) or recurrent (n = 161) infarction had angiocardiography at 4-8 weeks after index infarction and were followed for 8 (2-9) years. Coronary surgery was performed in 34%, as a clinical trial in 14%. Angiocardiographic and clinical factors were analysed by the proportional hazards model, taking cardiac death as the end point and considering (a) the whole period of observation, (b) the first five years after index infarction, and (c) the subsequent survival of the survivors at five years. There were 179 deaths, of which 79% were from cardiac causes; of the 141 cardiac deaths, 67% were sudden. End systolic volume remained the most powerful predictor of cardiac death over all time periods. Coronary stenoses (assessed by a scoring system) which were not predictive over 0-5 years became highly predictive after five years. Other independent adverse factors were continued cigarette smoking (19% smoked) and the withholding of β blocking drugs (taken by 34%). Trial surgery, age, and first or recurrent infarction were not predictive.

We conclude that coronary stenoses independently predict cardiac mortality but after a longer time course than ventricular dilatation.

Doppler assessment of effects on cardiac function of oral vasodilators started in early phase of acute myocardial infarction: randomised trial

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Serial changes in stroke volume and cardiac output were assessed by Doppler echocardiography of blood flow in the ascending aorta in patients entered in a randomised double blind trial of an oral angiotensin converting enzyme inhibitor or of an oral nitrate in suspected acute myocardial infarction. Eighty one patients randomised at a mean of 13 hours from the onset of pain to receive 28 days’ treatment of captopril (CAP) (12.5 mg three times a day after a 6-25 mg test dose; n = 27), isosorbide mononitrate (ISMN) (20 mg three times a day; n = 22), or placebo (n = 32) were studied. The baseline clinical characteristics and stroke distance of the three groups were similar. Changes in haemodynamic variables were assessed one hour after the first dose, at the time of discharge, and at six weeks—that is, two weeks after the end of trial treatment. At one hour the percentage changes (mean (SEM)) in systolic blood pressure was -11% (2) for CAP, -10% (2) for ISMN, and -1% (1) for placebo (p < 0.001 for CAP and for ISMN v placebo). At discharge and at six weeks there were no differences in systolic blood pressure between the three groups. The percentage changes in stroke volume were: (a) at one hour +8% (2) for CAP, +4% (2) for ISMN, and +2% (1) for placebo (p < 0.05 for CAP v placebo); (b) at discharge +18% (4), +10% (3), and +7% (3) respectively (p < 0.05 for CAP v placebo); and (c) at six weeks +22% (4), +16% (7), and +11% (3) respectively (NS for all comparisons). The percentage changes in cardiac output were: (a) at one hour +13% (3) for CAP, +2% (2) for ISMN and +2% (2) for placebo (p < 0.01 for CAP v ISMN and v placebo); (b) at discharge +23% (5), -1% (4), and -4% (4) respectively (p < 0.001 for CAP v ISMN and v placebo); and (c) at six weeks +24% (7), 0% (6), and +7% (5) respectively (p < 0.05 for CAP v ISMN and v placebo).

In summary, these data suggest that both CAP and ISMN produce a moderate reduction in blood pressure soon after treatment in acute myocardial infarction but that these effects do not persist. Captopril shows a marked increase in cardiac output soon after starting treatment and this effect persists after discontinuation of treatment. ISMN produces less striking haemodynamic improvement but at least shows no sign of reduction in cardiac output when compared with placebo. It seems that both vasodilators can be started safely in the early phase of acute myocardial infarction.

Early and late changes in diastolic filling pattern after myocardial infarction: importance of infarct size

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To characterise the early and late changes in left ventricular filling dynamics associated with myocardial infarction we recorded the Doppler echocardiographic filling pattern in 45 patients (mean age 65 (SEM 1.5) years) at one and six weeks after the acute event. Based on clinical criteria, patients were divided into those with large (group L; n = 12) and those with small infarctions (group S; n = 33). The difference in infarct size was reflected by the peak
enzyme activity (AST) in the two groups (553 (59) vs 212 (22), p < 0.001). These patients were then compared with 16 age matched normal controls (group C). The following filling variables were calculated from the mitral flow velocity waveform: peak early (PE) and peak atrial (PA) velocities (cm/s), early (Ei) and atrial (Ai) velocity integrals (cm). The PE/PA and Ei/Ai ratios were calculated to express the balance between early and atrial filling. To correct for the variation in heart rate, these ratios were divided by the diastolic filling period of the cardiac cycle (PE/PA\(_Ei/Ai\)). One week after myocardial infarction the PE velocities were higher in group L compared with groups S and C (75 (3), 67 (2), and 62 (4) cm/s respectively; p < 0.05 group L v group C; p < 0.05 group L v group S). However, there was no significant difference in Ei (9.2 (1), 9.5 (1), and 8.9 (1) cm). Thus, in group L early filling occurred during a shorter early filling period. Although the PA velocities and Ai in group L were not different from those in group S, they were significantly lower compared with those in group C (PA: 59 (5), 69 (2), and 76 (4) cm/s; p < 0.05 group L v group C; Ai: 4.0 (0.7), 5.3 (0.2), and 6.4 (0.4) cm/s; p < 0.01 group L v group C). Consequently, the PE/PA, PE/PA\(_Ei/Ai\), and Ei/Ai ratios were higher in group L compared with groups S and C. At six weeks these ratios decreased in group L (PE/PA, by 25%, p < 0.01; Ei/Ai, by 22%, p < 0.05) so that the differences between the groups were smaller.

These data suggest that, depending on the size of the infarct, patients with myocardial infarction exhibit a “restrictive” left ventricular filling pattern early after the acute event. This was manifested by the greater proportion of filling occurring in early diastole, reflecting an overall increase in chamber stiffness. Six weeks later the “restrictive” pattern is less pronounced, presumably due to the remodelling process after myocardial infarction.

**Combination treatment does not offer an advantage in managing chronic stable angina**

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The combination of \(\beta\) blockers and calcium antagonists is widely used in the management of angina pectoris, though there is little evidence to support its efficacy. This double blind randomised crossover placebo controlled study compared the effects of nicardipine, atenolol, and their combination in 30 patients with chronic stable angina and normal (52 (9-6)) left ventricular ejection fraction. Each treatment period lasted six weeks with dose titration after three weeks. Symptomatic limited treadmill exercise testing and radionuclide ventriculography at rest were carried out at the end of each treatment period. Total exercise duration was significantly prolonged by nicardipine and atenolol (616 s and 592 s respectively) when compared with placebo (529 s). Time to 1 mm ST segment depression was significantly prolonged from 406 s (placebo) to 472 s (nicardipine) and 466 s (atenolol). The combination of nicardipine and atenolol conferred no additional benefit (total exercise duration 610 s and time to 1 mm ST segment depression 483 s). Radionuclide ventriculography showed no significant change in left ventricular ejection fraction with any treatment. The peak filling rate and time to peak filling rate showed no significant change, but there was a significant increase in the first third filling fraction with atenolol (0.59) and the combination (0.6) compared with placebo (0.4). There was a significant increase in left ventricular end diastolic volume with atenolol (129 ml) compared with placebo (110 ml).

Thus nicardipine and atenolol are effective in prolonging exercise duration in patients with chronic stable angina while the combination offers no additional benefit. Neither drug seems to have an important effect on the parameters of diastolic function studied.

**Extent of coronary atherosclerosis is different in unheralded acute myocardial infarction compared with uncomplicated chronic stable angina**

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It is unclear whether coronary angiographic findings and risk factor profiles differ at initial presentation of acute versus chronic ischaemic heart disease. We studied 102 consecutive patients (males age ≤60, females age ≤65) who either had acute myocardial infarction as first ever manifestation of ischaemic heart disease with a concomitant coronary angiogram (55 patients; mean age 50-2 years) or had had stable angina for at least two years with a positive exercise test, no history of any acute event, no Q waves on electrocardiography or akinesis on ventriculography, and angiography performed ≥2 years from initial symptoms (47 patients; mean age at symptom onset 51-7 years). Risk factors were analysed and observers, blinded to all clinical data, evaluated these angiograms for (a) severity (number of vessel diseased, stenoses ≥50%, occlusions); (b) extent (with an index derived by assigning a score of 0–3 per segment depending on the proportion of lumen length irregularity and dividing the sum by the number of visualised segments); (c) pattern (discrete = ≤3 loci of disease never involving more than 50% of the length of any segment or diffuse = anything exceeding this). Patients with unheralded myocardial infarction had less vessel disease than those with uncomplicated stable angina (mean 1.3 (SD 0.8) v 2.1 (0.8), p < 0.001), fewer stenoses (2.1 (1.8) v 3.9 (1.8), p < 0.001), fewer occlusions (0.6 (0.6) v 1.0 (0.9), p = 0.01), and a lower extent index (0.6 (0.5) v 1.2 (0.5), p < 0.001). A discrete pattern was present in 54.6% of those with unheralded infarction and in only 8.5% of those with uncomplicated angina (p < 0.001). Age at symptom onset, sex distribution, serum cholesterol concentration, present and past smoking habit combined, and positive family history were similar in the two groups. Hypertension was found twice as frequently in angina (64.4% v 30.9%, p < 0.01), and a recent smoking history twice as often in infarction (60% v 31.1%, p < 0.01). There were seven diabetic patients in the angina group, and one in the infarction group.

Thus uncomplicated chronic stable angina is associated with appreciably more severe and extensive atherosclerosis and rarely a discrete pattern and a dissimilar risk factor profile compared with unheralded acute myocardial infarction. Such important differences suggest that acute and chronic manifestations of ischaemic heart disease are unlikely to be random expressions of a single underlying pathological process.
Recurrent ischaemic events after thrombolytic treatment: predictive value of symptoms, stress testing, and coronary arteriography

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Recurrent ischaemic events are common after thrombolytic treatment, and identification of patients at risk is important, although no diagnostic test has yet been validated for this purpose. We studied 101 patients treated by thrombolysis who underwent pre-discharge stress testing and early coronary arteriography. During 10 (7) months of follow-up 21 recurrent ischaemic events were documented: unstable angina (15), acute infarction (five), and cardiac death (one). Events occurred most commonly in patients with patent or high grade collateralisation of the infarct related artery (p < 0.02). However, none of the electrocardiographic variables measured during stress testing predicted events, although patients with patent arteries exercised longer (516 (186) v 434 (198) s, p < 0.05). We therefore examined the angiographic data and performed a morphological analysis of the infarct related coronary lesion. Patients with angina tended to have a tighter residual stenosis than those who remained free of symptoms (86% (15) v 78% (17), p < 0.05), but neither symptoms nor the severity of the stenosis predicted which patients were at risk of recurrent events. Indeed, none of 10 morphological features analysed was of any predictive value apart from arterial ectasia distal to the lesion (p < 0.01).

In conclusion, after thrombolytic treatment neither treadmill stress testing nor continuing exertional angina are of value for predicting which patients are at risk of recurrent ischaemic events after discharge from hospital. Angiography is more helpful because patients with residual perfusion of the infarct territory are of greater risk. Nevertheless, lesion morphology and the severity of the residual stenosis provide little additional guidance and should not affect decisions for revascularisation.

Cardiac structure and function in growth hormone deficiency

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It has recently been shown that cardiovascular mortality is increased in patients with hypopituitarism who have replacement therapy with thyroxine and adrenal steroids but not growth hormone (GH). We investigated the effects of GH deficiency on cardiac structure and function in 21 patients (nine men, 12 women; mean age 44 years, range 24–64) with hypopituitarism (mean duration 11 years, range 1–28) and no clinical evidence of cardiovascular disease, diabetes, or hypertension. Cardiac structure and function were assessed with cross sectional echocardiography and Doppler ultrasonography, and treadmill exercise tolerance was assessed with the Bruce protocol. The degree of GH deficiency, assessed by serum concentrations of insulin like growth factor 1 (IGF-1), was 82·4 (45) µg/l. Lean body mass calculated from total body potassium content was 48 (8) kg. All patients had a normal left ventricular mass index (90 (19)g/m²) and a normal left ventricular ejection fraction (66% (7')). There was, however, a significant correlation between left ventricular mass and serum IGF-1 concentration (r = 0.51, p < 0.03). Left ventricular mass and left ventricular diastolic function were related to lean body mass (r = 0.76 and 0.64, p < 0.003). Six patients had abnormal left ventricular diastolic function (E/A ratio 1.04 (0.2)). The mean exercise duration with the Bruce protocol was 9.0 (3.8) minutes and no patient had chest pain. A significant correlation was observed between the rate pressure product (maximum heart rate x systolic blood pressure on exercise) and serum IGF-1 concentration (r = 0.61, p < 0.003). Six patients developed planar ST segment depression > 0·1 mV during exercise testing (maximum ST segment depression 0·17 (0·03) mV). In five of these patients there was rapid resolution of ST segment depression immediately after exercise. One patient developed ST segment depression at four minutes with slow resolution; subsequent coronary angiography gave normal results. Exercise induced ST segment depression was not related to severity or duration of GH deficiency.

These results suggest that left ventricular mass and the maximum cardiac work achieved on exercise are inversely related to the degree of GH deficiency. Patients with hypopituitarism may often have ischaemic like ST segment changes during exercise testing. Follow up studies of these patients during GH replacement therapy are in progress.

Prediction of outcome in severe chronic heart failure

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The need to identify patients at higher risk and predict prognosis in severe heart failure has become increasingly important with the advent of cardiac transplantation. We undertook a retrospective study of 127 patients with chronic heart failure due to coronary artery disease or dilated cardiomyopathy referred to our exercise laboratory for assessment of functional capacity to identify variables predictive of outcome (death or transplantation). The mean follow up time was 14.6 months. The effect of the following variables on outcome were studied both by univariate and multivariate analysis: age, aetiology of heart failure, cardiothoracic ratio on chest radiography, left ventricular end systolic diameter on echocardiography, left ventricular ejection fraction (LVEF) on radionuclide ventriculography, mean dose of diuretic, plasma sodium and urea concentrations, and the peak oxygen consumption on exercise (VO₂). The group as a whole had severe heart failure with a median LVEF of 17% and a median VO₂ of 13.7 ml/kg/min. During the period of follow up 23 patients (18%) died and 18 (14%) underwent cardiac transplantation. Although all variables studied apart from the aetiology of heart failure affected outcome on univariate analysis, multivariate analysis identified three variables that were independent predictors of outcome. In order of importance these were plasma sodium concentration, LVEF, and VO₂. The predictive power of these variables for outcome was assessed by multivariate linear discriminant analysis. Seventy four per cent of the deaths or transplantations over the entire follow up period or one year could be predicted from the LVEF, plasma sodium concentration, and VO₂. When patients undergoing transplantation were excluded, 67% of the deaths could be predicted by the above variables.

In patients with severe heart failure the three variables identified are independent predictors of outcome and are useful in assessing the need for transplantation.
Characterisation of left ventricular filling abnormalities in hypertensive subjects

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Left ventricular filling and effect of left ventricular hypertrophy were studied in 70 untreated hypertensive patients and 40 normal controls who underwent cross sectional echocardiography and pulsed mitral Doppler studies. Peak early (E) and late (A) filling velocities, duration of early (TE) and late (TA) filling and total diastole (TD) were measured. Velocity-time integral of early (EI) and late (AI) filling, deceleration slope of early filling (Edec), E/A ratio, ratio of duration early and total diastole (TETD) and of late and total diastole (TATD) were calculated. Patients were classified into three groups: normal controls (group 1), hypertensive patients without left ventricular hypertrophy (n = 25) (group 2), hypertensive patients with left ventricular hypertrophy (n = 45) (group 3) by using echocardiographic left ventricular mass index. Left ventricular mass index (g/m²) in group 1 was 103.26 (5.8), 105.2 (4.29) in group 2, and 197.63 (74.66) in group 3 (group 1 v group 3, p < 0.01).

Impaired left ventricular filling develops in hypertension and may precede the development of echocardiographic left ventricular hypertrophy. Edec and E/A ratio may be a sensitive index of impaired left ventricular filling in such patients.

Long term effects on left ventricular function of treatment for childhood malignancy

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Anthracyclines and thoracic irradiation used in the treatment of childhood malignancy are known to cause early alterations in left ventricular function. The late effects are poorly documented. Ventricular systolic and diastolic function were assessed blindly with M mode and Doppler echocardiography in 44 symptom free patients (mean age 14.7 years, range 8–23) and age and sex matched controls between 2 and 17 years (mean 6.2 years) after chemotherapy for childhood malignancy. The patients received anthracyclines and thoracic irradiation (n = 10), anthracyclines alone (n = 20), or neither form of treatment (n = 14). Fractional shortening (FS) was significantly lower in the patients than in controls (control FS: mean 38.24% (SD 3.46), patient FS: 35.83% (5.47); p = 0.015). There was no significant difference in mitral half time or time from mitral valve opening to aortic valve closure (p = 0.142 and p = 0.53 respectively). There was a trend towards the reduction in FS being associated with thoracic irradiation (p = 0.103) rather than anthracycline (mean doxorubicin dose 256 (146) mg/m² and mean daunorubicin dose 248 (105) mg/m² treatment (p = 0.191).

This study suggests that treatment for childhood malignancy leads to long term reduction in left ventricular systolic function and that this reduction is more closely associated with thoracic irradiation than anthracycline administration.

Thallium-201 perfusion defects in hypertrophic cardiomyopathy

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The use of thallium-201 perfusion scanning in hypertrophic cardiomyopathy is uncertain. Myocardial ischaemia may be an important determinant of symptoms and prognosis. To determine the prevalence and clinical significance of thallium-201 myocardial perfusion defects in hypertrophic cardiomyopathy single photon emission computed tomography, analysed with bullseye polar coordinate maps, was performed in 80 patients aged 14 to 74 years (mean 42). Maximal treadmill exercise testing and cross sectional echocardiography were performed to determine presence of ST segment change and extent and distribution of left ventricular hypertrophy. Fifty three patients (66%) had regional perfusion defects; they were fixed in 28 (35%) patients, reversible in 32 (40%), and a combination of both in seven (9%). Reverse redistribution, a perfusion defect that develops or increases on the delayed image, was present in 28 (35%) patients. Reversible and fixed defects were localised to segments of the hypertrophied myocardium (23/32, 15/28), whereas reverse redistribution was more common in myocardial segments without hypertrophy (18/28; p < 0.01). There was no association of reversible or fixed defects to chest pain or ST depression (>2 mm) during exercise. Fixed defects were more common in patients with non-sustained ventricular tachycardia (10/15 v 18/65; p < 0.005), in those with marked functional limitation (6/12 v 22/68; p < 0.05), and in those with a history of syncope (13/27 v 15/53; p = 0.08). These three factors together with a family history of hypertrophic cardiomyopathy and sudden death, young age at diagnosis, and progressive left ventricular dilatation with wall thinning were considered to be risk factors for a poor prognosis. Eight out of nine (89%) patients with large fixed defects and seven out of 19 (37%) with small fixed defects had two or more risk factors, whereas only 12 out of 52 (23%) without fixed defects had two or more risk factors (p < 0.001).

These findings indicate that thallium-201 myocardial perfusion defects are common in hypertrophic cardiomyopathy and are associated with features of adverse prognosis but are not related to clinical markers of ischaemia. Prospective evaluation of their prognostic significance is warranted.

Senning operation for complete transposition: experience at Guy’s

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Seventy consecutive infants with complete transposition of the great arteries underwent an atrial switch repair by Senning's technique between 1980 and 1990. Associated
defects included ventricular septal defects in 20, left ventricular outflow tract obstruction in 10, coarctation of the aorta in two, and the Wolff-Parkinson-White syndrome in one. The age at operation was 7-4 (3) months (range 17 days–17 months) and weight was 6-7 (1-4) kg (3-8–9-8). There were two deaths in hospital (2.8%). During an average follow up of four years (45 days–9-6 years) none of these patients died and currently all but one has unimpaired exercise tolerance. Two patients had superior vena caval obstruction, which was successfully treated by balloon dilatation. Eight patients have arrhythmias—nodal rhythm in four, the sick sinus syndrome in three, and atrial flutter in one—but only three of these patients require anti-arrhythmic treatment.

In our experience Senning’s operation for complete transposition carries a low operative mortality and serious baffle complications requiring reoperation are rare. The functional state of the surviving patients during medium term follow up has been encouraging, with a low incidence of arrhythmias or right ventricular dysfunction.

Adenosine: selective pulmonary vasodilatation in patients undergoing assessment for cardiac transplantation

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Intravenous adenosine has been shown to decrease selectively pulmonary vascular resistance (PVR) in normal human subjects and in patients with primary pulmonary hypertension. This effect is of potential therapeutic value in the perioperative period in patients with elevated PVR undergoing orthotopic heart transplantation (OHT). In animal studies adenosine has been shown to be a renal vasodilator. The effect of adenosine infusion on human renal blood flow has not been reported. Clearly, renal vasodilatation might limit the therapeutic use of adenosine in patients undergoing OHT. This study assessed whether adenosine acted as a selective pulmonary vasodilator in seven patients undergoing assessment for OHT. A pulmonary artery thermodilution catheter was inserted and simultaneous measurements were made of systemic and pulmonary haemodynamic function and of renal blood flow by a continuous renal vein thermodilution technique previously validated in vitro and in animal and human studies. Adenosine (0-05 mg/kg/minute) caused selective pulmonary vasodilatation measured by PVR to systemic vascular resistance ratio (15 0-9 at baseline v 11-6 (6) with adenosine (p < 0-05)). There were no significant changes in other parameters measured. Respective values at baseline and with adenosine were: mean arterial blood pressure 86 (17) v 88 (19) mm Hg, CI 2-02 (6) v 2-13 (0-7) l/min/m², PVR 279 (166) v 216 (124) dyn.s.cm⁻², heart rate 86 (25) v 85 (20) beats/minute, renal blood flow 197 (73) v 186 (63) ml/minute, and renal oxygen consumption 5-1 (2-5) v 4-6 (2-2) ml/minute. No patients experienced any adverse symptoms or atioventricular block during adenosine infusion.

Previous reports have suggested that adenosine 0-03–0-05 mg/kg/minute is probably the optimal infusion rate for achieving selective pulmonary vasodilatation in humans. In this group of patients this dose resulted in an insignificant fall in renal blood flow and selective pulmonary vasodilatation, but the fall in PVR was small and failed to reach significance. In view of the absence of a fall in mean arterial blood pressure or of any adverse effects a trial of adenosine at higher doses is indicated in this group of patients.

Monoclonal antiplatelet antibody 7E3 (IIb/IIIa receptor blocker) produces rapid reduction in platelet aggregation in humans

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7E3 is a murine monoclonal antiplatelet antibody that is directed against platelet receptor IIb/IIIa. To determine the relation between the dose of 7E3 Fab and inhibition of platelet function a phase I study was performed. Seventy one patients with stable angina were given single doses of 7E3 Fab from 0-1 to 0-3 mg/kg or a loading dose of 0-25–0-3 mg/kg followed by a 0-15 mg/kg/min infusion of 7E3 for 12–36 hours. Platelet function was measured as platelet aggregation (PA) to 20 M ADP, bleeding time (BT), and free IIb/IIIa platelet receptors (FPR). Single doses of 0-1 to 0-3 mg/kg reduced the median PA from 89% to 11% of pre-dose values, increased the median BT from 5 minutes to C30 minutes, and reduced median FPR from 50% to 18% of pre-dose values. Continuous infusion caused rapid, sustained inhibition of platelet function for the entire infusion period, with median PA decreased to 10% of pre-dose. Return of BT from C40 to <12 minutes took 4–12 hours after single dose studies and 6–24 hours after infusion. No significant bleeding or allergic reactions were observed, although low titre human antimurine antibody developed in 16 out of 65 (25%) patients. Therefore, 7E3 Fab produced appreciable inhibition of platelet function at single doses C0-25 mg/kg which can be sustained by continuous infusion. This agent may have a role in the management of acute ischaemic events.

Risk stratification in unstable angina: who should be considered for early angiography?

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Chest pain suggestive of acute myocardial infarction remains the most common reason for admission to coronary care units. If myocardial infarction is subsequently excluded, when should such pain be diagnosed as “unstable angina” and who should be considered for early angiography? In a prospective study of all patients admitted to a coronary care unit during one six month period there were 530 cases of chest pain. In 304 acute myocardial infarction was subsequently confirmed, 32 had secondary angina (to an arrhythmia for example), and in a further 14 a specific non-cardiac cause was identified. The remaining 170 patients (180 admissions) were followed up for three years for the development of cardiac events (cardiac death or non-fatal infarction). These events occurred at a constant rate for eight weeks after admission (“early events”), after which the event rate slowed. Patients whose electrocardiogram (ECG) remained normal during their index admission had a benign prognosis whether there was a history of preceding effort angina (n = 35) or not (n = 29). In this group there were no early events and only a 3% cardiac event rate at three years. An abnormal admission ECG, whether the result of previous infarction (n = 39) or with reversible changes (n = 67), was associated with a much worse short and long term prognosis (12% events at two months, 32% at three years). After a review of published reports factors reported to be associated with a worse prognosis were studied in an attempt to predict this “at risk” group. The recurrence of
pain in hospital, or a cardiac enzyme activity raised to less than twice the upper limit of normal, identified 49 patients in whom 11 of the 13 early events occurred (sensitivity 85%, specificity 59%, positive predictive accuracy 22%). No other prognostic factors, either alone or in combination, gave a similar combination of sensitivity and specificity.

For patients presenting with chest pain in whom a myocardial infarct is subsequently excluded simple, non-invasive risk stratification permits the identification of patients with fundamentally different short and long term prognoses. Recurrent pain or a minor increase in enzyme activity identifies the group most likely to benefit from early revascularisation.

Implications of thrombolysis for risk stratification in patients after infarction
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Though the use of thrombolytic agents in acute myocardial infarction (AMI) is associated with an appreciable reduction in mortality, little is known about the effects on life threatening arrhythmic events (sudden death or sustained ventricular tachycardia) and risk stratification. As part of a prospective study at this hospital the effects of thrombolysis on arrhythmic events and risk stratification were investigated. Among 427 serial patients admitted with AMI eligible for thrombolytic treatment, 203 received thrombolysis (group T) and 224 did not (group N). The actuarial probability of life threatening arrhythmic events at two years was appreciably reduced in group T (4.5%) v group N (10.6%) (p < 0.001). Despite treatment with thrombolysis the incidences of arrhythmic markers such as late potentials, ventricular ectopic frequency (>10/h), impaired ventricular function (<40%), depressed heart rate variability, and a positive exercise test were similar in both groups. In group N the actuarial probability of arrhythmic events was increased in patients with frequent ventricular ectopic activity (24% v 7%, p = 0.008), positive late potentials (29% v 6%, p = 0.001), impaired heart rate variability (26% v 1%, p = 0.001), and poor left ventricular function (19% v 7%, p = 0.02), but in group T only impaired heart rate variability was associated with an increased probability of arrhythmic events (13% v 1%, p = 0.005).

Thrombolysis reduced the incidence of late arrhythmic events following MI but established methods of risk stratification, particularly those based on long term electrocardiographic recordings and the signal averaged electrocardiograms, may not be applicable in patients given thrombolysis.

Prognostic value of ambulatory ST segment monitoring after acute myocardial infarction
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We have assessed the prognostic value of ambulatory ST segment monitoring (early (6 days, n = 201) and late (38 days, n = 177)) in 203 patients with acute myocardial infarction when compared with clinical factors, coronary prognostic indices, exercise testing (n = 174), and radio-nuclide ventriculography (n = 134). The 29 patients (14%) with ST depression (STD) on early monitoring had more (p < 0.001) cardiac events (death, reinfarction, or coronary revascularisation) (13/29 (45%)) than those without STD (30/172 (17%)) and events were most common in those patients with three or more STD episodes a day (11/17 (65%) v 2/12 (17%), p < 0.03) or a maximum of at least 1.3 mm STD (10/15 (67%) v 3/14 (21%), p < 0.05). However, patients (56/177 (32%)) who developed STD on late monitoring experienced an increase in cardiac events only when they had three or more STD episodes a day (10/31 (32%) v 18/146 (12%), p < 0.01), at least 20 minutes of STD a day (8/25 (32%) v 20/152 (13%), p < 0.05), or a maximum STD of 1.6 mm or greater (8/25 (32%) v 30/152 (13%), p < 0.05). Furthermore, ambulatory monitoring had superior predictive value to clinical factors, coronary prognostic indices, and left ventriculography but similar prognostic value to exercise testing.

Thus, any STD on ambulatory monitoring early after myocardial infarction identifies patients who are at increased risk whereas STD later carries prognostic value only when it is prolonged, pronounced, or frequent. Ambulatory monitoring may be a useful alternative to exercise testing for identifying patients after myocardial infarction who might benefit from early coronary angiography.

Prognostic significance of heart rate variability in myocardial infarction
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Heart rate variability in the early phase of myocardial infarction reflects cardiac autonomic balance and may carry prognostic significance. We studied heart rate variability in 34 patients with anterior and 36 patients with inferior myocardial infarction by Holter tape recording during the first day of hospital admission. By excluding the RR intervals with lengths outside 20% of the previous cycle to avoid ectopy and sensing artefacts, the following calculations were made in order to express heart rate variability: (a) mean RR interval; (b) standard deviation of the mean RR interval (SD); (c) standard deviation of the mean difference of each RR interval from the preceding one (SDdiff). These parameters were calculated for all patients during a four hour night time period (0100-0500). The presence of heart failure and the use of β blockers was similar in the two groups at the time of the recording. Patients with anterior infarction when compared with those with inferior infarction showed a shorter mean RR interval (743 (SEM) (22) vs 849 (20) ms; p = 0.001), a smaller SD (39.6 (3.1) vs 66.2 (4.6) ms; p < 0.001), and a smaller SDdiff (19.8 (4.1) vs 33.4 (3.4) ms; p = 0.001). During the hospital stay subsequent heart failure or death occurred more frequently in those patients with low heart rate variability (SD below the median value of 50 ms) (44% v 8%; p < 0.01) independently of infarct site. Low SD had 83% sensitivity and 63% specificity whereas low SDdiff (below 23 ms) had 61% sensitivity and 52% specificity in predicting a worse clinical outcome. These data show that there is a difference in heart rate variability between anterior and inferior myocardial infarction which may reflect the differences in autonomic balance during the early phase of infarction; low variability independently of infarct site is associated with a complicated course.
Evaluation of patient benefit and resource use after early treatment of myocardial infarction with heparin and recombinant tissue type plasminogen activator (Actilyse): study of heparin and Actilyse processed electronically (SHAPE)

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A total of 758 patients with suspected acute myocardial infarction admitted to 32 general hospitals were considered for inclusion in a double blind study comparing recombinant tissue-type plasminogen activator (rt-PA) 100 mg plus heparin with placebo plus heparin. The usual standard treatment for each hospital was continued normally. The original intent was to recruit some 3000 patients but the trial had to be halted prematurely on ethical grounds. The patient data were collected by using records on a personal computer linked by modem to a central site. In all, 164 patients were excluded from the main analysis. Of the 594 patients who satisfied the entry criteria by a 3:1 allocation ratio, 435 were randomly allocated to rt-PA and 159 to placebo. The primary assessment of patient benefit was measured with the New York Heart Association functional classification. The benefit was measured over the 12 months from treatment and compared with the assessment before admission. There was no statistical difference found between the two groups. Other indices of patient benefit were also examined and no difference was found. Twelve per cent of patients given rt-PA had a bleeding complication compared with 3% given placebo. The incidence of stroke was very low in both groups. There was little difference in the use of resources either in the initial length of hospital stay or in the subsequent need for readmission, angiography, angioplasty, or bypass surgery. There was no difference in the proportion of patients who returned to work between the placebo or the treatment group. Death was not a primary end point. There was some survival benefit for the rt-PA group, although it did not reach significance.

Relations between heart rate, ischaemia, and drug treatment during daily life in patients with coronary artery disease

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Previous studies have shown that little if any increase in heart rate occurs one minute before the onset of ischaemia in ambulant patients with coronary artery disease (CAD). This study has tested the hypothesis that there are characteristic relations between heart rate and ischaemia in ambulant patients with CAD. Twenty one patients with proved coronary disease had 212 episodes of ischaemia during 504 hours of continuous electrocardiographic monitoring. An important increase in heart rate (74 (11) to 95 (14) beats/minute, p < 0·001) occurred between five and 30 minutes before the onset of ischaemia. A significantly higher heart rate at onset of ischaemia was seen during Bruce protocol exercise testing than during daily life (117 (12) v 90 (15) beats/minute, p < 0·01). However, when a less strenuous but more prolonged exercise protocol was used in a subgroup of patients (n = 12) ischaemia occurred at a heart rate that was significantly lower than during the Bruce protocol (88 (14) v 103 (15) beats/minute, p < 0·05) and was not significantly different from the threshold heart rate at onset of ischaemia during daily life (88 (14) v 84 (12) beats/minute, NS). As part of two placebo controlled trials, treatment with both propranolol and glyceryl trinitrate altered the distribution of ischaemic events by heart rate, but in opposite directions. Though propranolol largely eliminated events occurring at high (>100 beats/minute and moderate (80–100 beats/minute) heart rates, the number of events at low (<80 beats/minute) heart rates was increased. In contrast, glyceryl trinitrate reduced episodes at low and moderate heart rates only.

Important increases in heart rate occur before the onset of ischaemia during daily life but this increase occurs much earlier than has been reported. Duration of heart rate increase seems to influence the heart rate threshold for ischaemia, and this may contribute to the occurrence of ischaemia at lower heart rates during daily life than during exercise testing. Finally, different classes of drugs have characteristic effects on ischaemia occurring at different heart rates.

Inhibition and summation in human heart by long duration subthreshold conditioning pulses

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Inhibition (prolongation of refractoriness) and summation (shortening of refractoriness) have previously been reported to a limited extent in human myocardium by using bipolar conditioning stimuli of conventional (2 ms) pulse width. In 32 patients undergoing clinical electrophysiological studies we studied the effect of long duration, constant current subthreshold pulses on atrial (n = 22) and ventricular (n = 10) refractory periods. Continuous atrial or ventricular pacing (S1S1 = 500–600 ms) was performed throughout to minimise variability in refractoriness. Effective refractory period (ERP) was determined with a 2 ms pulse at an amplitude of twice the late diastolic threshold (LDT). A long duration conditioning pulse (Sc; duration = S1S2) was introduced. Initial Sc amplitude was 10% of LDT; amplitude and duration of Sc were varied stepwise and the effect of Sc observed. Inhibition was observed in all patients, the atrial ERP being prolonged by a mean of 98% from 238 (SD43) ms to 470 (100) ms with an Sc of mean amplitude 55% of LDT. In 10 patients reversal of the polarity of Sc resulted in shortening of the ERP (summation) by a mean of 27%, from 208 (24) ms to 151 (22) ms. Similar results were produced by ventricular stimulation (ERP was prolonged in all patients, from 239 (36) ms to 475 (88) ms, and shortened in five patients, from 259 (25) ms to 200 (12) ms). With unipolar stimulation cathodal current always produced inhibition; summation, when it occurred, was produced by anodal current.

Inhibition and summation may be produced in the same heart by reversal of stimulus polarity. Long duration current pulses can produce much greater degrees of inhibition and summation than conventional pulses.
Double blind comparison of DDI, DDI with rate hysteresis, VVI, and VVI with rate hysteresis in control of symptoms in carotid sinus syndrome

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DVI pacing has been shown to be superior to VVI pacing in controlling symptoms in the carotid sinus syndrome (CSS). DDI pacing with rate hysteresis (H) provides the opportunity of physiological pacing at high rate during attacks without the disadvantage of undue pacing every time the rate goes below the programmed rate as in pacing without H. This study was designed to perform a double blind comparison of the efficacy of DDI with H/DDI-H, programmed rate 80, H rate 40, DDI at 60 ppm, VVI with H (VVI-H, programmed rate 80, H rate 40) and VVI 60 ppm. Seventeen patients who had had pacemakers implanted 28-9 (27) months before for the carotid sinus syndrome syncope and pre-syncope were considered for the study. Preinclusion evaluation comprised carotid sinus massage (CSM), supine blood pressure and blood pressure five minutes after 80° tilt, retrograde atrioventricular conduction with and without carotid sinus massage, and DDI pacing during carotid sinus massage to identify patients with vasodepressor component. Two patients were excluded because of negative carotid sinus massage and one patient for marked sinus bradycardia. Fourteen patients, mean age 72-7 (8-8) years (two women), were included in the study and were randomised in a double blind fashion to one of the pacing modes for a period of six weeks each. During these periods they kept a record of episodes of mild dizziness, pre-syncope, syncope, palpitations, and shortness of breath in a diary. Thirteen patients completed the study; one patient withdrew because of hypertensive stroke. Total number of symptomatic episodes were: (a) DDI-H mode mild dizziness 70, pre-syncope 9, syncope 0, palpitations 16, shortness of breath 38; (b) DDI mode mild dizziness 46, pre-syncope 22, syncope 1, palpitations 36, shortness of breath 65; (c) VVI-H mode mild dizziness 62, pre-syncope 36, syncope 5, palpitations 76, shortness of breath 86; and (d) VVI mode mild dizziness 78, pre-syncope 20, syncope 0, palpitations 84, shortness of breath 61. One patient could not tolerate VVI pacing and had to have the next mode within two days and another patient developed atrial fibrillation in the final pacing mode (VVI-H). Overall the least symptomatic mode of pacing was DDI-H (p < 0-001).

It is concluded that DDI-H is the best mode of pacing for symptomatic carotid sinus syndrome and is now our pacing mode of choice.

"Subclinical" pacemaker syndrome: randomised study of "symptomless" patients with VVI pacemakers upgraded to dual chamber devices

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Sixteen patients aged 41-84 (69% men) who had had long term pacing for more than three years in VVI mode and had no evidence of the pacemaker syndrome had their pacemakers upgraded to DDI devices during routine generator change. Assessment was before (#VVI pre) and after upgrade in three pacing modes (VVI post, DDI, and DDD) in a randomised double blind crossover design. Patients with chronic atrial fibrillation or the pacemaker syndrome were excluded. Subjective, clinical, objective (stress tests), radiographic (chest x ray film), and echocardiographic (M mode, cross sectional, colour flow, and continuous wave Doppler echocardiography) assessments were undertaken after four weeks of out of hospital activity in each mode. Perceived general wellbeing and exercise tolerance was better in DDD mode than in VVI pre or post or in DDI (p < 0-01). Symptoms were less in DDD mode (p < 0-05). After study completion 75% preferred DDI and 12% DDI and the remainder had no preference. Seventy two per cent found VVI post least acceptable whereas none found DDD least acceptable. Treadmill exercise tolerance was greatest in DDD mode (p < 0-001) but did not differ in the remaining modes. Chamber dimensions (echocardiography) and cardiothoracic ratio (chest x ray film) did not differ in any mode. Improved cardiac output was seen at rest in DDD mode (p = 0-03) compared with VVI pre and post modes but not DDI mode. Mitral and tricuspid regurgitation was least in DDD mode but did not correlate with symptoms.

Thus patients who are receiving optimal pacing in VVI mode benefit subjectively and objectively from upgrade to DDD mode whereas DDI has little effect. This suggests the existence of a "subclinical" pacemaker syndrome that becomes apparent only when physiological pacing is introduced.

Physician implanted defibrillator: first clinical experience of a new transvenous device

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A pacemaker/cardioverter/defibrillator was implanted without a thoracotomy in three male patients with a history of drug resistant ventricular tachycardia and sudden cardiac death. This new device utilises two pace/sense/defibrillate electrodes positioned via the subclavian vein in the right atrial appendage and in the right ventricular apex. A monophasic bidirectional shock is delivered between these and a subcutaneous axillary patch. The generator is situated in an abdominal pocket. Implantation took between 2.5 and 4 hours and was performed under general anaesthesia. x Ray screening was required for between 5 and 35 minutes. During intraoperative testing there was a loss of sensing and pacing postshock in two patients. This was corrected by repositioning the right ventricular electrode (total five minutes). A good defibrillation threshold was achieved in all patients (10 J, 10 J, 20 J) and was maintained at the one month follow up. The implant procedure was uncomplicated and patients were fit for discharge two days after operation. In one patient a lead complication required repositioning after one week.

The implantation of a transvenous defibrillator is a safe and effective alternative to the standard thoracotomy approach.

Prophylactic use of implantable cardioverter defibrillator after myocardial infarction: predicting cost in high and low risk patients

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Interest is growing in the prophylactic use of the
implantable cardioverter defibrillator (ICD) in patients at high risk of sudden death. We costed ICD use in myocardial infarction survivors by using data from our post-myocardial infarction database of 525 patients. All cause cumulative mortality after one year (Y1) was 8.4%, after two years (Y2) 11.5%, and after three years (Y3) 13.7%. Sudden death mortality was 3.8% (Y1), 4.5% (Y2), and 4.5% (Y3). Patients at higher risk could be identified. In the group with left ventricular ejection fraction <40% (EF < 40) (n = 201) mortality from sudden death was 7.5% (Y1), 7.5% (Y2), and 7.5% (Y3) while a combination of reduced heart rate variability, >10 ventricular ectopics per hour, and positive late potentials (n = 25) identified a group (HRG) with sudden death mortalities of 22.8% (Y1), 29.9% (Y2), and 29.9% (Y3). We costed the use of the ICD in all patients and in groups EF < 40 and HRG over a three year period assuming an ICD life of three years, 100% prevention of sudden death, no antiarrhythmic drug treatment, and transthoracic implantation. Costs are ICD and patches (£10,700), surgery (£3,000), extra seven days as an inpatient (£1,400), outpatient follow up over three years (£1,400). Total implant and follow up cost was £16,500. Screening costs were £50 (EF < 40 group) and £130 (HRG group) per patient screened. Implantation in all patients saved 2-7 life years per 100 implants (LY%) at a cost per life year of £6,040,000. In the EF < 40 group the ICD saved 10-7 LY% at a cost of £15,500 per life year. In the HRG group (in which 33% of all sudden death occurs) the ICD saved 58-3 LY% at a much reduced cost of £33,000 per life year but was still expensive when compared with other accepted invasive treatment.

Pending a reduction in this cost by improved selection of patients at high risk of sudden death, there is no general indication to implant an ICD in high risk patients after myocardial infarction but a limited trial to clarify the true costs may be justified.

Anatomical problems associated with implantation of cardioverter defibrillator

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A Guardian cardioverter defibrillator (ICD) was implanted in nine patients, all men (mean age 60 (6) years, range 50–69), over a 15 month period. Three patients (33%) suffered out of hospital ventricular fibrillation, one (11%) had exercise induced ventricular fibrillation and two (22%) exercise induced ventricular tachycardia, and three had haemodynamically unstable ventricular tachycardia. During the first implantation severe postoperative bleeding occurred with suturing of the epicardial patches, and all subsequent patches were stitched to the pericardium. In one patient the generator eroded through the rectus sheath, was repositioned within the thorax, where it also eroded, and was subsequently explanted. In a further case the generator was electively implanted in the thorax because of restricted space in the rectus sheath and for the same reason in another patient the generator was sutured anteriorly to the sheath. During a mean follow up of 11 months (3–17) there were seven inappropriate shocks, three during atrial flutter (one patient) and four due to lead fracture (two patients). There were no deaths.

In this series a common problem was related to the size of the ICD generator precluding its implantation in the rectus sheath. This was overcome by repositioning in other body cavities. The use of an ICD is associated with treatable morbidity but there were no deaths in this follow up period.

Physiological properties of human hypertrophic myocardium and impaired contractility

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Hypertrophy may be associated with changes in inotropy, intracellular pH (pHi), and sodium concentration ([Na\textsuperscript{+}]). Strips of human left ventricle removed at valve replacement were perfused with Tyrode’s solution (pH 7.35 in 5% carbon dioxide and 95% oxygen at 37°C) and stimulated at 1 Hz and isometric twitch (T) and mechanical restitution curves (MRC) analysed. pHi and [Na\textsuperscript{+}] were measured by using ion selective electrodes in quiescent preparations. Tension was reduced in pressure overloaded myocardium (0.72 kN/kg (n = 20) v controls, 1.72 (n = 15); p < 0.05) and negatively correlated with cell diameter (R = −0.66, p = 0.02 (n = 11)). MRC time constants (τ\textsubscript{T}, τ\textsubscript{R}) correlated with cell diameter (τ\textsubscript{T} R = 0.62, τ\textsubscript{R} = 0.81 (n = 11)). Mean pHi was 7.27 (SD 0.19) (n = 7) mean pH\textsubscript{i}, 7.42 and [Na\textsuperscript{+}], 13.31 (SD 4.13) μmol\textsuperscript{−1} (n = 6), [Na\textsuperscript{+}], correlated with cell diameter (R = 0.98, p = 0.02). Reducing extracellular pH (pH\textsubscript{e}), by raising carbon dioxide content, led to the largest fall in tension (% control T/unit pH\textsubscript{e}) in volume overloaded myocardium (108% (n = 15) v controls, 73% (n = 9) p = 0.05). In pressure overloaded myocardium T/pHi was inversely related to hypertrophy on electrophysiologic voltage criteria (R = 0.52, p = 0.03 (n = 18)). In resting muscle pH\textsubscript{e}, correlated with pH\textsubscript{i} and buffering capacity “pH\textsubscript{i}/pH\textsubscript{e}” correlated with T/pH\textsubscript{e} slopes of contracting muscle.

It is proposed that altered homeostasis of pH\textsubscript{i} and [Na\textsuperscript{+}] in hypertrophy could explain abnormalities of contractility.

Platelet and white cell accumulation in early infarction

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Both white cells and platelets have been implicated as contributing to myocardial damage after infarction. In nine pigs (20–39 kg) the left anterior descending coronary artery (LAD) was occluded and the area of myocardium at risk determined by intravenous thallium–201, given five minutes after the occlusion. Autologous white cells were labelled with technetium–99m and platelets with indium–111 and reinfected before occlusion. The animals died or were sacrificed at a mean time of 85 minutes (12–120 minutes) and the hearts were extracted, opened, and laid flat on a γ camera and imaged to determine the area
Glucose tolerance test and insulin concentrations in British Asian and white patients and in Asian patients in India with coronary artery disease

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Blood glucose and insulin concentrations were measured 0, 1, and 2 hours after a 75 g oral glucose challenge in a consecutive series of 56 British Asian (BA) and 65 randomly selected white patients (WP). These were compared with 47 BA and 57 white controls (WC) randomly sampled from the community. A consecutive series of 28 patients in India were compared with 28 randomly selected controls, measurements for these subjects being at 0 and 2 hours. All patients had angiographically confirmed coronary artery disease. Most BA subjects had migrated from the north-west of the Indian subcontinent, and subjects resident in India were from the same geographical area. These groups have not been previously compared. Significance was set at a conventional 5% level. Impaired glucose tolerance and overt diabetes were significantly more common in BA and Asians in India (AI) than in white subjects—that is, 40.7%, 46.4%, and 18% respectively. This was more common in patients than in controls—namely, 24.6% v 10.5% in white subjects, 42.8% v 38.2% in BA, and 57.1% v 35.7% in AI. Serum glucose concentration at 0 hours was borderline significantly higher for WP than controls but was very significantly higher in BA and AI patients than controls—5.0 v 4.6, 5.6 v 5.0, and 5.5 v 5.1 respectively. At one hour BA patients had significantly higher values than controls (10.0 v 8.5) unlike white patients (7.5 v 7.6). At 2 hours values were only borderline significantly higher in WP than WC (5.8 v 5.1) but very significantly higher in BA (7.3 v 6.1) and AI patients (8.2 v 7.4). The geometric mean of insulin concentrations was significantly higher in patients than in controls in all the groups at 0, 1, and 2 hours—13 v 7, 78 v 55, and 47 v 28 for white subjects; 23 v 16, 107 v 96, and 70 v 52 for BA; and 18 v 14, 70 v 48 for AI at 0 and 2 hours. These concentrations were significantly higher at all times in Asians than in white subjects both patients and controls.

We conclude that impaired glucose tolerance and diabetes is significantly more common in Asians than in white subjects and more so in AI. Insulin resistance is seen not only in Asian patients but also in white patients, with significant hyperinsulinaemia also found in Asian controls as compared with white controls.

Apolipoprotein (a) concentrations and susceptibility to coronary artery disease in patients with peripheral vascular disease

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Patients undergoing surgery for peripheral vascular diseases often have generalised atherosclerosis and a high incidence of significant coronary artery disease. Apolipoprotein (a) (Apo(a)) concentrations are genetically determined and have been strongly associated with the presence of coronary artery disease in the general population. The close structural homology that has been shown between Apo(a) and plasminogen has been suggested as an important link between lipoprotein metabolism, the clotting or fibrinolytic system, and susceptibility to coronary artery disease. The aim of this study was at establishing whether an association exists between Apo(a) concentrations and coronary artery disease in patients with atherosclerotic peripheral vascular disease. We studied 38 consecutive patients under consideration for peripheral vascular surgery, all of whom underwent clinical assessment and coronary arteriography. A serum sample from each patient after fasting was analysed for concentrations of total cholesterol, high density lipoprotein cholesterol (HDLC), Apo(a), apoprotein A-I (Apo A-I), apoprotein B (Apo B), and triglyceride. Apo(a) was measured by a two site immunoa radiometric assay using monocl onal antibodies to two different epitopes of Apo(a) (Pharmacia Diagnostics AB). The within assay coefficient of variation was 3.8%. Of the 38 patients, 27 had significant coronary artery disease while 11 did not. These two patient groups were of similar age and sex distribution and had similar patterns of peripheral vascular disease and smoking habits. None of the patients had diabetes mellitus, but a history of hypertension was found more frequently in patients with coronary artery disease (χ², p < 0.01). Apo(a) concentrations were significantly greater in patients with coronary artery disease (median 328 U/l (range 33–1638) v 122 U/l (19–206), p < 0.002) (Mann–Whitney U test) whereas HDLC concentrations were significantly lower in this group (mean 0.97 (SD 0.22) v 1.25 (0.49), p < 0.05 (unpaired t test)). No significant difference was observed in the distribution of total cholesterol, Apo A-I, Apo B, or triglyceride between the two groups.

Thus, we conclude that high concentrations of Apo(a) and low concentrations of HDLC are significantly associated with the presence of coronary artery disease in patients with surgically correctable peripheral vascular disease. Measurement of Apo(a) concentrations may prove to be a useful additional discriminator in the detection of patients with coronary artery disease within this group.

Free radical production during human myocardial reperfusion

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Oxygen free radical production has been shown during myocardial reperfusion in animal models. Peak radical detection in the coronary sinus occurs 2–5 minutes after...
reperfusion, thus excluding confusion with ischaemic washout (5–15 seconds). We studied free radical activity in the blood of 15 patients undergoing percutaneous transluminal angioplasty to proximal anterior descending lesions with the highly specific technique of electron spin resonance spin trapping. Sequential coronary sinus sampling alone was performed in 10 patients and in a further five patients paired aortic and sinus samples were obtained. Phenylbuthylhydrazine was used to spin trap free radicals present in the blood and the samples were then evaluated by electron spin resonance. In nine of the 15 patients free radical activity was detected in the coronary sinus blood, with peak detection frequency between 2 and 4 minutes after balloon deflation. Radicals were not detected in any of the aortic samples or in the coronary sinus samples taken before and during balloon inflation.

This study provides the first unequivocal evidence of free radical production during human myocardial reperfusion.

Dissociation between angiographic findings and functional assessment of myocardial ischaemia soon after successful coronary angioplasty

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To understand better the mechanism responsible for exercise induced myocardial ischaemia after successful coronary angioplasty (PTCA), 13 patients who underwent single vessel PTCA were studied. Exercise testing was performed before and on day 7 after PTCA, which was repeated after 10 mg sublingual isosorbide dinitrates if the test gave positive results. Quantitative coronary arteriography was also performed on day 8 after PTCA in the basal state (B), after intracoronary infusion of 0.9% saline and 1, 5, 10, 20 µg ergometrine, and after 300 µg glyceryl trinitrate (GTN).

All antianginal drugs except for aspirin were stopped 48 hours before both phases of the study. All patients had a positive exercise test (≥1 mm ST segment depression) before PTCA but on day 7 seven patients had a positive exercise test with chest pain (group 1) and six patients had a negative exercise test (group 2). In group 1 all positive exercise tests on day 8 became negative when repeated after nitrates. There was no significant difference in the basal luminal diameter before, immediately after, and eight days after PTCA between the two groups. Intracoronary ergometrine was associated with a dose dependent constriction of the angioplasted segment with no significant difference in the magnitude of the response between the two groups (maximum constriction for group 1 was 19% (3) (p < 0.001 v B) and in group 2 was 20% (4%) (p < 0.006 v B)). No angina, ischaemic ST changes, or occlusive or subocclusive spasm occurred in any patient of either group. The degree of dilatation induced by glyceryl trinitrate was also similar in both groups.

Thus, soon after PTCA exercise testing may be positive despite successful dilatation. The lack of hyperreactivity of large epicardial vessels to the powerful vasoconstrictor stimulus of ergometrine indicates that the mechanism responsible for exercise induced myocardial ischaemia after PTCA lies in small coronary vessels, an abnormality amenable to be abolished by glyceryl trinitrate.

Acute effects of transition to a Fontan circulation

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The immediate effects of the Fontan operation on left ventricular function were studied in five patients by using simultaneous high fidelity intraventricular pressure measurements and M mode Doppler epicardial echocardiograms recorded before and after pulmonary bypass. The Fontan operation had no effect on left ventricular end diastolic pressure or systolic pressure or on load dependent indices of ventricular function (shortening fraction, rate of change of dimension, rate of posterior wall thickening, and thinning), but large changes in left ventricular geometry occurred. Maximum cavity dimension fell from 3.6 (0.62) cm to 3.0 (0.68) cm (p = 0.046).

Maximum posterior wall thickness increased from 11 (3.6) mm to 14 (2.1) mm (p = 0.026) and minimum posterior wall thickness increased from 7.1 (3.6) mm to 10.4 (1.5) mm (p = 0.003). Doppler echocardiography with simultaneous intraventricular pressure measurement showed gross isovolumic intraventricular flow suggestive of incoordinate wall motion in all patients.

The Fontan operation causes a sudden reduction in left ventricular preload, which in the presence of a maintained shortening fraction leads to a "hypertrophic" and incoordinate left ventricle.

Left ventricular dysynchrony after the Fontan operation: evidence for incoordinate systolic and diastolic wall motion

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Thirty patients were studied between one day and six years after the Fontan procedure (FP) for evidence of regional abnormalities of ventricular wall motion. Left ventriculograms from 14 patients after FP and 11 patients with univentricular atrioventricular connection before FP were digitised frame by frame. Strict criteria for incoordinate wall motion were used (outward movement of >50% of total outward movement of four adjacent segments before mitral valve opening or inward movement of >50% of total inward movement in four adjacent segments after minimum cavity dimension) so that minor abnormalities were not included. There were major abnormalities of regional wall motion in 12 of the 14 patients after FP but in only three of the 11 patients before surgery. Doppler inflow velocities were recorded in 16 patients with simultaneous phonocardiogram and echocardiogram. Abnormal systolic base to apex flow reflecting incoordinate contraction was detected in 15 patients. This had a mean velocity of 23 cm/s (16–34) and lasted for 65% (40–83%) of the total electromechanical systole. Abnormal intraventricular flow from base to apex during isovolumic relaxation was detected in 11 patients with a mean velocity of 19 cm/s (10–27). These abnormal flow transients were not detected in any of the 10 normal children or six patients with a univentricular atrioventricular connection before FP.

Major abnormalities of regional ventricular motion, which may have important implications for global ventricular function and efficiency, are common after FP.
Transoesophageal echocardiography: new diagnostic technique in evaluation and follow up of Fontan procedures

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Transoesophageal echocardiography (TOE) was used prospectively in 18 patients (aged 1–6–34 years; mean 12–6 years) to determine whether this technique may be superior to transthoracic echocardiography (TTE) in the assessment of the immediate (five patients) or intermediate results (13 patients) after a wide range of Fontan type procedures. The findings were correlated with one another and cardiac catheterisation (11 patients). Atrial shunting was documented by TOE in three patients and by TTE in only one. Two had this subsequently confirmed by cardiac catheterisation; the third underwent reoperation based on the TOE study alone. Right atrial thrombus formation was detected by TOE in three patients and by TTE in one patient. Repeat TOE studies were used to evaluate thrombolytic treatment in two, which was successful in one. Spontaneous right atrial contrast was identified in an additional two patients only by TOE. Atroventricular valve regurgitation (11/18) was better defined by TOE than by TTE studies (5/18). A coronary artery fistula was identified by TOE in two patients and by TTE in none. Of the total of 29 Fontan and Glenn connections established in these 18 patients, 25 (86%) were able to be evaluated by TOE and only 14 (48%) by TTE. Posterior Fontan connections were able to be evaluated by TOE in 10/10 patients (TTE 5/10), and Glenn shunts in 8/9 patients (TTE in 3/9). Anterior Fontan connections were better shown by TTE (6/8 patients) than by TOE (5/8). Pulmonary artery obstruction was documented by TOE in three patients and by TTE in one. This was confirmed by subsequent cardiac catheterisation in all three and was excluded in the remaining eight patients who had catheterisation. Transoesophageal pulsed wave Doppler interrogation of pulmonary artery and pulmonary vein flow patterns consistently allowed a detailed evaluation of the Fontan circulation. Whereas pulmonary artery flow patterns varied according to the procedure used, the corresponding pulmonary vein flow patterns were found to be independent of the type of Fontan connection used.

TOE is an important diagnostic and monitoring technique in patients requiring Fontan procedures. In this series it proved to be largely superior to TTE and of substantial additional value to cardiac catheterisation. Pulsed wave Doppler studies allow a detailed evaluation of haemodynamic characteristics after different types of Fontan procedures.

Management of pulmonary artery stenosis after arterial switch operation for transposition of the great arteries

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The arterial switch operation is the treatment of choice for transposition of the great arteries and is now performed with a low mortality. One of the recognised complications is pulmonary artery stenosis (PAS), and we have found this in 16 out of 84 survivors. The following differences were observed between those infants with PAS and those without (NPAS). The mean age at operation of the PAS group was 14.8 (SD 11.2) days and for NPAS 271 (1085) days (p = 0.05). The mean period of ventilation for PAS was 3.8 (29) days and for NPAS 2.5 (19) days (p = 0.04). The mean time taking intravenous inotropic drugs for infants with PAS was 5.06 (SD 3.3) days and for those without 3.1 (1.8) days (p = 0.002). The mean postoperative Doppler velocity was 3.13 (0.9) m/s for PAS. Twelve infants underwent cardiac catheterisation at a mean of 252 (185) days after surgery and six had balloon dilatation. Of those with PAS at the anastomosis site, four out of five had successful dilatation, and of those with PAS at the origin of the branch pulmonary arteries, four out of six had successful dilatations. None of the three patients with long segment PAS had successful dilatation. Six patients proceeded to surgery. There were no complications and only one restenosis occurred after reoperation, which was dilated successfully.

We suggest a risk factor for the PAS group is a younger age at surgery and they are more likely to require prolonged postoperative ventilation or inotropic support. Balloon dilatation should be undertaken for main or branch origin stenosis. Balloon dilatation or surgery is safe and effective.

Abnormal right ventricular diastolic function is common after relief of severe outflow tract obstruction

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With Doppler echocardiography and simultaneous respirometry and electrocardiography right ventricular diastolic function was studied in seven symptom free patients at a median interval of five years after complete correction of pulmonary atresia with intact septum (three) or critical pulmonary stenosis (four) and in seven age and sex matched controls. Tricuspid and pulmonary flow velocities were measured, and the atrial contribution to forward flow in the pulmonary artery was assessed with planimetry. Three inspiratory and three expiratory cardiac cycles were analysed and averaged. Relief of right ventricular outflow tract obstruction was complete in all patients. All, however, continued to show evidence of right ventricular diastolic abnormalities. There was obvious forward flow in the pulmonary artery coincident with atrial systole, which accounted for 23% (6.7–42%) of the total pulmonary flow in the patient group. This was not detected in controls. Though mean tricuspid E wave deceleration and E/A ratio was similar in patients and controls, a significant decrease in E wave deceleration time was observed in the patient group during inspiration (p = 0.008).

Even after complete relief of right ventricular outflow tract obstruction in infancy abnormalities of right ventricular diastolic function, characteristic of a restrictive process (prominent atrial contribution to pulmonary flow and a shortening in tricuspid E wave deceleration during inspiration), are common even in symptom free patients.

Congenital heart disease: nutritional state of children undergoing cardiac surgery

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Nutritional state is a major determinant of the magnitude
of the metabolic response to injury, malnutrition being associated with poor wound healing, reduced immunity, and impaired respiratory function. We are currently studying the energy requirements of children with congenital heart disease before and after surgery by the doubly labelled water technique; as a preliminary we investigated their preoperative nutritional state. Forty children and 29 variables were studied (19 males, 21 females, mean age 1-75 years, range 2 days to 4-77 years). Body weight was less than or equal to the 10th centile in three and to the third centile in 15 (37-5%). Results for height were (respectively) 1 and 8 (20%) and for triceps and subscapular skinfold thickness 6 and 3 (7-5%) and 4 and 6 (15%). Bicarbonate concentrations were low in 18; chloride was raised in 29. Total protein and albumin concentrations were subnormal in 13 and in 19 (47-5%) respectively. Transferrin was low in five (12-5%), zinc in seven (17-5%), copper in four, and magnesium in one. Phosphate was raised in 26, calcium in 11, aspartate transaminase activity in nine, alanine transaminase activity in two, and bilirubin in two. C reactive protein was raised above 10 mg/l in three patients; urinary 3-methylhistidine (a marker of whole body protein breakdown) was raised in these and in five others (20%). Overall, in 60% of patients the values of seven or more variables were abnormal.

These results support the clinical impression that many children undergoing cardiac surgery are severely undernourished. This is in contrast to previously reported findings in adults.

Early use of captopril limits left ventricular remodelling after myocardial infarction
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Captopril treatment started one to three weeks after myocardial infarction may limit left ventricular remodelling. Angiotensin II concentrations peak within a few days of infarction and the earlier use of captopril may be advantageous. In a double blind study 90 patients (82 men, age range 40-75) were randomly assigned to treatment with captopril or placebo within 24 hours of myocardial infarction, continuing for one year. No patient had to be withdrawn from captopril treatment because of acute hypotension, and over 12 months withdrawals and deaths were balanced between the treatment groups. Serial cross sectional echocardiography was used to assess ventricular remodelling. After 12 months of treatment left ventricular end diastolic volume index (EDVI) had increased (8-4 (1-9) ml/m² in the captopril group v 19-0 (2-6) ml/m² with placebo, p = 0-002). Left ventricular end systolic volume index (ESVI) increased by 5-4 (1-3) ml/m² in the captopril group v 14-7 (2-3) ml/m² with placebo (p = 0-001). The resulting mean volume indices were significantly lower in the captopril group: EDVI 76-9 (3-0) ml/m² v 89-5 (3-1) ml/m², p = 0-005; ESVI 47-0 (3-8) ml/m² v 59-9 (3-4) ml/m², p = 0-005. In the patients with anterior myocardial infarction, anterior segment length increased by 4 (2) mm in the captopril group v 17 (4) mm with placebo (p = 0-009). In the subgroup with inferoposterior myocardial infarction the posterior segment length increased by 4 (2) mm in the captopril group v 13 (3) mm with placebo (p = 0-03).

Thus captopril treatment started within 24 hours of myocardial infarction is safe and significantly attenuates ventricular remodelling over one year.

Influence of early vasodilator treatment on myocardial infarct size and the inflammatory response
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To test the hypothesis that captopril and nitrates may reduce infarct size and that captopril may scavenge free radicals or suppress inflammation, we have conducted a double blind randomised study in which 105 patients with acute myocardial infarction were assigned to treatment with placebo (n = 36), isosorbide mononitrate 20 mg three times a day (n = 33), or captopril 12-5 mg three times a day (n = 36). Treatment was started within 24 hours of the onset of pain (mean 14-4 h) and was continued for 28 days. Infarct size was assessed two to four days after the onset of pain by tomographic technetium-99m pyrophosphate imaging. Quantification of infarct size was by voxel counting. Vasodilator treatment had no influence on infarct size (placebo 58-9 (9-0), nitrate 65-8 (5-2), captopril 58-8 (7-8) cm³). The inflammatory response was quantified by estimating plasma neutrophil elastase activity, a measure of neutrophil activation, and the plasma concentration of the phospholipid diene conjugated isomer of linoleic acid, a product of free radical lipid attack. The average neutrophil elastase activity over the 48 hours after trial entry was similar in the three groups (placebo 40-0 (3-6), nitrate 52-3 (5-5), captopril 41-6 (2-5) ng/ml). There was no evidence of suppression of free radical production with similar values of the ratio of the diene conjugated to the diene unconjugated isomer of linoleic acid over the same time period (placebo 2-8 (0-2), nitrate 2-9 (0-2), captopril 2-9 (0-3) (x 10⁻⁷). We conclude that early oral vasodilator treatment has little or no effect on infarct size or infarct associated inflammation.

One year comparative study of captopril and flosequinan in patients with chronic heart failure
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Two hundred and nine patients with chronic heart failure, whose symptoms remained despite at least 80 mg frusemide daily and who were not taking vasodilators were randomised double blind to either flosequinan or captopril for one year. Before randomisation each patient completed a single blind placebo period until their exercise tolerance had plateaued. The patients were stratified according to whether they were capable of performing at least three minutes of treadmill exercise to either a treadmill group or if they could not to a corridor walk test group. The treadmill group underwent exercise tests at weeks 2, 4, 6, 8, 13, 26, 39, and 52 according to a modified Bruce protocol whereas the walk test group completed a six minute test only at the same times. One hundred and two patients were randomised to flosequinan; 65 were withdrawn, of whom 22 died. Forty three patients were withdrawn from captopril, of whom 17 died. Withdrawal from flosequinan was due to worsening heart failure in 11 and adverse events in 28 whereas the corresponding numbers in the captopril group were nine and 15. In those patients capable of treadmill testing with their last exercise time taken as end point
there was no difference in the increase in treadmill exercise time; in the flosequinan group the mean baseline exercise time was 593 s and the end point 709 s (n = 31), and in the captopril group the baseline was 572 s and the end point 738 s (n = 36) (p = 0·57). Values were similar in both groups in the patients who completed the corridor walk test only. The distance walked at baseline was 208 m and at the end point 271 m in the flosequinan group and 252 m and 326 m in the captopril group (p = 0·71). Analysis of the exercise times at each visit for those patients who continued in the study also showed no differences.

Flosequinan had equal efficacy with captopril in the patients who were able to continue treatment but it was associated with a greater withdrawal rate, predominantly due to adverse events, over the one year period of this study.

Comparison of a new neutral endopeptidase inhibitor with frusemide in left ventricular dysfunction

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Atrial natriuretic factor has significant diuretic and vasodilatory properties and is degraded by neutral endopeptidase. Therefore, a specific inhibitor of this enzyme might have beneficial effects in left ventricular dysfunction by increasing circulating atrial natriuretic factor concentrations. We compared such an inhibitor (candoxatril) with frusemide in 18 patients with previous myocardial infarction. All patients had left ventricular dysfunction, defined as an end diastolic dimension > 55 mm; fractional shortening < 25%; and a reduced exercise capacity with a maximum oxygen consumption of < 25 ml/kg/min. Patients were randomised in single blind fashion to (a) candoxatril 200 mg twice a day, (b) candoxatril 400 mg twice a day, or (c) frusemide 20 mg twice a day. After 10 days atrial natriuretic factor concentrations increased significantly by 155% (p < 0·05) and 210% (p < 0·01) with candoxatril 200 mg and 400 mg respectively. With frusemide, concentrations decreased by 40% (p < 0·05). There was a significant increase of 329% in plasma renin activity with frusemide but no significant change with candoxatril. At four hours after dosing mean pulmonary wedge pressure decreased by 41% from 13·1 to 7·7 mm Hg (p < 0·05) and by 45% from 15·5 to 8·5 mm Hg (p < 0·05) after candoxatril 200 mg and 400 mg respectively. With frusemide there was a smaller decrease of 15% from 11·5 to 9·8 mm Hg (p < 0·05). Similar changes were noted for right atrial pressure recordings. This reduction was sustained by candoxatril at six hours but became attenuated after four hours with frusemide. Mean arterial pressure fell by 10·5 mm Hg (p < 0·05), 13·3 mm Hg (p < 0·01), and 3·7 mm Hg (NS) with candoxatril 200 mg, candoxatril 400 mg, and frusemide respectively. No significant changes in heart rate or cardiac output were noted. After dosing urine volume increased by 376%, 201%, and 498% over the first three hours and by 337%, 151%, and 270% over the next three hour period for candoxatril 200 mg, candoxatril 400 mg, and frusemide respectively. Sodium excretion was similarly increased by 213%, 236%, and 367% for the first three hour period and by 222%, 233%, and 214% for the second three hours respectively.

Both candoxatril and frusemide lower filling pressures and induce a natriuresis. Candoxatril in contrast to frusemide is not associated with adverse neuroendocrine effects and its haemodynamic effects are more prolonged. Therefore, neutral endopeptidase inhibitors may have advantages over standard diuretic treatment in left ventricular dysfunction.

Decreased overall sympathetic activity during inhibition of angiotensin converting enzyme in patients with chronic heart failure

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Angiotensin converting enzyme inhibitors improve symptoms and survival in chronic heart failure, some of which benefit may be due to improved autonomic balance. We used whole body titiated noradrenaline (NA) kinetics to evaluate the short (48 hours) and medium term (six weeks) effects of angiotensin converting enzyme inhibition with ramipril on overall sympathetic activity in 21 patients with chronic heart failure (aged 68 (3) years) stabilised by diuretic treatment (69 (6) mg frusemide). At each visit radiotracer NA kinetics (assessed in arterial plasma) were measured at rest and at the same level of supine bicycle exercise. In eight patients given placebo no changes in NA kinetics occurred over the six week treatment period (whole body NA spillover at rest 240 (32), 251 (34), and 230 (18) ng/min/m² at baseline and after two and 42 days treatment respectively; NS; NA spillover during submaximal exercise 561 (65), 584 (187), and 619 (96) ng/min/m² respectively, NS. Pretreatment values were, however, lower than those in the 13 patients who received ramipril 5–10 mg daily. In the ramipril treated patients there was a decline with treatment in resting and exercise arterial plasma NA concentration (339 (29), 315 (37), and 303 (35) pg/ml at the three time points at rest, p < 0·05; 681 (48), 557 (64), and 562 (84) respectively during exercise, p < 0·05) and in whole body NA spillover to arterial plasma, both at rest (385 (39), 354 (43), and 312 (32) ng/min/m², p < 0·05) and during submaximal exercise (733 (46), 728 (114), and 612 (81) ng/min/m², p < 0·05). This decline was more pronounced at six weeks than at 48 hours. Whole body NA clearance did not change during the treatment period in either group.

Angiotensin converting enzyme inhibition with ramipril in patients with chronic heart failure is associated with a decline in overall sympathetic tone. This effect is more prominent at six weeks than at 48 hours, which may be relevant to the delayed clinical benefit of angiotensin converting enzyme inhibition.

Is routine withdrawal of digoxin necessary before elective cardioversion?

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Digoxin treatment is often withheld before direct current (DC) cardioversion because of the risk of ventricular arrhythmias. To test the necessity for this we randomly allocated 35 patients admitted for DC cardioversion for atrial fibrillation (AF) either to continue taking digoxin (group 1) or to stop treatment for 48 hours (group 2). All patients had continuous electrocardiographic monitoring from one hour before cardioversion until two hours after. Four patients were also taking amiodarone 200 mg once
daily, two in group 1 and two in group 2. There were 17 patients in group 1 and 18 in group 2. Mean heart rate was similar before cardioversion (97 beats/min in group 1 v 95 beats/min in group 2) and after (83 ± 85 beats/min), and there was no difference between potassium concentrations in the two groups (4.36 ± 4.17 mmol/l). Overall success for conversion to sinus rhythm was 60% and 65% in group 1 and 56% in group 2. In group 1 mean digoxin concentration was 1.79 nmol/l (range 1.0–5.4 nmol/l) and in group 2 0.34 nmol/l (0.1–0.5 nmol/l), which was significantly different from the value in group 1 (p < 0.001). There were no sustained ventricular arrhythmias in either group. The mean number of ventricular ectopics in group 1 before DC shock was 80 (0–595) and after was 50 (0–346). The number of ventricular ectopics did not significantly differ in group 2 (50 (0–156) before cardioversion and 77 (0–480) after). There was no correlation between the number of ventricular ectopics and serum digoxin concentrations. These findings show that withdrawal of digoxin does not influence ventricular ectopy during elective cardioversion and may be unnecessary.

Coronary angiography in Glasgow: relation to coronary heart disease and social class

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Standardised mortality ratio (SMR) for coronary heart disease correlates highly with social deprivation score (SDS). We examined their influence on coronary angiography rates in 1986 and 1987 in Greater Glasgow Health Board residents aged 35–64. SDS for each patient was derived from SCOTDEP scores (range 1 to 7—low to high SDS) from area postal codes. Coronary angiography rates were obtained from OPMS 3 code 306.9. SMRs in men were 52, 72, 88, 107, 120, 133, and 128 for SDS 1–7 respectively. Mean angiography rate a year and number performed a year were 4.5 per 1000 and 692. When adjusted for the different SMR, used as the criterion of need for angiography, predicted rates were 2.3, 3.2, 3.9, 4.8, 5.3, 5.9, and 5.7 per 1000 for SDS 1–7 respectively. Observed rates were 3.6, 4.5, 4.7, 4.5, 5.2, 5.1, and 4.1 per 1000 for SDS 1–7 (excess 33, deficit 46 angiograms a year (15% and 72% of predicted) for comparable sized SDS 1 v 7). SMRs in women were 38, 65, 73, 102, 96, 141, and 144 for SDS 1–7 respectively. Mean angiography rate a year and number performed a year were 1.65 per 1000 and 390. When adjusted for the different SMR, predicted rates per 1000 were 0.9, 1.5, 1.7, 2.3, 2.2, 2.3, and 3.3 for SDS 1–7 respectively. Observed rates were 1.7, 1.4, 1.2, 2.2, 2.4, 2.3, 3.0, and 2.7 for SDS 1–7 respectively (excess 24, deficit 18 angiograms a year (200% and 83% of predicted) for SDS 1 v 7). These data show a relative excess of referral for coronary angiography, particularly in women, in patients from areas of low social deprivation. This was not apparent from crude angiography rates. If, as seems likely, these rates approach the ideal then this suggests a significant need is not being met in patients from areas of high social deprivation.

Admission to hospital with suspected myocardial infarction, 1973–89: from the Nottingham heart attack register

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The Nottingham heart attack register was established in 1973 to monitor admissions to the Nottingham hospitals for suspected myocardial infarction. Analysis of over 20000 admissions and the cases of over 8000 people who were declared dead on arrival was undertaken to identify trends in patient behaviour, involvement of the general practitioner and ambulance service before admission, management in hospital, and outcome. There was a fivefold increase in admissions, exceeding 4000 per year in 1989. The median delay from symptom onset to arrival in hospital decreased from over four hours to under three. A general practitioner was called to over 60% of those admitted. Nottingham ambulances conveyed an increasing proportion of an ever increasing number of patients, reaching 85% of all admissions by 1989; the number of 999 calls almost doubled. The number of men admitted always exceeded the number of women admitted, and men (particularly younger men) were always more likely to be admitted to a coronary care unit (CCU); by 1989 these differences were slight. Three quarters of patients with a confirmed myocardial infarction were treated initially in a CCU. Acute myocardial infarction was diagnosed on discharge in a quarter of admissions, a third having a possible myocardial infarction. Mortality declined generally from 18% to 10%, but men always fared better than women and those under 65 better than those over 65. CCU mortality fell from 18% to 10%, ward mortality fell from 27% to 10%, and myocardial infarction mortality was constant at 20%. Drug prescribing changed markedly. In 1973, 30% of patients received either digoxin or an antiarrhythmic drug, but only 10% by 1989; diuretic use was constant at about 45% and β blockers and anticoagulants were prescribed more frequently, in over a quarter by 1989. Temporary pacing, inotropic drugs, and intravenous vasodilator drugs were used infrequently.

Blood selenium state of controls and patients with ischaemic heart disease and of healthy volunteers in Ayrshire and a survey of dietary selenium

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There is evidence that the atherogenic process is initiated by the free radical lipid peroxidation of low density lipoprotein and that this process can be inhibited by antioxidants—for example, vitamins A, C, and E. A strong inverse relation has been shown between mortality from ischaemic heart disease and plasma vitamin E concentrations (WHO/MONICA). Selenium, through its presence in the structure of the antioxidant enzyme glutathione peroxidase, is also involved in the damage limitation pro-
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However, this may not have been entirely comparable. The mean whole blood glutathione peroxidase activity for the 354 patients in 1985 was 8-16 U/ml and was highly significantly (p < 0.001) lower in patients with ischaemic heart disease (6-54 (0.41)) than in controls (9.57 (0.43)). In 1988 the mean activity was 6-08 (0.065) U/ml and was inversely correlated with white bread consumption and directly with wholemeal bread but not with oily fish consumption. Significant relations were also found with social class, age, and place of residence but not with a history of angina or previous heart attack. The numbers in these latter categories were low, however. Dietary selenium has declined from 43 μg/day in 1985 to around 30 μg/day in 1990 because of decreased use of imported Canadian wheat flour in bread making. The proportion of dietary selenium provided by cereals has fallen from 47% to 24%. The lower mean glutathione peroxidase activity recorded in 1988 is consistent with the decrease in dietary selenium since the previous survey in 1985. The two populations, however, may not have been entirely comparable.

Analysis of heart disease mortality data: inference on causality and prospects for primary prevention

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An important consideration in support of causality of association in epidemiological studies is specificity of the association between the putative “risk marker” and the disease under study. Nevertheless, many studies, both observational and experimental, investigate mortality from a single disease without comparison with a control disease or with “all causes.” Reappraisal of methods of analysing mortality data and of presenting the results of analysis as (age standardised) proportions of all cause mortality creates case-control comparisons and helps to distinguish between more deaths and younger deaths, thereby overcoming an important limitation of the familiar standardised mortality ratio (SMR). Results of these analyses show that cigarette smoking, an important risk marker for heart disease, is not associated with more deaths from heart disease but rather with younger death from a number of causes (including heart disease). The lifetime risk of heart disease death is inversely associated with smoking: never 35%, light 34%, medium 32%, heavy 29%.

On present evidence and for the foreseeable future heart disease is not preventable: the later stages (severe disabling disease) and the final manifestation (death) may be postponable, which is not the same thing. These findings have implications both for preventive medicine and for health care planning.

Epidemiology of heart valve surgery in Ireland, 1956–85: a 30 year perspective

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Because of its small size Ireland affords a unique opportunity for population based research. From the mid-1960s to 1985 virtually all adult heart valve surgery was performed in one centre. The operative records for this centre and all the other available operative records for the country were reviewed. Data were entered on precoded data sheets, stored on an Amdahl 5860 mainframe computer, and analysed with the statistics analysis system (SAS) package. With triennial national census data, procedure rates per 100 000 of the population were calculated. The total number of operations increased from 27 in 1956 to 201 in 1979 and thereafter levelled off at a mean of 196 operations a year. The five year procedure rate per 100 000 population was 6-9 in 1956–60 and increased to 28-9 in 1980–5. The procedure rate for mitral valvotomies peaked at 18.5 in 1961–5 and fell to 2.5 in 1981–5. The mitral valve replacement rate increased from 0-2 in 1961–5 to a peak of 9-7 in 1976–80 and fell to 8-8 in 1981–5. The aortic valve replacement rate increased during each successive five year period, from 0-1 in 1961–5 to 17-6 in 1981–5. The double valve replacement rate remained approximately 30 for the three five year periods from 1971 to 1985. The aetiology of the disease in patients undergoing valve surgery changed dramatically; 68% had rheumatic valve disease in 1976 v 30% in 1985 and 10% had degenerative disease in 1976 v 40% in 1985. A progressive increase in mean age was observed also.

This review provides a unique national perspective on the trends in valve surgery over 30 years and affords an opportunity for rational health planning for the future.

Failure of provision of antibiotic prophylaxis for at risk cardiac patients

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Patients at risk of infective endocarditis may not be aware of the need for antibiotic prophylaxis and not receive appropriate advice or treatment. Questionnaires were sent to general practitioners and dentists and 189 at risk patients (aged 12–92 years, mean 62). Only 46% of patients recalled any advice about prophylaxis and 26% recalled written advice. Thirty per cent remembered receiving repeated advice. Only 21% could accurately recall specific instructions for prophylaxis. Half the patients attended a dentist, but only 12% had done so within one year and 39% and not attended in five years. Half told their dentist about their heart condition, 40% of these brought a doctor’s note, and only 44% of all patients recalled receiving antibiotics before treatment. General practitioners’ replies (262/480; 55% in 200 practices) indicated that 97% gave antibiotic advice but only 3% in writing. Only 50% took a dental history. Dentists’ replies (72/240; 30% in 120 practices) indicated that 94% identified at risk patients on their registries. Only 14% of general practitioners identified such cases, but 75% could adapt their register to do so. Most dentists (96%) and 57% of general practitioners would prescribe antibiotics recommended by the British Society for Antimicrobial Chemotherapy. Only half of the general practitioners and dentists thought that they received adequate advice from their cardiac centre. Up to half of the general practitioners and dentists did not know all of the cardiac conditions requiring prophylaxis.

This study shows important failures in dental care and provision of antibiotic prophylaxis for at risk patients. Improved communications are needed to address these problems.
Early experience with directional coronary atherectomy

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We assessed the safety and efficacy of the Simpson atherectomy catheter in 11 patients with eccentric lesions in a major coronary artery. Atherectomy was attempted in seven left anterior descending (LAD) vessels (seven lesions), one LAD graft, and three right coronary (RCA) vessels (four lesions). Two patients had angioplasty of other lesions. All patients were fully heparinised during the procedure and for 24 hours afterwards. A guiding catheter of 9-5 (RCA) or 11 (LAD) French gauge was introduced into the target vessel and the lesion was crossed with a 0-014 inch high torque floppy wire. The primary success rate (stenosis reduced to < 50%) was 10/12 (83%). However, three of these vessels (all LAD) became occluded after 10 minutes (reopened by angioplasty), 24 hours (reopened by angioplasty with small enzyme activity increase), and 5 days (patient received internal mammary graft six weeks later) with no long term sequelae for the patients, who are now symptom free. The remaining six patients were followed up for a total of 25 months. Five remain well while one returned after six months with symptomatic restenosis at the atherectomy site, which was successfully treated by angioplasty. An average of 7-8 (range 4–12) cuts produced 3-8 (range 1–8) tissue pieces per patient. The number of tissue pieces and residual stenosis was not related (r = 0.3), suggesting that the mechanical displacement of atheroma (Dotter effect) is important in obtaining a good result. Individual histological features were present with varying frequency: fibrous tissue (100%), smooth muscle proliferation (50%), haemosiderin (30%), calcification (20%), cholesterol (20%), thrombus (20%), internal elastic lamina and part of media (10%). Two patients suffered complications, one left main stem dissection requiring non-emergency bypass grafting and one femoral artery occlusion.

The Simpson atherectomy catheter is a safe and practical form of treatment for discrete (< 10 mm long) eccentric coronary artery lesions.

Excimer laser coronary angioplasty: initial experience in the United Kingdom

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Since February 1990 the 200+ dymer (Advanced Interventional Systems) excimer laser has been used to treat 58 patients in 63 procedures (52 in men, 11 in women; mean age 55-4 years, range 32–78). Thirty procedures (48%) were high risk (one or more of (a) left ventricular ejection fraction (LVEF) 35%; (b) triple vessel coronary artery disease; (c) unstable angina; (d) need to treat a stenosis in the sole remaining coronary conduit). Nineteen procedures (31%) were in patients with present or recent unstable angina, 23 (37%) in patients turned down for (further) coronary surgery. LVEF averaged 55% (range 27% to 78%). There was a high incidence of previous myocardial infarction (43%), previous bypass graft surgery (CABG) (37%), previous balloon angioplasty (PTCA) (32%). Fifteen laser treated lesions in 11 patients were restenoses after PTCA and seven lesions in five patients required repeat excimer laser coronary angioplasty (ELCA) or PTCA, or both, for restenosis after ELCA. Of the 112 lesions available for treatment, 29% were short (< 5 mm long), 49% were intermediate (5–15 mm long), and 22% long (> 15 mm long). Fifty seven lesions were treated by ELCA alone (reducing mean per cent stenosis from 74 (SD 13-2) to 24 (10-5)), 37 by ELCA and PTCA (stenosis reduced from 82 (12-4) to 23 (20-7)), and 16 by PTCA alone (stenosis reduced from 72 (11-5) to 15-3 (13-4)). In this high risk group of patients there were three procedure related deaths (one ELCA related, 10 hours after the procedure, and two PTCA related, one 72 hours after the procedure and the other during the procedure); one late death 10 weeks after the procedure; two acute thrombotic closures due to inadequate early heparin dose; three extensive and six minor dissections; one perforation; five spasm; two late small coronary artery aneurysms; two myocardial infarction (one ELCA and one PTCA related); two distal coronary emboli. No patient required emergency coronary artery bypass grafting.

Long term follow up of self expanding stents

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Coronary artery stents were developed to treat abrupt vessel closure during coronary angioplasty (PTCA) and to control restenosis. Between 1986 and 1989, 132 patients underwent stent implantation with 171 self expanding mesh stents. Stent implantation into native coronary vessels was undertaken as a primary procedure to treat acute myocardial ischaemia in 29 patients (after PTCA in 24 and unstable angina in five) with 34 stents. Elective stent insertion for native vessel restenosis was performed with 71 stents in 61 patients, and 66 stents were deployed electively in saphenous vein coronary bypass graft (CABG) stenosis in 42 patients. The postimplantation course during a follow up period of 1 to 34 (mean 17) months was uncomplicated in 101 (76.5%) patients. Thrombotic stent occlusion before discharge occurred in eight (6.1%) patients and was treated conservatively in two, by PTCA in four, and by CABG in three (after unsuccessful PTCA in one case). Surgical repair of the femoral artery was required in eight patients (6.1%) because of persistent bleeding in the presence of anticoagulant treatment. Among the group who underwent urgent stent implantation, restenosis requiring repeat PTCA occurred in one (4%) patient and an additional four patients (13%) required further intervention (PTCA or GABG) for other disease. After elective stent implantation into native vessels symptomatic restenosis occurred in four (6.6%) patients and intervention for different disease was required in a further four (6.6%). After stent implantation into coronary artery bypass grafts restenosis occurred in three (7%) and an additional six (14.3%) patients underwent repeat intervention for different lesions. There were nine deaths (mortality 6.8%) during follow up, three in each group. Management of anticoagulation after stent implantation may be difficult but the PTCA restenosis rate is reduced considerably, and this may be the procedure of choice for the management of CABG stenosis.
Combined coronary angioplasty and ultrasound imaging catheter: initial in vivo studies in humans

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Intravascular ultrasound allows direct visualisation and characterisation of the arterial wall and measurement of luminal cross sectional area and wall thickness. This has particular potential for coronary angioplasty procedures. We have tested a new combined coronary angioplasty and ultrasound imaging catheter (Endosonics) which allows immediate assessment of the vessel wall during and after balloon angioplasty. It consists of a 2-5 or 3.0 mm percutaneous transluminal coronary angioplasty balloon with an integral synthetic aperture transducer. The balloon profile is 0.044 inch and the transducer profile 0.072 inch. It uses a standard 0.014 inch guide wire. This combined catheter was used to perform coronary angioplasty in 10 patients. Trackability and movement over the wire within the coronary vessels was good. Pushability against the lesions was similar to that of a standard balloon catheter. In one patient we were unable to cross the lesion because of the high balloon profile. Satisfactory images were obtained in eight patients providing information on the vessel wall and luminal diameter. Ultrasound imaging influenced our management in two out of the eight cases. In one a significant stenosis was present that was not convincingly shown on angiography. In another there was a significant residual stenosis on ultrasonography requiring redilatation with a larger balloon resulting in definite improvement on ultrasound despite what appeared to be a good initial angiographic result. In two patients no images were obtained, in one for unknown reasons and in one because persistent manipulation of the catheter in attempting to cross the lesion led to loss of the signal.

We conclude that this combined catheter assists in the performance of percutaneous transluminal coronary angioplasty and may allow characterisation of the vessel wall not achievable with standard angiography. In some cases, however, image quality was hampered by the presence of air bubbles trapped in the balloon. Future technical developments should include lower balloon and transducer profiles and improved balloon venting mechanisms to allow optimal image quality.

Can ω 3 fatty acids reduce percutaneous transluminal coronary angioplasty restenosis rate?

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Restenosis of a coronary artery diluted by coronary angioplasty (PTCA) occurs in up to 40% of lesions. We investigated whether ω 3 fatty acids (Maxepa) administered 1–2 days before and for six months after angioplasty could reduce this restenosis rate. A total of 120 consecutive patients who underwent PTCA to one or more stenoses were randomly assigned to standard treatment plus 1 g eicosapentaenoic and 1 g docosa-hexaenoic acid daily (group A, n = 60) or to standard treatment alone (group B, n = 60). There was no statistical difference between groups in baseline characteristics. Quantitative angiography at a mean 31–4 weeks after angioplasty occurred in all patients in group A but in only 53 in group B. Primary angiographic success was defined as a lesion of >50% diameter stenosis reduced to half of the initial diameter stenosis and restenosis as a loss of >50% of initial angiographic improvement in those lesions with a primary success. In group A 106 lesions were dilated, with angiographic success in 79. Restenosis occurred in 27-8% of these. In group B 96 lesions were dilated, but only 87 had angiographic follow up. Angiographic success occurred in 60, of which 28.3% restenosed (NS; group A v B). There was no significant difference between group A and group B in the mean diameter stenosis before and immediately after angioplasty or at follow up angiography. Twenty seven patients required a further revascularisation procedure in the year after angioplasty (22 v 15, A v B). Return of anginal symptoms during the six months after angioplasty occurred in 51.7% of group A and 55% of group B (NS).

In conclusion, administration of capsules containing ω 3 fatty acids in the quantity used 1–2 days before angioplasty and continued for six months conferred no benefit in restenosis rate, recurrence of symptoms, or need for a further revascularisation procedure.

Restenosis after coronary angioplasty: role of preangioplasty stenosis morphology

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To assess the role of precoronary angioplasty (PTCA) stenosis morphology on restenosis, 41 patients (47 stenoses) who underwent repeat angiography ≥3 months (mean 11 (1-5)) after PTCA were studied. Coronary stenosis diameter, area, symmetry, and morphology were assessed by computed quantitative coronary angiography before and immediately after PTCA and on follow up angiography. Before PTCA 18 stenoses were concentric (symmetric narrowings with smooth borders), 12 eccentric (asymmetric narrowings with smooth borders), and 17 irregular (three or more serial severe, closely spaced obstructions in a coronary artery) or type II eccentric (asymmetric narrowings with scalloped or multiple irregular borders). Restenosis occurred in 18 lesions: two (11%) concentric, four (33%) eccentric and 12 (70%) irregular or type II (p < 0.05), while 29 lesions remained unchanged. Stenosis diameter, area, and symmetry before and immediately after PTCA were similar in the 18 patients with and the 23 patients without restenosis. The follow up angiogram showed that 11 (61%) stenoses in the restenosis group and 18 (63%) in the non-restenosis group had similar morphology to that before PTCA. Restenosis occurred in seven (30%) patients with chronic stable angina in and in 11 (61%) with unstable angina (p < 0.05). In patients with stable angina one (8%) concentric stenosis, two (25%) eccentric stenoses, and four (80%) irregular lesions restenosed. In patients with unstable angina one (25%) concentric, two (50%) eccentric, and eight (66%) irregular lesions restenosed.

Stenoses that were irregular before PTCA tended to adopt an irregular morphology if they recurred, whereas concentric stenoses rarely recurred. These findings indicate that irregular and type II eccentric stenoses are associated with a higher risk of restenosis than are concentric stenoses. In most cases the morphology of a restenosed lesion is similar to that observed before PTCA.
Cardiac manifestations of Marfan’s syndrome: improved evaluation with transoesophageal echocardiography

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Aortic root pathology is common in Marfan’s syndrome but is not well visualised by conventional transthoracic echocardiography. Transoesophageal echocardiography (TOE) can provide high resolution imaging of the heart and great vessels and may be valuable for the diagnosis of aortic dissection in such patients. We performed TOE in 14 patients (aged 19–56 years) known to have Marfan’s syndrome. Eight patients had suspected aortic dissection, four had inadequate results from transthoracic studies, and two patients had endocarditis postoperatively, one after aortic root and valve replacement and one after mechanical mitral valve replacement for myxomatous valve degeneration. Excellent visualisation was obtained in all patients with TOE. Aortic dissection was shown in seven patients (type I dissection in six, chronic type III dissection in one). In all seven patients the extent of the dissection, entry and exit points, true and false lumen, and the presence of aortic regurgitation or pericardial effusion, or both, were identified in addition to diagnostic confirmation. The TOE findings of aortic dissection were confirmed at surgery in five patients, at necropsy in one patient, and on computed tomography in the patient with type III dissection. In the four patients with inadequate results from transthoracic echocardiographic studies TOE allowed assessment of aortic root dimensions, the presence of mitral valve prolapse, and aortic regurgitation. The patient with endocarditis after root replacement had an aortic root fistula shown on TOE, with flow identified between the layers of the Dacron wrap and the native aortic root. The remaining patient with suspected endocarditis on a mechanical mitral valve replacement had vegetation shown at TOE which had not been seen on transthoracic imaging. In both patients the TOE findings were confirmed at the time of surgery.

TOE can provide important and rapid diagnostic information in patients with Marfan’s syndrome and has altered the approach to diagnosis and follow up in such patients.

Biplane transoesophageal echocardiography: valuable new diagnostic information or simply more of the same?

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With the introduction of a second ultrasound array scanning in the longitudinal plane, the morphological and functional information which may be obtained during a transoesophageal (TOE) study is potentially increased. To determine what, if any, new diagnostic insights might be obtained by this addition, we carried out a prospective study to compare and contrast the findings obtained by an initial transverse plane study with (a) information from a subsequent longitudinal plane study alone and (b) information derived by integrating both imaging planes. All patients had confirmation of the biplane TOE findings at either catheterisation or surgical inspection, or both. Sixty one patients were included in the study (age range 9–78 years). Referral diagnoses included suspected mitral prosthetic dysfunction (17), mitral stenosis (four), mitral regurgitation (all being considered for valve repair) (seven), acute infarct complications (four), atrial septal defects (nine), complex congenital heart disease (11), aortic coarctation (three), aortic dissection (three), and suspected endocarditis (three). When the information derived from each plane was compared with the definitive diagnosis (integrated biplane TOE and correlative catheterisation or operative findings, or both) complete diagnostic information was derived from the transverse plane alone in only 78% of patients and from the longitudinal plane alone in only 65%. Clinically important new (21%) or additional (36%) morphological information was obtained from long axis scanning in 37/61 patients. Morphology better studied by long axis scanning included native mitral and tricuspid valve leaflet and subvalve morphology (17/28); anterior and posterior sites of mitral paravalvar leakage (8/17); lesions of the apex, posterior, and anterior walls of the left ventricle (3/3); defects in the anteroinferior atrial septum (4/9); the right ventricular outflow (61/61); proximal left pulmonary artery (40/61); and ascending aorta (1/3). The maximal diagnostic accuracy value biplane TOE was obtained only when morphological and haemodynamic information obtained from both imaging planes was integrated. This gave a diagnostic accuracy of 98% for biplane TOE v 86% for cardiac catheterisation in the 39 patients who had subsequent detailed surgical description.

Transoesophageal echocardiography in patients with focal cerebral ischaemic events: glamorous toy or clinically useful tool?

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The detection rate of cardiac sources of emboli (SOE) with precordial echocardiography (PE) in patients with focal ischaemic cerebral events is low. To investigate the role of transoesophageal echocardiography (TOE) 131 consecutive patients with such events were studied with both PE and TOE contrast studies. TOE detected 18 potential right to left (R-to-L) shunts and two cases of valve vegetations not detected by PE, and spontaneous contrast echoes (SCEs) were found in 27 out of 28 patients with a large left atrium—three with left atrial thrombus. A clinical cardiac abnormality had been found in 53 patients; mitral valve prolapse (MVP) was confirmed in four; 25 patients with chronic atrial arrhythmias had a large left atrium (24 with SCEs, three with left atrial thrombus); valve disease was confirmed in 14; and 10 had potential R-to-L shunts. Seventy eight patients had no clinical cardiac abnormality: six had MVP, 17 had potential R-to-L shunts, and one had a left ventricular regional wall motion abnormality. TOE is thus more sensitive than PE for the detection of potential SOE in these patients. However, except for the detection of a R-to-L shunt, the yield in patients with no clinical cardiac abnormality is low. Moreover, the abnormalities detected in those with overt cardiac disease merely confirm the clinical diagnosis. Patients with left atrial spontaneous contrast echoes may benefit from anticoagulation but this requires further study. Until more data are available on this feature and the role of R-to-L shunts in this population, the role of echocardiography (precordial or transoesophageal) remains limited.
Transoesophageal versus transthoracic echocardiography in assessment of systemic and pulmonary venous connections

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To determine the diagnostic accuracy of transoesophageal echocardiographic (TOE) and transthoracic (TTE) studies in the definition of either systemic or pulmonary venous connections, 86 unoperated children (aged 0-2-14.8 years, mean 3.8 years) with congenital heart disease were prospectively studied by both techniques. The results obtained were correlated with one another, subsequent surgical inspection (n = 53), which served as the gold standard, and cardiac catheterisation (n = 78). Normal systemic and pulmonary venous connections were defined by TOE in 72 of the 86 patients and all were confirmed by surgical inspection or cardiac catheterisation, or both. Systemic venous connections could be defined by TOE in all. The drainage of all four pulmonary veins could be documented by TOE in 92% of all children studied. Nineteen anomalous venous connections were documented by TOE in 14 patients. These were confirmed in all but one child who awaits surgical correction. In contrast, TOE allowed the definition of only eight of these 19 anomalous venous connections (42%). Partial anomalous pulmonary venous connections were documented by TOE in six out of six patients, by TTE in only two out of six. In one patient in whom TTE suggested total anomalous pulmonary venous drainage the TOE study defined a mixed pattern of drainage, which was confirmed at surgery. Anomalies of the superior caval vein system were documented by TOE in nine patients, whereas these were identified in only three by TTE. Anomalies of the inferior caval vein (three patients) were equally well identified by either technique. When compared with angiocardiography TEE provided additional valuable morphological information on the venous connections relative to the atrial septum in complex congenital heart disease. None of the patients in whom TOE showed normal venous connections was found either by surgical inspection or cardiac catheterisation to have anomalous venous connections.

TOE is a highly sensitive and most versatile tool in the preoperative definition of systemic and pulmonary venous connections. In this series it was largely superior to TTE and of additional value to cardiac catheterisation and angiocardiography.

Can intravascular ultrasonography affect the outcome of vascular procedures?

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Recent interventional techniques demand greater operational feedback, beyond the limits of conventional imaging systems. We assessed intravascular ultrasonography (IVUS) in five coronary and 18 peripheral arteries (23 patients) during varying combinations of laser and balloon angioplasty (PTCA, n = 21), atherectomy (n = 6), and endovascular stent implants (n = 8). IVUS was performed with a rotating 20 MHz probe. This was compared with angiography (all cases) and angiography (five cases). Dis- eased normal arteries and stents were well defined with IVUS in 21 out of 23 patients (two failures: one mechanical, one poor access). Wall morphology, plaque mapping (eccentric v concentric), and tissue characterisation was possible in all 21 cases. On line measurements allowed luminal cross sectional area, diameter, and percentage stenosis calculations in 20 cases. The immediate effect of vascular manipulations was evident in all. Successful PTCA was associated with significant wall disruption (plaque rupture, splitting of intima or media) in 12 out of 15 cases. In atherectomies IVUS was very useful in showing the extent of debulking, wall thinning, residual disease, and the relative lack of wall disruption compared with PTCA. Likewise, IVUS showed stent deployment and expansion in eight out of eight cases v six out of eight with angiography. Online data were valuable in selecting the most appropriate mode of treatment and the balloon or stent size and in assessing the therapeutic outcome, complications, and extent of residual disease not apparent on angiography or angiography.

Morphological assessment of pulmonary vascular disease by intra-arterial ultrasonography

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Intra-arterial ultrasonography allows direct and accurate visualisation of vessel wall morphology. To evaluate its potential role in pulmonary vascular disease we studied eight patients (age range 7-59 years) undergoing routine diagnostic right and left heart catheterisation. Cardiac pathologies were dilated cardiomyopathy (two patients), ventricular septal defect (two), atrial septal defect (one), primary pulmonary hypertension (one), multiple pulmonary emboli (one), and mitral stenosis (one). Real time, cross sectional images of the pulmonary artery (PA) and its branches were obtained with a 20 MHz ultrasound transducer rotating in a 100 cm long, 2 mm in diameter sterile sheath which was advanced into the pulmonary artery under fluoroscopic guidance. Seven out of eight studies were successfully completed; in one patient the right heart was very dilated and adequate positioning of the transducer was not possible. Normal arterial, cross sectional morphology was seen in three patients, two with normal PA pressures and one whose mean PA pressure was 60% of mean systemic arterial pressure because of atrial septal defect. In three patients with systemic level PA pressures owing to ventricular septal defect (two) and primary pulmonary hypertension (one) thickening of the intimal and medial layers and areas of intimal proliferation were seen. In the patient with multiple pulmonary emboli, intravascular, mural thrombus was detected at several sites.

Intra-arterial ultrasonography can differentiate normal from abnormal pulmonary arterial wall morphology in patients with and without pulmonary hypertension. It may thus become an important investigation in the diagnosis and assessment of pulmonary vascular disease.