ANNUAL MEETING OF THE BRITISH CARDIAC SOCIETY

Riviera Centre, Torquay, South Devon
17, 18 and 19 May 1994

PROGRAMME AND ABSTRACTS OF PAPERS

The Meeting will be held in the Forum, the Arena, the Grace Murrell, the Burdett and the Grosvenor Hotel. All Plenary Sessions and formal lectures will take place in the Forum.

Posters will be on display (Tuesday 17, Wednesday 18 and Thursday 19) in the Exhibition Hall and authors will be in attendance.

Catering facilities will be in the Exhibition Hall.

There is a plan of the Riviera Centre on the inside back cover of this programme.

The Society thanks Bayer UK for the conference bags.

The contact phone number during the conference is 0803 299992.

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<table>
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<th>BRITISH CARDIAC SOCIETY</th>
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<td><strong>OFFICERS:</strong></td>
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<td>Mr D J Parker</td>
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<td>Dr R Balcon</td>
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<td>Prof R W F Campbell</td>
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<td>Dr D S Dymond</td>
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<td>Dr J C F Cleland</td>
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<td>Honorary Secretary</td>
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<td>Assistant Secretary</td>
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The British Cardiac Society
9 Fitzroy Square, London
W1P 5AH

Telephone: 071-383 3887
Fax: 071-388 0903
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H Swanton
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H D Tunstall-Pedoe

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D Ward
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R West
D J Wheatley
R G Wilcox
T Williams
D Wood
D Yellow

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### ANNUAL MEETING AT TORQUAY 17–19 MAY 1994: PROGRAMME

**Tuesday 17 May**

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<td>8.25</td>
<td>Welcome by the President</td>
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<td>8.30 – 10.00</td>
<td>Plenary Session</td>
<td>Perspektive in intravascular and transesophageal ultrasound</td>
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<tr>
<td>Speakers: Dr P Kearney (Edinburgh), Dr Carlo Di Mario (Rotterdam), Dr Sanjiv Kaul (USA), Dr George R Sutherland (Edinburgh). Chairmen: Dr A G Fraser and Mr M Monaghan</td>
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<td>10.00 – 11.15</td>
<td>Coffee</td>
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<td>Rosetor</td>
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<td>Papers 126–131 Paediatric Cardiology II</td>
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**Thursday 19 May**

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<tr>
<td>8.00 – 9.30</td>
<td>Plenary Session</td>
<td>The Management of acute myocardial infarction: Short and long term considerations</td>
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<td>10.30 – 12.00</td>
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<tr>
<td>10.00</td>
<td>Bradycardia Seminar</td>
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<td>Defibrillator Seminar</td>
<td>Grace Murrell</td>
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<td>11.15</td>
<td>Coronary revascular surgery – Who needs it?</td>
<td>Dr Iain Todd (Edinburgh)</td>
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<td>12.00 – 13.30</td>
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<td>Cardiac Technicians’ Committee Meeting</td>
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<td>Intervention Cardiology II</td>
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| 8.30-10.00 | **Forum**  
Plenary Session  
Perspectives in intravascular and transesophageal echocardiography  
(chairmen: Dr A G Fraser and Mr M Monaghan)  
1 Intravascular ultrasound imaging – clinical or research tool?  
Dr Peter Kearney (Mainz/Edinburgh)  
2 Intracoronary Doppler – current status and future potential  
Dr Carlo di Mario (Rotterdam)  
3 Intracoronary contrast agents in the evaluation of myocardial perfusion  
Dr Sanjiv Kaul (Charlottesville, USA)  
4 Transesophageal echocardiography – state of the art  
Dr George R Sutherland (Edinburgh) |
| 10.00-11.15 | **Exhibition Hall**  
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St Cyres Lecture  
 Prof Gunter Breithardt  
Management of patients with sustained ventricular tachycardia or previous cardiac arrest – the changing scenario in the 1990s  
(chairman: Dr J Somerville)  
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British Cardiovascular Intervention Society  
Council Meeting |
| 17.30-18.30 | **Grosvenor Hotel**  
British Paediatric Association – Business Meeting |
ENHANCED EXPRESSION OF SMOOTH MUSCLE CELL GAP JUNCTIONS IN THE DEVELOPING Atherosclerotic PLAQUE

J N Severs, J Blackburn, N S Peters, C R Green*. Department of Cardiac Medicine, National Heart & Lung Institute, London and *Department of Anatomy, School of Medicine, University of Auckland, New Zealand.

The pathogenesis of atherosclerosis involves complex interactions between the cells of the arterial wall. One form of interaction — direct intercellular communication via gap junctions — has been implicated in the control of growth and differentiation in many systems. Evidence from recent in vitro studies suggests that increased expression of gap junction proteins in arterial cells is associated with enhanced growth factor production and synthesis of extracellular matrix components. To investigate gap junction expression in the pathogenesis of human atherosclerosis, lesions representing the different stages of the disease were obtained from coronary arteries of hearts removed from patients undergoing cardiac transplantation. Twelve hearts, each providing 1 to 3 segments of coronary artery, were used in the study. Sections were examined by confocal laser scanning microscopy after immunofluorescent labelling with a specific antibody against connexin43 (the major gap-junctional protein of smooth muscle cells) to permit high definition visualisation of immunostained gap junctions through the depth of the specimen. Electron microscopy was conducted in parallel. Fatty streak lesions showed substantially increased expression of immunodetectable connexin43 gap junctions in the intima compared with the levels detected in normal arterial segments. With progression of atherosclerosis through the preatheroma stage to atheroma, a decline in the quantity of immunolabeled junctions was observed, first from the subendothelial layer of the intima, and then from the muscularis layer. Concomitant with this decline, the distribution of the junctions became more patchy, and individual junctions larger. The overall level of gap junction immunostaining nevertheless remained persistently higher at all stages of lesion growth compared with that seen in undiseased specimens. Enhanced expression of gap junctions between smooth muscle cells may play a role in maintaining the synthetic phenotype during growth of the atherosclerotic plaque.

THE EFFECT OF RECOMBINANT GROWTH HORMONE ON CARDIAC STRUCTURE AND FUNCTION IN GROWTH HORMONE-DEFICIENT ADULTS

R Port, JU Weaver*, JP Monson, PG Mills. Departments of Cardiology and P Endocrinology, The Royal London Hospital, London E1 1BB.

The life expectancy of growth hormone (GH) deficient adults is reduced due to cardiovascular disorders. Replacement therapy with recombinant GH (rhGH) is now a therapeutic option. In a double-blind placebo-controlled trial 19 patients with hypopituitarism, on appropriate adrenal, thyroid and gonadal therapy, received 6 months treatment with rhGH. All patients were subsequently treated with rhGH for a further 6 months (open study). Mean age of the patients was 45 yrs (range 20-60 yrs), (BMI 13%) with a > 2 yera duration of GH deficiency. Patients with clinical evidence of cardiac disease, hypertension and diabetes mellitus were excluded. Doppler and 2-D echocardiography were used to assess left ventricular (LV) dimensions, systolic and diastolic function. Exercise tolerance was assessed by treadmill testing using Bruce protocol. Serum IGF-I levels were normalised in all patients. Results are expressed mean +/- SEM and analyzed by Student’s t-test. rhGH treatment did not significantly alter resting HR & BP. Peak exercise tolerance was increased from 9.50+/-0.65 to 11.91+/-0.63 (p<0.001). Maximum cardiac work (peak HR x peak BP) was increased from 29.77+/-1.24 to 38.65+/-1.41 (p<0.01). Fractional shortening was significantly increased from 33.70+/-2.42 to 37.96+/-2.27% (p<0.05). These were however no significant changes in LV dimensions, wall thickness or mitral valve inflow velocities measured. In the placebo group, no changes in exercise tolerance, Doppler or 2-D echocardiographic indices were seen.

This study suggests that treatment with rhGH can improve LV systolic and diastolic function and that the associated improvements in both exercise tolerance and maximum cardiac work.

HYPERTHYROIDISM AND THE CARDIOVASCULAR SYSTEM


To investigate the effects of hyperthyroidism on the cardiovascular system, 10 patients with Graves’ hyperthyroidism (group 1, overt hyperthyroidism) with no history of heart disease were examined. All patients were studied at presentation and at 1 and 2 months during treatment with Carbimazole (CMZ). In addition, 10 subjects who were receiving sufficient thyroxine to suppress thyroid stimulating hormone (TSH) were examined at presentation and at 6 and 12 months (group 2, subclinical hyperthyroidism). Data from groups 1 and 2 were compared with a control group of 20 healthy subjects who were age and sex matched. At presentation, mean serum free thyroxine (4T4) were significantly higher in groups 1 and 2 (both p<0.001) but mean free triiodothyronine (4T3) were not significantly different (both p=0.05). Maximum 24 hour ambulatory blood pressure and pulse monitoring revealed a significantly higher mean 24 hour systolic blood pressure (24hrSBP) in both groups 1 and 2 (24.1±0.14 and 24.1±0.11, respectively, p<0.05). Mean 24 hour diastolic blood pressure (24hrDBP) was higher only in group 1 (24.8±0.97 vs 24.1±0.16, p<0.001). Echocardiography revealed higher mean left ventricular mass index (LVMi) in group 1 (11.91±0.63) and group 2 (11.61±0.63, p=0.02) and group 2 (10.33±0.25, p<0.05) than controls (7.9±0.14, p<0.01). Symptomatic activity assessed by Valsalva manoeuvre, head-up tilt, isometric forearm exercise, cold pressor test and 2-D echocardiography did not differ significantly between the 3 groups. With antithyroid treatment in group 1, mean FT4 and mean FT3 fell significantly after one month (both p<0.001) and again after the second month (both p=0.006) to control levels. Mean 24hrSBP and mean 24hrDBP fell significantly by one month (24.1±0.14 to 11.8±18.11±2.3mgHg in group 1 and 24.1±0.11 to 4.1±2.4mgHg in group 2 with p<0.001) with a further fall by the second month (11.8±15.9 to 9.9±13.9, p<0.05 and 8±11.8 to 7±14.6, p<0.001) to control levels. Mean LVMi did not change significantly after 2 months. Our findings indicate that overt hyperthyroidism increases LVMi, 24hrSBP and 24hrDBP. The latter two can be reversed within 2 months using standard antithyroid treatment but left ventricular mass index remained elevated. Subclinical hyperthyroidism also caused an increase in 24hrSBP and 24hrDBP. In view of these data it is reasonable to suggest that further investigation, further consideration of the cardiovascular risks associated with an increase in 24hrSBP and LV mass is warranted. Although overt hyperthyroidism mimics sympathetic overactivity, our findings suggest that the sympathetic nervous system does not play a major role in its clinical manifestations.

THE PROGNOSTIC IMPORTANCE OF ABNORMAL LIVER FUNCTION TESTS IN CHRONIC HEART FAILURE

P D Batin, M Wickens**, D McEntegart**, L Fullwood, A J Cowley Cardiac Medicine, University Hospital and **Medical Statistics, Boots PLC, Nottingham.

Chronic heart failure (CHF) has a high prevalence and is associated with considerable mortality and morbidity. Previously described prognostic variables involve complicated measures and techniques and are therefore unfeasible in many practitioners. The purpose of this study was to examine the prognostic importance of a number of simple variables which are generally available to most physicians. Five hundred and fifty-two (410 males) patients, mean (SD) age 62 (9) years with CHF (New York Heart Association (NYHA II-IV) were included in the analysis. CHF was secondary to ischaemic heart disease (IHD) in 338, dilated cardiomyopathy in 99, valvular heart disease in 42 and hypertension in 20 patients. Non-laboratory variables (demographic, aetiology of CHF, treatment) and laboratory variables (haematology and biochemistry) were analysed for prediction of survival. The total exposed time until death or censored survival was 1148 years. Two hundred and eighteen (39%) patients died, the median survival time estimated from Kaplan-Meier function was 48 months. Univariate analysis of non-laboratory and laboratory diastolic dose (p<0.0001), NYHA class (p=0.001), age (p=0.001) and male gender (p=0.004) were all predictors of prognosis. Treatment with digoxin had no effect on survival (p=0.85). Laboratory variables with the greatest prognostic value were measures of liver function tests bilirubin (p<0.001), aspartate transaminase (AST) (p=0.004) and plasma urate (p=0.001). Of less prognostic importance were serum sodium (p=0.04), ESR (p=0.03) and plasma urea (p=0.04). Multivariate analysis showed that AST was the most powerful predictor of mortality (X2 17.4, p<0.001), plasma bilirubin (X2 14.9, p=0.001), age (X2 10.9, p=0.002) and serum urate (X2 6.9, p=0.009). This large series of patients with CHF demonstrates the prognostic importance of simple and widely available tests. Abnormalities of liver function tests are strongly predictive of mortality.
PARTIAL EXPRESSION OF THE INSULIN RESISTANCE SYNDROME IN POSTMENOPAUSAL WOMEN WITH SYNDROME X

IF Godlisd, D Crook, B Lees, GMC Rosano, DC Lindsay, DC Lefroy, NS Peters, JC Stevenson. Wynn Institute for Metabolic Research and Department of Cardiac Medicine, National Heart and Lung Institute, London, U.K.

Syndrome X (angina-like chest pain, exercise ECG typical of ischaemia and angiographically normal coronary arteries) is predominantly seen in women and may be accompanied by disturbances in metabolic risk factors for arterial disease, typically including insulin resistance. Whether these disturbances comprise the putative "insulin resistance syndrome" has yet to be established.

Metabolic risk factors were compared between 20 non-obese, post-menopausal, Caucasian women with syndrome X and 20 healthy postmenopausal women, matched for age and weight. Insulin resistance was measured by the minimal model method and body fat distribution by dual energy X-ray absorptiometry.

In the syndrome X group, IVGT insulin and C-peptide areas were 53% (28.1 ± 17.0 pmol/ml · min, p < 0.01) and 36% higher (102.6 ± 75.8 pmol/ml · min, p < 0.05), respectively and insulin sensitivity, S, (inversely related to insulin resistance) was 40% lower (1.83 ± 3.04 min·1 μU·ml-1, p < 0.05) than in the control group. Fasting triglycerides were 44% higher (1.58 ± 1.10 mmol/l, p < 0.05); HDL3 cholesterol was 10% lower (0.95 ± 1.06 mmol/l), p < 0.05), and apoAI was also 10% lower (39.2 ± 43.5 mg/dl, p < 0.05). HDL and LDL cholesterol did not differ between the groups. Women with syndrome X did not differ from controls in blood pressure, body fat distribution or serum uric acid.

Women with syndrome X were insulin resistant but did not exhibit the full range of disturbances characteristic of the insulin resistance syndrome. Insulin resistance appears to be a consistent feature of arterial disease but the extent to which disturbances in other metabolic risk factors are expressed may be more variable than hitherto supposed.

THE INFLUENCE OF COMPETITIVE PULMONARY BLOOD FLOW ON THE BIDIRECTIONAL SUPERIOR CAVOPULMONARY SHUNT: A MULTI-INSTITUTIONAL STUDY

Z. Slivik, AP Salmon, JG LeBlanc, P Horvath, B Hucin, J Skovranek, RK Lamb, JL Montero, BR Keeton, SA Webber

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The bidirectional superior cava pulmonary shunt (BCPS) is being increasingly applied as an interim palliation for children with complex congenital heart disease. It is common practice to interrupt the alternate sources of pulmonary blood flow (PBF) at the time of BCPS, though the need and advantage for this has not been studied. Furthermore the BCPS can be performed in many patients through a right thoracotomy (Abrams technique 1967), further emphasizing the importance of defining the effects of competitive flow. We have therefore studied the early and medium term clinical and haemodynamic findings in 95 patients (age 3 weeks-25 years, median 1.7yrs) undergoing BCPS at 3 institutions from Aug '87-Aug '93. Preoperatively PBF was dependent on antegrade ventricular flow (47 pts), systemic-pulmonary shunts (28 pts) or mixed sources (20 pts). In 28 pts (39%) BCPS was the primary palliative surgical procedure. This was performed through a sternotomy in 79 cases and competitive flow was interrupted in 57(72%). In 16 patients BCPS was performed through a right thoracotomy leaving competitive flow from the ventricle (9 pts), systemic-pulmonary shunts (2 pts) or mixed sources (5 pts). There were 4 early deaths; none related to persistence of competitive flow. Prolonged effusion occurred in 10 pts, 7 with and 3 without competitive flow (p < 0.00). One repeat required ductal ligation 2 days after BCPS. All survivors achieved good or excellent palliation.

EVIDENCE AGAINST SYSTEMIC ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH MICROVASCULAR ANGINA

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Microvascular angina (MVA) is associated with impaired coronary perfusion reserve, and has been shown in one study to be associated with impaired coronary endothelium-dependent and -independent vasodilators in 11 patients (7 male, mean age 52y, range 42-62y) with previously characterised MVA (typical effort angina, positive exercise thallium scans, normal coronary angiograms) and 11 control subjects (matched for age, sex, blood pressure and serum cholesterol). 5 patients with MVA had impaired glucose tolerance. All medication was withdrawn 248 hours before the study. Incremental concentrations of acetylcholine (ACH; endothelium-dependent vasodilator) and sodium nitroprusside (SNP; endothelium-independent) were infused into the left brachial artery at a constant rate of 0.5 ml/min with subjects supine following a 20 min rest. Left radial artery blood flow was calculated from the diastolic-interstitial radial artery diameter imaged using a high resolution Duplex ultrasound scanner (Diasonics, Spectra) and from the Doppler velocity waveform (Scimed, PCDOPS). ACH (7.5, 15, 30 μg/min) increased radial artery blood flow similarly in MVA and controls (+0±5, 36±20, 31±2% in MVA vs. 26±22, 25±22, 25±22 in controls) as did SNP (1.25, 3.75, 11.25 μg/min; 32±18, 59±19, 80±22% in MVA vs. 12±31, 46±16, 95±23% in controls). This study provides no evidence that MVA is associated with systemic endothelial dysfunction.

THE ATRIOPULMONARY OR THE TOTAL CAVOPULMONARY CONNECTION FONTAN: WHICH IS BETTER?


Royal Brompton and Great Ormond Street Hospitals, London.

We have previously demonstrated a close relationship between respiratory motion and pulmonary blood flow after total cavopulmonary anastomosis (British Heart Journal 1991;65:213-7). In this study we have compared the resting, submaximal (submax) and maximal (max) exercise pulmonary haemodynamics of 23 atrio-portal (AP) Fontan children, 20 with total cavopulmonary connection (TCP) and 105 healthy control children. All underwent a graded workload protocol with respiratory mass spectrometry to measure metabolic gas exchange and pulmonary blood flow was measured with an automated acetylene rebreathing technique during exercise. There was no difference in maximal exercise performance in the Fontan groups. Effective pulmonary blood flow was equal but low at rest in both Fontan groups but relatively declined in the AP group (p < 0.05) and relatively improved in TCP group during submax exercise, compared to controls. As chronotropic incompetence was equal in both Fontan groups, blood flow improvement in the TCP was due to increased stroke volume (p < 0.05). There was a significantly greater respiratory rate at the same minute volume and carbon dioxide production in this TCP group (p < 0.05), compared with AP and control groups. In order to compensate for their poorer cardiac output APs had a greater A-V oxygen difference at maximal exercise than the TCP group (p < 0.05). During recovery there was a prompt return to normal respiratory rate in the TCP group (p < 0.05) but evidence of more prolonged recovery of oxygen debt in the AP group (p < 0.05).

Although similar at maximal exercise, submax exercise haemodynamics are superior in the TCP patients compared with the AP group. Exercise tachypnoea in the TCP group may be an adaptive response to increase pulmonary blood flow after this operation.
**HYPOLISTIC LEFT HEART SYNDROME; EARLY RESULTS FOLLOWING THE INTRODUCTION OF A MODIFICATION OF THE NORWOOD PROTOCOL**

PA Bu-Lock, O Silvester, E Logue, JV deGiovanni, JGC Wright, B Seitha, WJ Brawn.
Birmingham Children's Hospital, Birmingham, UK.

The results of surgical palliation for hypoplastic left heart syndrome (HLHS) in the UK have been dismal. Since 1st January 1993, we have offered a modification of the Norwood protocol to all neonates presenting to our unit with HLHS or variants thereof. Stage 1 surgery consists of application of the Damus/Norwood arch repair without use of exogenous material, ductal ligation, coarctectomy, atrial septectomy and insertion of a 3.5mm Gortex shunt between the innominate artery and the right pulmonary artery. Cardiac catheterisation is performed early (3 months) & is closely followed by Stage 2 surgery. Arterial resection is performed as necessary and the Gortex shunt is replaced by a superior cavo-pulmonary (CP) connection, to offload the ventricle and prevent subsequent pulmonary artery distension.

So far, 16 neonates (11 with HLHS and 5 with univentricular heart and severe systemic outflow obstruction) have been transferred to our unit. Nine were on Prostaglandin infusions, 5 were acidotic, 2 were ventilator and inotrope dependent. In 3 infants, congenital heart disease had been detected antenatally. Parents declined surgery for 2 infants. Fourteen underwent Stage 1 surgery after stabilisation with prostaglandin, inotropes and ventilation. There were 3 post-operative deaths. Two post-operative deaths occurred, one at 6 hours, and one, unexpectedly, at 14 days. Thus 9 (75%) survived Stage 1 surgery. Three patients underwent elective CP shunt procedures at 3-5 months of age following cardiac catheterisation. Another had a CP shunt performed on the 19th post-operative day for failure to wean from the ventilator. All survived. The other Stage 1 survivors await cardiac catheterisation and surgery. Principle risk factors so far identified are similar to those reported from the USA, ie severe tricuspid regurgitation from a structurally abnormal tricuspid valve as well as poor pre-operative condition.

Successful medium-term palliative surgery for the hypoplastic left heart syndrome can now be offered in the UK. The role of very early cavo-pulmonary shunting merits further investigation.

**COMBINED ATRIAL AND ARTERIAL SWITCH PROCEDURE FOR CONGENITAL CORRECTED TRANSPOSITION WITH VENTRICULAR SEPTAL DEFECT.**

O Stümper, JGC Wright, Jv deGiovanni, ED Silove, B Seitha, WJ Brawn.
The Children's Hospital, Birmingham, UK.

Four children with congenital corrected transposition (cct TGA) and ventricular septal defect underwent combined atrial and arterial switch procedure, to establish the left ventricle as the systemic ventricle after surgery.

Two suffered from severe tricuspid regurgitation and one from gross right ventricular failure preoperatively. One child was operated electively following previous pulmonary artery banding. Age at operation ranged from 0.8 - 3.1 (mean 2.2) years. Post surgical follow-up ranged from 3-18 (mean 9) months.

There were no early or late deaths. Bypass time ranged from 145 - 194 (mean 167) mins. Progression of conduction abnormalities were encountered in 2 pts. In-hospital stay ranged from 8 to 17 (mean 13) days.

Cathoioderatico ratio decreased from a mean of 0.65 (range 0.6 to 0.71) preoperatively to 0.58 (range 0.52 to 0.6) at last follow-up. Latest follow-up examinations excluded residual lesions in all patients. Three patients are in functional class I and one child is in functional class II.

**DIAGNOSTIC PROPERTIES OF THE RIGHT VENTRICULAR 15-34 YEARS AFTER REPAIR OF TETRALOGY OF FALLOUT**

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We have previously shown that transient right ventricular (RV) restriction is common following corrective surgery for Tetralogy of Fallot (TOF) and prolongs the post-operative course. In this study we assessed RV Doppler/echo indices of diastolic function in 31 patients aged 16-46 years (mean 29.1), 15 to 34 years (mean 23.3) after repair. All patients were operated upon by a single surgeon. Their mean age at operation was 3.9 years. Nine patients exhibited transmural Doppler flow, N-mode, cross sectional echo-cardiographic and pulmonary artery (PA) and superior vena cava Doppler flow signals were assessed. Patients were considered to have right ventricular restriction if antegrade diastolic flow was detected in the main pulmonary artery, coinciding with atrial systole(A wave), throughout the respiratory cycle.

2 patients were excluded because of an atrial septal defect and 1 because of moderate RV outflow obstruction (> 40 mmHg). Of the remaining 28 patients, 27 were in sinus rhythm. 12 of these (42.8%) had definite evidence of restriction with an A wave in the PA during expiration, which was significantly augmented during inspiration (P<0.01). In all 12 cases there was an SVC flow reversal coincident with atrial systole, whereas in the non-restrictive group both retrograde SVC flow was observed. The former group had undergone an earlier repair and was significantly shorter in the restrictive group compared to the non-restrictive group (P<0.001). Sixteen patients had normal pulmonary Doppler flow patterns. All patients had Doppler evidence of turbulent flow and its duration was shorter in the restrictive group (P<0.01) because of the influence of the A wave. The cardiac output ratio (CTR) was significantly lower in the restrictive group (P<0.01) suggesting less severe RV. There was no significant difference in age, age at operation, or time since operation when comparing those with and without restriction.

We conclude that right ventricular restrictive physiology late after TOF repair is common. Although it reflects abnormal haemodynamics, the A wave contributes to forward flow and shortens the duration of PR. Loss of sinus rhythm may therefore be detrimental in these patients. The pathogenesis of this phenomenon of RV restriction early and late after TOF repair remains unclear.

**MODERATED POSTER**

Are there different mechanisms for stretch-induced ventricular premature contraction and fibrillation?

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Stretch-induced ventricular arrhythmias, including ventricular premature contraction (VPC) and fibrillation (VF) has been shown experimentally. As there are different mechanisms underlying these arrhythmias, we studied this possibility further in isolated guinea-pig heart using Langendorff apparatus.

Hearts (n=30) were perfused with oxygenated (95%O2-5%CO2) modified Krebs-Henselei solutions. The myocardium was stretched by suddenly increasing left ventricular loading via a saline filled latex balloon every two minutes for 30 minutes, then repeated in a solution containing 10 and 20 uM gadolinium (Gd3+), a stretch-activated channel blocker. The volume of balloon inflation triggering the most VPCs was determined by step-wise increase increments within physiologic limits. Monophasic action potential and ECG were recorded from the epicardium using suction electrodes. Stretch-induced VPCs were significantly inhibited by Gd3+ (Fig 1A), however, Gd3+ had no effect on the incidence of stretch-induced VF (Fig 1B).

Fig 1. Effects of Gd3+ on stretch-induced VPCs (A) and VF (B). These results suggest that the underlying mechanism of stretch-induced VPCs may be triggered by activation of a Gd3+-sensitive stretch-activated ion channel. However, the stretch-induced VF reflects some other effect of myocardial stretch, which leads to electrophysiologic changes predisposing to reentry and VF.
MODERATED POSTER


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Chesterfield Royal Hospital, Chesterfield, UK.

Sudden cardiac death is a substantial problem. Apart from b2 adrenergic blockade, the prevention of sudden death with antiarrhythmic drugs is disappointing. One of the stronger correlations of this is left ventricular function, and it is becoming clear that which arrhythmias could be generated and which is well established is mechanoelectric feedback. We investigated the effect of B2 adrenergic stimulation on mechanoelectric feedback by measuring the change in action potential duration on acetic occurrence during dobutamine infusion. We also investigated the effect of dobutamine and mechanoelectric feedback on action potential recovery. We used steady state pacing and single premature beats. For the single premature beats, the beat to beat interval, or test pulse interval, was plotted against action potential duration to form an electrical restitution curve. We performed our investigations in the in vivo heart (n=25). Pigs were anaesthetised (N2O, 11 %; 1% Halothane) and their chests opened. Spindled monophasic action potentials were recorded from the anterior surface of the right ventricle. Monophasic action potentials were recorded from the left ventricle and the aortic root. We used an aortic clamp. Acute occlusion shortened the action potential duration (p<0.001). This increased with increases in the rate of dobutamine infusion (p<0.05). The mean shortening during control recordings was 5.0 ms. Dobutamine stimulation increased it to 7.0, 8.0, and 10.0 ms at infusion rates of 5, 10, 15 and 20 mg/kg/min respectively. Dobutamine stimulation decreased the initial phase of the restitution curve at short test pulse intervals. Isoproterenol increased mechanoelectric feedback (p<0.001). Increased mechanoelectric feedback increased the plateau of the restitution curve (p<0.01) and this was more marked after dobutamine.

In conclusion, mechanoelectric feedback increased during B2 stimulation and induces changes in the recovery of excitability and which would predispose to the generation of arrhythmias by reentry and possibly the alteration of the dynamics of arrhythmias, once initiated, from periodic to chaotic.

MODERATED POSTER

INCREASED INHOMOGENEITY OF INTRAVENTRICULAR CONDUCTION IN HYPOFUNCTIONAL CARDIOMYOPATY IS ASSOCIATED WITH RISK OF SUDDEN DEATH. RESULTS IN 104 PATIENTS

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INTRODUCTION: Increased latency and duration of paced right ventricular electrograms in response to premature stimulation in patients with hypokinetic cardiomyopathy is strongly associated with ventricular fibrillation. In 37 patients, these variables were used to discriminate patients into three groups: VF survivors had the greatest increase in electrogram latency at long R-S intervals and increase in electrogram duration (Group 1). Patients with non-sustained VT on ambulatory monitoring (NSVT) and a family history of SD (FHSFD) had less pronounced changes in electrogram duration and latency-duration (Group 2) and patients with no risk factors (no RF) and controls, showed least changes in electrogram latency and duration (Group 3). RESULTS: These discriminant criteria have been used in 104 patients with HCM. 7 patients out of 8 with VF (Group 1) are discriminated from the remaining population (p<0.001) 3 patients with either a FHSFD or NSVT also lie in this group. A new group (modified VF group) can be constructed that contains all 8 patients with VF. Three VF patients in this group were studied prior to their VF arrest. This group includes a further 6 patients of whom 3 have NSVT, 2 have a FHSFD and one has no RFs. 21 patients have NSVT. 1 patient lies in the VF group, 4 in the modified VF group, 13 lie in group 2 and 3 lie in group 3. CONCLUSIONS: (i) The classification of patients according to electrogram fractionation using 104 patients is similar to that obtained from 37 patients. (ii) Less than 19% (9/96) patients who have not suffered VF are included in the high risk modified VF group. As 3/8 VF patients who define this group were studied prior to their arrest, the non-VF patients may be at high risk of sudden death. (iii) 24% (5/21) patients with NSVT lie in the modified VF group. Since NSVT patients have a 20% 3 year mortality, this technique may identify high risk patients with NSVT.

(iv) These results justify a prospective trial of ICDs in patients with HCM.

Circulation 1992;86:467-474

MODERATED POSTER

IMPROVED PREDICTION OF PAROXYSMAL ATRIAL FIBRILLATION BY ANALYSIS OF MULTIPLE SIGNAL AVERAGED P WAVE VARIABLES.

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Although analysis of the signal averaged P wave (SAPW) in patients with paroxysmal atrial fibrillation (PAF) reveals important differences from normal controls the ability of single time or frequency domain variables to separate patients from normal is low. Discrimination may be improved if multiple variables are assessed. We analysed the time and frequency domain characteristics of SAPW from 115 patients and used multivariate techniques to identify important predictive variables. Subjects were divided into those with normal cardiovascular systems (group A) comprising 24 with PAF and 34 controls and those with cardiopulmonary disease (group B) comprising 31 with PAF and 26 controls. Signal averaging used a P wave template derived from the most frequent P wave morphology in any recording. Data was examined using both logistic regression and linear discriminant analysis.

In both group A and group B significant increases in P wave duration, peak spatial velocity, and absolute power were noted in patients with PAF:

<table>
<thead>
<tr>
<th>Group</th>
<th>Control</th>
<th>PAF</th>
<th>Group</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>145(2)*</td>
<td>137(2)</td>
<td>155(3)*</td>
<td>144(2)</td>
</tr>
<tr>
<td>PSV</td>
<td>18(1)*</td>
<td>15(1)</td>
<td>20(1)*</td>
<td>16(1)</td>
</tr>
<tr>
<td>P6;</td>
<td>32(3)*</td>
<td>25(2)</td>
<td>38(3)*</td>
<td>28(3)</td>
</tr>
<tr>
<td>P60;</td>
<td>4.6(0.5)*</td>
<td>3.3(0.3)</td>
<td>4.8(0.6)*</td>
<td>3.5(0.3)</td>
</tr>
<tr>
<td>P90;</td>
<td>1.9(0.2)*</td>
<td>1.3(0.1)</td>
<td>2.0(0.2)*</td>
<td>1.5(0.1)</td>
</tr>
</tbody>
</table>

DUR = P wave duration after high pass filtering at 40Hz. PSV = Peak spatial velocity (mV/s). P30, P60, P90 = Total absolute power (μV²/s) in frequency bands between 30, 60 or 180Hz and 500Hz. All values are mean(SEM). “p<0.05” was used to identify significant differences.

P wave duration and magnitude were independent predictors of PAF class. P wave duration and P60 combined identified patients with PAF with a sensitivity of 76%, specificity of 62% and diagnostic accuracy of 72% in the same patient duration alone had a sensitivity of 71%, specificity of 61% and diagnostic accuracy of 66%. Analysis of both P wave duration and magnitude improves the discriminant ability of SAPW for PAF.

MODERATED POSTER

THE EFFECTS OF HYPOTHYROIDISM ON THE VULNERABILITY TO VENTRICULAR FIBRILLATION IN DOGS

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Sun Yat-sen Memorial Hospital, Guangzhou, China.

It has been shown that thyroid function has a significant effect on the heart and it has been suggested that suppression of thyroid function may have a detrimental effect on the heart. However, a comparative study of the effects of hypothyroidism and amiodarone on vulnerability to ventricular fibrillation is still lacking. In this study, twenty four adult dogs were randomly divided into three groups: a hypothyroid group following total thyroidectomy (n=9), an amiodarone group (n=7, 400 mg per day, 4 weeks) and a control group (n=8). Both amiodarone and control groups were subjected to sham surgery. Five to eight weeks after surgery the following electrophysiological parameters were measured: (1) right ventricular effective refractory period (ERP), (2) dispersion of monophasic action potential (MAP) duration (from 1 right and 3 left ventricular sites) and (3) ventricular fibrillation threshold (VFt). Effects on ischaemic/reperfusion arrhythmias were also assessed.

Results:

<table>
<thead>
<tr>
<th>Groups</th>
<th>Controls</th>
<th>Hypothyroid Amiodarone</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERP (ms)</td>
<td>135±12</td>
<td>179±18**</td>
</tr>
<tr>
<td>MAP95 (ms)</td>
<td>123±10</td>
<td>151±26**</td>
</tr>
<tr>
<td>MAP99 (ms)</td>
<td>158±11</td>
<td>191±31</td>
</tr>
<tr>
<td>MAP99-50 (ms)</td>
<td>35±4</td>
<td>41±12</td>
</tr>
<tr>
<td>MAP Disp (ms)</td>
<td>17±6</td>
<td>20±4</td>
</tr>
<tr>
<td>VFt (mA)</td>
<td>25±6</td>
<td>37±5**</td>
</tr>
</tbody>
</table>

Incidence of VF:

<table>
<thead>
<tr>
<th></th>
<th>ischaemic</th>
<th>reperfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>VFt</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

Incidence of VF:

| VFt | 4 | 3 | 2 |

*p<0.05; **p<0.01

Conclusions. These observations suggest a significant antiarrhythmic effect of hypothyroidism similar to amiodarone.
ALDOSTERONE BLOCKADE INDUCES MAGNESIUM RETENTION AND REDUCES VENTRICULAR ARRHYTHMIAS IN HEART FAILURE

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Congestive heart failure (CHF) is a condition with a high mortality and morbidity. Neurohormonal suppression with ACE inhibitors confer additional mortality advantages over mixed vasodilator combinations. Aldosterone has properties which are likely to be detrimental in CHF and are distinct from angiotensin II. These include magnesium, induction of ventricular arrhythmias and inhibition of myocardial uptake of catecholamines in both animal models and in human heart failure. Aldosterone escapes suppression from ACE inhibition, 3-6 months after initiation of treatment. We have therefore, assessed the effects of aldosterone antagonism on magnesium balance and ventricular arrhythmias in human heart failure. 42 patients with NYHA II-III CHF were randomised in a double-blind manner to 8 weeks treatment with placebo or spironolactone 50-100 mg over and above ACE inhibition. Serum magnesium, 24 urinary magnesium excretion and Holter monitoring was undertaken at baseline, four weeks and eight weeks. Assessment was made of NYHA class, weight, blood pressure and electrolytes were also made. Treatment with spironolactone induced a significant increase in serum magnesium, a reduction in urinary magnesium excretion and a decrease in ventricular ectopic beats (MANOVA). Low grade or occurrence of non-sustained ventricular tachycardia did not change. There were no significant differences in potassium, serum creatinine and weight, although mean BP fell with spironolactone. Treatment was well tolerated. Although NYHA class did not significantly differ between treatment groups, four patients improved one class in the spironolactone limb.

Spironolactone-treated group

<table>
<thead>
<tr>
<th>Mg p (mmol/l)</th>
<th>Baseline</th>
<th>8 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.88 (0.84, 0.95)</td>
<td>0.99 (0.94, 1.04)</td>
</tr>
<tr>
<td>%4 VPB</td>
<td>1.42 (2.83, 3.39)</td>
<td>2.31 (1.78, 2.83)</td>
</tr>
<tr>
<td>%4 VPB</td>
<td>-27 (-35,-1)</td>
<td></td>
</tr>
</tbody>
</table>

Results are presented as mean (95% CI).

Conclusion. Treatment with an aldosterone antagonist over and above an ACEI may confer symptomatic benefit in some patients but significance changes in magnesium balance and ventricular arrhythmias occur which may confer advantages in reduction of the risk of sustained ventricular arrhythmias and sudden death. These questions will be answered in a larger mortality study.

LONG TERM OUTLOOK FOR TACHYARRHYTHMIAS DETECTED IN UTERO

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Since 1982, 97 fetuses with an atrial tachycardia have been seen in our centre. In each case, the fetal arrhythmia was evaluated by two dimensional and M-mode echocardiography. The gestational age at presentation was between 19 to 42 weeks (mean 31.6 weeks). Eighty one fetuses (82%) had a supraventricular tachycardia and 16 (16%) had atrial flutter with varying degrees of atrioventricular block. There was evidence of fetal hydrops in 40 (40%) at presentation. Antiarrhythmic treatment was given by oral therapy to the mother in 85 cases (86%) and by direct administration to the fetus in 2. Digoxin alone (n=28) or in combination with verapamil (n=28) was used in the majority of cases (72%), flecainide was used in 24% and amiodarone in 2%. Fetuses who did not receive antenatal treatment delivered within 72 hours of presentation. Maternal therapy resulted in conversion of the tachycardia to normal sinus rhythm in 75%. Intrauterine death occurred in 6 fetuses, there was 1 stillbirth and 4 died in the neonatal period. One pregnancy was terminated electively for multiple fetal anomalies. Of 85 fetuses (86%) who survived beyond the neonatal period there were 2 infant deaths. In the postnatal period, 53 of the 85 survivors were started on antiarrhythmic therapy, 23 were not in sinus rhythm at birth and recurrence of the arrhythmia occurred in 15, in the remainder treatment was prophylactic. Mean duration of therapy in these infants was 10.6 months and extended to a maximum of 5 years. No postnatal treatment was given in 31 infants, all of whom had no documented evidence of tachycardia postnatally. Follow up period has been from 2 weeks to 7 years (mean 6 months).

In conclusion, the long term prognosis for antenatally detected tachycardias is good, particularly when control is achieved before delivery or in the immediate postnatal period.
**RELATIONSHIP BETWEEN CORONARY STENOSIS MORPHOLOGY AND DEGREE OF VASOMOTION IN PATIENTS WITH VARIANT ANGINA**

D Tousoulis, L Chen, G Davies, JC Kaski, St George's Medical School and RPMS, London

In patients (pts) with chronic stable angina, eccentric stenoses have a larger potential for dynamic changes of calibre in response to vasoactive stimuli than concentric stenoses. Whether the same phenomena is present in pts with variant angina is not known. The vasomotor response of eccentric (asymmetric narrowings) and concentric (symmetric narrowings) stenoses to ergonovine and isosorbide dinitrate (ISDN) was studied at the spastic site in 16 variant angina pts (14 male, 2 female, mean age 51±6 years). Coronary diameter of eccentric (n=8) and concentric (n=8) stenoses that ranged from 20 to 63% luminal diameter reduction were measured by computerized quantitative angiography before and after ergonovine and ISDN. Ergonovine (20 μg i.c) caused total coronary occlusion in 2 of 8 (25%) eccentric and in 3 of 8 (37.5%) concentric (p=NS). Stenoses. Mean (x±SEM) diameter reduction with ergonovine was 55±10% and 58±10%, in eccentric and concentric, respectively (p=NS). ISDN (1-2 mg i.c), which relieved spasm in all pts, increased coronary diameter by ±10% (from baseline before spasm) in 4 of the 8 (50%) eccentric and in 3 of the 8 (37.5%) concentric (p=NS). Mean diameter of eccentric increased from 1.44±0.12 to 1.61±0.14 mm after ISDN (12.5±0%) and diameter of concentric increased from 1.49±0.17 to 1.71±0.17 mm (12.3±2%) (p=NS). The results of this study indicate that in pts with variant angina both eccentric and concentric stenoses have the potential for changing their calibre dynamically in response to vasoactive stimuli. The magnitude of dynamic changes of calibre was similar in eccentric and concentric stenoses. Thus in patients with variant angina the stimulation of hyperreactive vascular smooth muscle in the vessel wall (or adjacent to it) may result in dramatic changes of coronary calibre irrespective of stenosis morphology.

**PATHOPHYSIOLOGY OF TRANSIENT MYOCARDIAL ISCHAEMIA IN UNSTABLE ANGINA**


Transient myocardial ischaemia (TMI) in stable angina is mainly due to increased myocardial demand with a morning peak in TMI. In unstable angina (UA) and non-Q MI (NQ), thrombosis and vasospasm are considered to be important mechanisms causing TMI. We have assessed the change in heart rate and the circadian variation of TMI in 256 patients admitted with UA and NQ. 44 patients had a total of 176 episodes of TMI (32 UA patients with 132 episodes; 12 NQ with 44 episodes). The heart rates (HR) at 10, 5 minutes prior to and at the onset of TMI were recorded for each episode. We prospectively considered five and ten beat increases in HR at the onset of TMI to represent increased myocardial demand. Circadian distribution of TMI was plotted based on three-hourly grouping of episodes.

**RESULTS:** Peak activity of TMI in UA and NQ was between 12 midnight and 9 am.

**Conclusion:** Increased HR leading to TMI is less frequent in UA and NQ compared to previously published data in stable angina (70 - 80%). In UA and NQ the distribution of TMI is mainly in the early morning when vasoconstrictor tone is high. TMI in UA and NQ could be commonly caused by coronary blood flow reduction due to spasm or thrombosis rather than increased demand consistent with the pathology of acute plaque rupture. The detection and characterisation of TMI in this manner for UA and NQ may help in identifying the underlying pathophysiology thus providing a rationale for targeted drug therapy.
DIASTOLIC ABNORMALITIES OF LEFT VENTRICULAR SUBENDOCARDIAL FUNCTION IN UNSTABLE ANGINA.

M Y Henein, D Patel, K Fox, D G Gibson. The Royal Brompton National Heart and Lung Hospital, London.

Left ventricular (LV) long axis (LAx) function, representing that of the subendocardium, is often abnormal in coronary artery disease and improves with angioplasty. To assess its function in unstable angina (UA), rest pain in previous 24 hours, we compared 38 (UA) patients age 58 ± 12 vs. 18 matched patients with chronic stable angina (CSA) age 57 ± 10 and 21 normals age 51 ± 11 ys. 2D guided M-modes of LV long axis (LAx) at 3 sites, left, septal and posterior were recorded in the absence of chest pain or ST shift along with phonocardiogram to identify A2 and ECG. 21/38 US pts showed prolonged LAx shortening after A2 by > 3 mm at one or more of the 3 sites by 3-5 mm, not seen in CSA pts, p < 0.001, though minor shortening < 3 mm occurred in 7. The onset of diastolic lengthening was thus delayed by 90 ± 20 ms in UA compared with 75 ± 15 ms in CSA p < 0.001. This delayed LAx shortening in UA lasted 150 ± 20 ms or 25 ± 9 % of total diastolic time, taken as A2 to onset of succeeding Q wave while that in CSA was 100 ± 15 ms or 19 ± 4 % p < 0.001. All these 21, 14 other UA and 8 CSA pts showed less severe LAx abnormalities including delayed onset of shortening after Q wave, reduced peak lengthening rate, and increased atrial component of lengthening. 3 pts with UA and 3 with CSA had normal LAx function.

Conclusion: In patients with UA, even in the absence of chest pain or ST shift, LV long axis frequently shows a major disturbance of relaxation, not seen in CSA. It occupies 25% diastolic time and may thus directly impair coronary flow to already ischaemic regions, perpetuating relaxation abnormalities and thus setting up conditions for instability.

LONG-TERM FOLLOW-UP AFTER PERCUTANEOUS MITRAL COMMISSUROTOMY WITH THE INOUE BALLOON.


We evaluated the long-term outcome of our first 300 consecutive patients (pts) undergoing percutaneous mitral commissurotomy (PMC) with the Inoue balloon. There were 256 females and 44 males, the mean age was 44±9,6 years (range 18-69), 52 pts had previous surgical commissurotomy, 96 pts were in atrial fibrillation, 16 pts had a history of embolism. PMC was carried out with the success rate of 84% (no significant mitral regurgitations (MR) and mitral valve area (MVA) > 1,5 cm²). 270 pts were available for serial clinical and echocardiographic studies at 6 months (mo) intervals post PMC with the mean follow-up of 24,0±13,5 months. (12 pts refused returning, 18 operated for MR less than 6 mo post PMC). 247 pts (92%) were in NYHA class I or II. MVA decreased from 2,01±0,35 cm² immediately after PMC to 1,81±0,3 at follow-up. 22 pts had mitral valve replacement, 35 (12,0%) had restenosis (MVA at follow-up < 1,5 cm² with a 50% loss of the initial gain in MVA), 2 pts experienced an embolic event, 2 pts had myocardial infarction, no pts died.

The estimated event free survival (no mitral valve replacement, embolism, myocardial infarction, restenosis) according to the Kaplan-Meier curve was 87%, 80%, 68% and 63% at 12, 24, 36 and 54 mon respectively. The estimated survival without restenosis was 93%, 86%, 77%, 73% at 12, 24, 36 and 54 mon respectively. The Cox proportional hazard univariate and multivariate analysis did not identify any clinical, echocardiographic hemodynamic or procedural factor as an independent predictor of restenosis free or event-free survival.

Conclusions: PMC provides good long-term clinical and echocardiographic results. Restenosis free or event-free survival could not be predicted on the basis of any clinical, hemodynamic, echocardiographic or procedural variable.

ENDOCARDITIS AND HUMAN IMMUNODEFICIENCY VIRUS INFECTION.

PF Currie, GR Sutherland, AJ Jacob, RP Brettle*, JE Bell*. NA Boro. Dept of Cardiology, Edinburgh Royal Infirmary, *Regional Infection Unit, City, Hospital and *Department of Pathology, Western General Hospital, Edinburgh.

Post mortem (PM) studies have suggested that endocarditis is a frequent finding in AIDS patients. Nonbacterial thrombotic endocarditis (NBTE) has been described in up to 5% of cases. However, we suggest that both infective endocarditis (IE) and NBTE are less common than previously thought. Moreover, in this group IE appears to be a consequence of intravenous drug use (IVDU) rather than HIV infection itself. In the last 4 years 280 patients with HIV infection (mean CD4 count 143 cells/mm² (range 0-940)) have taken part in a prospective echocardiographic survey. Despite the high rate of previous IVDU in this cohort (69%), only 4 cases (1.4%) of IE have been identified in this way. The incidence of clinically proven IE has also fallen from 7 cases in 1984, to a single case in 1993 and this trend has mirrored a decline in the popularity of injection drugs. We have performed 110 autopsies on subjects from all the major risk groups and at all stages of HIV infection, but have seen no thrombotic vegetations consistent with a diagnosis of NBTE.

RISK FACTORS/CLINICAL STATUS

<table>
<thead>
<tr>
<th>No. of Pm's</th>
<th>Homosexual AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IVDU/AIDS</td>
</tr>
<tr>
<td></td>
<td>IVDU+Pro-AIDS</td>
</tr>
<tr>
<td></td>
<td>Blood product recipient/AIDS</td>
</tr>
<tr>
<td></td>
<td>African AIDS</td>
</tr>
</tbody>
</table>

The unique haemostatic defect in aortic valve stenosis. J O'Brein*, J Brunt, M Rutherford*, J Watkins. Departments of Haematology* and Cardiology, St Mary's Hospital, Portsmouth.

Aortic valve stenosis (AVS) is associated with a tendency to bleeding from intestinal angiodyplasia which is usually relieved by aortic valve replacement. We have investigated the haemostatic defect in patients with AVS which may contribute to this phenomenon.

In 15 adult patients with AVS and 10 age and sex matched controls, there were no differences in blood count, basic clotting tests, plasma Von Willebrand factor and citrated plasma rich platelet aggregation with ADP, adrenaline, arachidonic acid or ristocetin. Two high shear tests were also performed. In (1), citrated blood was forced at 40 mmHg through a 10 μ filter and in (2) native blood was forced at constant speed through a 13 cm column of fine glass beads (Adeplast Ltd). Shear activates platelets leading to retention and % platelet retention in the filter between 20 and 40 seconds and in the column between 15 and 20 seconds was recorded.

Results: Filter %

<table>
<thead>
<tr>
<th></th>
<th>Column (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVDU patients</td>
<td>51.9 ± 12.4</td>
</tr>
<tr>
<td>Controls</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>80.9± 11.7</td>
<td>85.5± 10.1</td>
</tr>
</tbody>
</table>

Standard bleeding time at 40 mmHg pressure (Simplate II) was also longer in the AVS patients compared with controls, p<0.05. These findings suggest that the high shear haemodynamics of AVS modify platelet function in vivo in a manner detectable only by high shear tests in vitro. Preliminary data suggests that this effect is reversed following aortic valve replacement.
AORTIC VALVE REPLACEMENT IN PATIENTS WITH AORTIC STENOSIS AND SEVERE LEFT VENTRICULAR DYSLAERDYSYNY: PROGNOSTIC INDICATORS
HM Connolly, JK Oh, TA Orszulak, SL Osborn, VL Roger, DO Hodge, RK Bailey, JB Steward, AJ Tajik
Mayo Clinic, Rochester, Minnesota, United States of America

The outcome of aortic valve replacement in patients with severe pressure gradient (ejection fraction ≤ 35%) and marked left ventricular (LV) dysfunction (ejection fraction ≤ 35%) is not well known. Thus we reviewed 154 such patients (male 107/female 47), mean age 73 years, (range 32-93), who were operated on between 1985-1992. We describe the outcome, and prognostic variables of these patients. Pre-operative (presp) hemodynamics demonstrated the following mean values: ejection fraction 0.63±0.22, mean transvalvular gradient 43±18 mm Hg, and cardiac output 3.9±1.3 l/min. Coronary artery disease requiring bypass was present in 78 patients (51%).
The in-hospital mortality was 11% (17/154), and 50 patients (32%) were dead at follow-up, mean 2.1 years (up to 8.2 years). Overall five year mortality was 58%. In-hospital mortality was significantly associated with lower mean preop mean pressure (p<0.005) and cardiac output (p<0.03) by univariate analysis. The only predictor of overall long-term mortality was the presence of significant coronary artery disease (22 vessels or left main). Five year survival with significant coronary artery disease was 39% vs 69% without significant coronary artery disease (p=0.005).
By univariate analysis postoperative (pstop) ejection fraction (n=109), mean 39±15% was significantly related to a higher preop peak aortic pressure (p<0.001), and a higher mean gradient (p<0.01); and inversely related to LV mass index. Preoperative paroxysmal atrial arrhythmias were related to peak aortic valve gradient (p<0.002), and aortic valve area (p=0.01).

CONCLUSION
1) Operation for AS with reduced LV function (ejection fraction ≤ 35%) can be performed at an acceptable risk. 2) In-hospital mortality is associated with lower preop cardiac output and mean gradient. 3) Overall long-term mortality is related to ischemic tissue necrosis. The postoperative ejection fraction is related to preop AV hemodynamics, coronary artery disease, and gender.

PHASIC CORONARY FLOW VELOCITY AT REST AND DURING STRESS IN PATIENTS WITH AORTIC VALVE STENOSIS
M K Kyriakidis, P N Petroplakias, C A Testolouris, C V Kouroulias, P K Toustouzas
Department of Cardiology, Hippokration Hospital, University of Athens, Athens, Greece

Alterations in phasic coronary flow (such as an early systolic retrograde wave) have been demonstrated at rest in patients with aortic valve stenosis (AVS) but have never been studied in man under conditions of stress. To investigate these phenomena we studied 32 patients, mean age 63±25 years, with moderate to severe pure AVS and normal coronary arteries. TwO patients (group A) had paroxysmal atrial fibrillation (AF) and exertional symptoms (angina and/or dyspnea) while 12 (group B) were asymptomatic. The study involved bimanual cardiac catheterization and all measurements were obtained at rest, during atrial pacing-induced tachycardia and during incremental intravenous dobutamine (DOB) infusion (5-30 μg/kg/min). Intracoronary Doppler flow velocimetry in the proximal LAD was used to determine phasic and mean coronary flow velocity (FV) along with hemodynamic parameters. Results were:

<table>
<thead>
<tr>
<th>G r o u p</th>
<th>G r o u p A vs G r o u p B</th>
<th>P (n=12)</th>
<th>P R E S T</th>
<th>P A C E</th>
<th>D O B</th>
<th>P R E S T</th>
<th>P A C E</th>
<th>D O B</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>79</td>
<td>123</td>
<td>118</td>
<td>76</td>
<td>126</td>
<td>122</td>
<td>126</td>
<td>122</td>
</tr>
<tr>
<td>LVSP (mmHg)</td>
<td>220</td>
<td>273</td>
<td>256</td>
<td>191</td>
<td>254</td>
<td>248</td>
<td>238</td>
<td>248</td>
</tr>
<tr>
<td>mean SGR (mmHg)</td>
<td>77</td>
<td>75</td>
<td>115</td>
<td>55</td>
<td>54</td>
<td>94</td>
<td>79</td>
<td>94</td>
</tr>
<tr>
<td>peak SV FV (cm/sec)</td>
<td>-15</td>
<td>-14</td>
<td>-41</td>
<td>-6</td>
<td>-5</td>
<td>-28</td>
<td>-16</td>
<td>-28</td>
</tr>
<tr>
<td>peak DA FV (cm/sec)</td>
<td>65</td>
<td>73</td>
<td>80</td>
<td>29</td>
<td>40</td>
<td>69</td>
<td>69</td>
<td>69</td>
</tr>
<tr>
<td>Mean FV (cm/sec)</td>
<td>31</td>
<td>35</td>
<td>38</td>
<td>14</td>
<td>25</td>
<td>33</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>Valve area (cm²)</td>
<td>0.61</td>
<td>0.56</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1.87</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mass index (g/m²)</td>
<td>200</td>
<td>187</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*p<0.05 vs Group B, p=0.001 vs REST

The EF of correlate with the stress response in patients with AVS.

A NEW PACING ALGORITHM FOR THE SUPPRESSION OF ATRIAL FIBRILLATION
F D Murgatroyd, A K B Slade, S Jones, R Nitzsche, E Rowland, A John Cann, M Limousin, P Ritter, for the Chorus Multicentre Study Group
Department of Cardiological Sciences, St George's Medical Hospital London, School and Clinique Val d'Oise, Paris, France

Rapid pacing is used acutely for arrhythmia suppression, but is usually unsuitable for long-term therapy. We report initial experience with a new pacing algorithm intended to suppress atrial fibrillation (AF) by increasing the heart rate only in the presence of atrial premature complexes (APCs). On sensing an APC, it causes (i) elimination of any subsequent pause; (ii) a 12.5% acceleration of the heart rate for 20-50; (iii) further modest acceleration if other APCs occur during this period, otherwise (iv) it allows a gradual deceleration if the rhythm remains stable.

The algorithm was tested in 50 patients, aged 26-85 (mean, 64) years, implanted with a Chorus RM dual chamber pacemaker (ELA Medical, France) and atrial arrhythmias. After loading the algorithm into the random access memory of the pacemaker, it was programmed to switch on/off every 2 hours during a 24-hour period of ambulatory recording. The resulting recordings were analysed for the frequency and duration of atrial arrhythmias: comparison was made between arrhythmias commencing with the algorithm active versus inactive.

Results: No patient was aware of the algorithm functioning. 25 recordings which showed atrial arrhythmias or >10 APCs/hr were analysed for the effects of the algorithm. The effects of the algorithm were: atrial bigemini reduced in 7 patients, increased in 3; salvo (APCs >2 beats, <30s) reduced in 5 patients, increased in 1; episodes of AF >30s reduced in patients, increased in 6, total duration of AF reduced in 11 patients, increased in 4. In all patients with >5 episodes of AF in total, the frequency of AF was reduced when the algorithm was active.

We conclude that pacing acceleration triggered by APCs is well tolerated and appears to have an antiarrhythmic action, and that a longer term trial of this pacing algorithm is therefore warranted.
INTRAVASCULAR FIBRIN TURNOVER AND THROMBOGENESIS IN ATRIAL FIBRILLATION IS REDUCED BY CARBODIVERSION

Department of Cardiology, Stobhill Hospital, Glasgow; and "University of Medicine, Royal Infirmary, Glasgow

Cardioversion of atrial fibrillation (AF) carries a serious risk of major thromboembolism and stroke. To determine whether or not the procedure alters plasma levels of fibrin D-dimer (DD) a marker of intravascular fibrin turnover and thrombus formation and plasma fibrinogen (PF) [associated with stroke and thromboembolism], we performed a prospective study in 19 patients with AF in whom cardioversion had been performed. Each patient was studied prior to the procedure and one hour after cardioversion. The results show that plasma fibrinogen levels (PF) were significantly reduced at one hour after cardioversion compared with baseline values, and fibrin D-dimer (DD) levels were not significantly changed. The effect of cardioversion is likely to be due to the acute hemodynamic changes associated with AF, and it may be that the reduction in fibrin D-dimer is due to the acute hemodynamic changes associated with AF and the subsequent cardioversion. This study suggests that cardioversion is a safe and effective procedure for the treatment of atrial fibrillation.

NORMAL RIGHT ATRIAL SIZE IS REQUIRED FOR SUCCESS IN RADIOFREQUENCY ABLATION OF ATRIAL FLUTTER.

J.P. Mounsey, N. Mathew, D. DaHines, J.P. DiMarco. Department of Cardiology, University of Virginia Hospital, Charlottesville. Virginia. USA.

Classical atrial flutter is caused by a right atrial macroreentry circuit. Ablation may be achieved by interruption of the zone of slow conduction in the isthmus between the tricuspid annulus and the inferior vena cava. We report predictors of success in 20 patients. All had classical atrial flutter (cycle length 254.4±73ms) resistant to medical therapy (previously 2±1 drugs); age was 63±10 yrs. 5 had no other heart disease, 8 had ischaemic heart disease, 4 were hyperensive, 2 had valvular heart disease and 1 had cardiomyopathy. 5 had a history of atrial fibrillation (AFib). Ablation was successful in 11 (55%) of cases overall (1 after a second procedure). Predictors of procedural success are shown in the table. (p values are from Fisher's exact test.)

Efficacy of Sequential "Fast" and "Slow" Pathway Ablation as a Means of Creating Complete Heart Block in Patients with Atrial Fibrillation.

G.E. Payne, J.D. Skehan, C.J. Garrett, Groby Road Hospital, Leicester

The results of radiofrequency (RF) catheter ablation for atrioventricular (AV) nodal tachycardia have suggested that anatomical substrates of the "fast" and "slow" AV nodal pathways involve anterior and posterior right atrial inputs to the node, rather than being confined to the compact node itself. The purpose of this study was to examine the role of these anatomical inputs to the AV node in patients without AV nodal tachycardia or demonstrable dual AV nodal physiology. Ten consecutive patients (pts) with symptomatic paroxysmal atrial fibrillation undergoing complete AV junction ablation were studied. Mean age was 63 years and 7 were male. Dual AV nodal pathways were excluded by a baseline electrophysiology (EP) study in sinus rhythm. Following EP study, RF energy delivery was applied in the anterior "fast pathway" position, to prolong the AH interval by at least 50% above baseline. After repeat assessment of AV nodal function, the ablation catheter was moved posteriorly and RF energy applied to the septal annulus of the tricuspid valve in a stepwise manner according to the technique of "slow pathway" ablation described by Akhtar. The endpoint was the development of complete heart block (CHB) or the recording of a His bundle electrogram on the ablation catheter. AH prolongation was achieved in all 10 pts with a mean of 5 applications of RF energy in the anterior "fast pathway" position. Subsequent ablation of the anatomical equivalent of the "slow pathway" resulted in 7 of the 10 pts (mean of 5 further RF pulses). The resulting escape rhythm in these pts was narrow complex with a mean RR interval of 110±10ms. Three pts needed standard His bundle ablation for creation of CHB. In 2 of these there was no underlying escape rhythm. Conclusion: The anatomical equivalents of "fast" and "slow" AV nodal pathways may operate the principal or only input to the compact node even in pts without dual AV nodal pathways.

LONGTERM SUCCESS OF CARDIOVERSION IN PATIENTS WITH CHRONIC ATRIAL FIBRILLATION.

University College Hospitals, London, *Kent & Canterbury Hospital, **JH Hospital, Tokyo, Japan & Toku Medical School, Japan

Cardioversion of atrial fibrillation (AF) is usually restricted to patients in whom AF is of recent onset and many clinicians argue against cardioversion if AF has been present for more than a year. However, it may be the association of chronic AF with cardiac disease, rather than the duration of AF itself, which determines the poor outcome suggested by earlier studies. The aim of this study was, therefore, to investigate rates of cardioversion and maintenance of sinus rhythm (SR) in a homogeneous group of patients with chronic AF and "normal" left ventricular function. We report a retrospective series of 92 patients followed from 1979-1993. The study was limited to patients (aged 48.1±11.3 years; 55 men) presenting with thyrotoxicosis induced AF, but no other heart disease, who had remained in AF for 12 months or more (38.7±26.3 months; range 12-120) despite being euthyroid for at least 3 months. Cardioversion was attempted using 600mg of oral Disopyramide (DS) per day for 3 days: if unsuccessful the patients were given DC shock. If SR was established the intention was to maintain patients on 300mg of DS daily for at least 3 months. 85 patients (92%) were successfully cardioverted: 13 reverted to SR with DS alone. The duration of AF prior to cardioversion was longer in the 7 who remained in AF (67.6±43.3 vs 36.4±23.2 months; p<0.0001). 29 euthyroid patients relapsed into AF: no further cardioversion was attempted. Episodes of AF due to recurrent thyrotoxicosis were managed as at presentation. At last follow up (78.6±37.7 months; range 7.7-155.7, 56 of the initial 92, or 61%, were in SR. Of interest no significant arrhythmias were induced by 93 patient years of DS. The study shows that cardioversion is highly effective even in longstanding AF. The excellent rates of cardioversion and maintenance of SR suggests that the duration of AF per se may be a less important determinant of longterm outcome than has previously been suggested.
An abnormal signal averaged P wave (SAPW) indicates vulnerability to paroxysmal atrial fibrillation (AF). We investigated the characteristics and evolution of the SAPW following cardioversion from chronic AF. The SAPW was recorded from 12 subjects at 3hrs, 24hrs and 4 weeks after cardioversion. A P wave template derived from the most commonly occurring P wave morphology was used for averaging. The (mean±range) age of the subjects was 58±45–71; 11 were male. 5 were taking amiodarone, 2 sotalol and 1 flecainide. 7(58%) subjects reverted to AF during the 4 week observation period. The SAPW 3hrs after cardioversion was abnormal in all subjects. But by 24hrs significant decreases in peak spatial velocity and both low and high frequency power occurred in the group who remained in sinus rhythm at 4 weeks compared to no change in those who reverted to AF:

<table>
<thead>
<tr>
<th>Reverted</th>
<th>Sinus</th>
</tr>
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<tbody>
<tr>
<td>3hrs</td>
<td>24hrs</td>
</tr>
<tr>
<td>3hrs</td>
<td>24hrs</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Dur:</td>
<td>155(8)</td>
</tr>
<tr>
<td>PSV:</td>
<td>21(3)</td>
</tr>
<tr>
<td>P20:</td>
<td>67(15)</td>
</tr>
<tr>
<td>P60:</td>
<td>4.00(6)</td>
</tr>
</tbody>
</table>

P wave duration after high pass filtering at 40Hz. PSV: Peak spatial velocity (mV/s). P20, P60: Power from 20 and 60Hz to 150Hz (μV²/s).

"*" p < 0.05 vs Sinus at 3hrs.

The SAPW following cardioversion in patients who remain in sinus rhythm shows reduced power and spatial velocity at 24hrs in contrast to those who revert to AF. Serial SAPW after cardioversion from AF can identify patients who remain vulnerable to AF and are at risk from recurrent arrhythmia.

### (38) POSTER

**MEMBRANE-BOUND CARBONIC ANHYDRASE AND CARDIAC pH REGULATION**

**J I Vandenberg, N D Carter**, A A Grace
Department of Biochemistry, University of Cambridge and
*Medical Genetics Unit, St George's Hospital Medical School

We have previously shown that the CO₂/HCO₃⁻/buffer system contributes to pH regulation in the heart both during normal perfusion and during perfusion after myocardial ischaemia. Carboxic anhydrase (CA) was recently demonstrated to be present in mammalian cardiac muscle. The aims of this study were to determine the functional location of CA in cardiac tissue (i.e. intracellular versus extracellular) and whether CA in the heart contributes to pH recovery following reperfusion of the ischaemic myocardium.

In the Langendorff-perfused ferret heart, switching perfusion between a 25 mM HCO₃⁻/5% CO₂ buffered solution and a nominally HCO₃⁻/CO₂ free HEPES-buffered solution caused a transient rise in pHₐ measured using 3¹P NMR spectroscopy, with an initial dPH/dt of 0.01±0.03 (n=9) pH units min⁻¹. In the presence of the membrane permeable CA inhibitor, 6-ethylxazolimide, initial dPH/dt was reduced to 0.28±0.02 pH units min⁻¹ (n=5, p<0.05, vs. control) and in the presence of the membrane impermeable inhibitor, 2-benzene sulfonamido-1,3,4-thiadiazol-5-sulfonamide (CL-11,366) it was reduced to 0.22±0.04 pH units min⁻¹ (n=5, p>0.05 vs. control). During perfusion, after myocardial ischaemia, recovery of pHₐ (controls: dPH/dt = 0.21±0.01 pH units min⁻¹, n=9) was significantly enhanced in the presence of both 6-ethylxazolimide (0.17±0.01 pH units min⁻¹, n=6) and CL-11,366 (0.15±0.02 pH units min⁻¹, n=5). These results demonstrate that the heart contains CA, that it is accessible to both membrane permeable and membrane impermeant inhibitors (consistent with an extracellular location for CA in the heart) and that CA facilitates pHₐ recovery after reperfusion of the ischaemic myocardium.

### (39) POSTER

**BASAL RELEASE OF ENDOTHELIN FROM ENDOCARDIAL ENDOTHELUM DELAYS ONSET OF MYOCARDIAL RELAXATION**

H G Evans, M J Lewis, A M Shah
Cardiovascular Sciences Research Group, University of Wales College of Medicine, Cardiff, CF4 4XN.

In both isolated myocardial preparations and in intact hearts, the endocardial endothelium (EE) releases agents which influence myocardial contraction. We have recently reported that unstimulated cultured EE cells release endothelin basally. In the present study, we investigated the contractile effects of endothelin released from EE in situ in ferret papillary muscle preparations (0.1±0.1 nM, low P20, 30sec, but also high P20, 100sec, low with indoethacin 10mM and acetobolitin 1mM). Incubation of EE-intact muscles with the specific ETA receptor antagonist, BQ123 (10μM) for 1h, resulted in characteristic effects of endothelin release, both the time to onset of relaxation and the time to 50% tension decline were reduced (-12.3±1.8% to -13.7±1.1%; both p<0.01; n=6), but there was no change in peak tension (-2.2±2.6%, or in rate of tension development (7±2.3%, both p>ns). In EE-damaged muscles (1sec exposure to 0.5% Triton X-100), 1h exposure to BQ123 produced no significant change in any of the parameters (eg. time to onset of relaxation -2.6±0.9%; time to 50% tension decline -4.8±1.1%; p=ns; n=6). We have previously reported similar myocardial relaxant effects with interventions that raise cyclic GMP content, eg. nitric oxide. However, BQ123 caused no change in cyclic GMP content (radioimmunoassay), either in EE-intact or EE-denuded muscle groups (303±287; 248±242 respectively, both p=ns). Thus, suggesting a significant role of cyclic GMP in the effects of BQ123. These data suggest that (1) EE in situ releases endothelin basally, resulting in delayed onset of myocardial relaxation, without change in the synthesis phase of twitch contraction. (2) This suppression, there is no evidence for significant endothelin release from microvascular endothelium within the myocardium. Endothelin released by EE may exert significant para-cardiac myocardial contraction, independent of any local vasocostructor activity.

### (40) POSTER

**ENDOGENOUS NITRIC OXIDE ENHANCES LEFT VENTRICULAR RELAXATION IN THE ISOLATED HEART**

R M Grocott-Mason, P B Anning, M J Lewis and A M Shah
Cardiovascular Sciences Research Group, University of Wales College of Medicine, Heath Park, Cardiff.

Nitric oxide (NO) modulates relaxation of isolated myocardial preparations. We recently reported that the exogenous NO-donor, sodium nitroprusside (SNP) selectively enhanced early left ventricular (LV) relaxation in the isolated ejecting guinea pig heart, independent of increases in coronary flow (CF). In the present study we examined the effects of endogenous NO on LV performance in the same preparation (constant loading and heart rate; Krebs buffer + indoethacin 1μM; 37°C). LV pressure (P) was measured with a 2F Millar catheter in the LV cavity and early LV relaxation characterised by a monoeponential time constant, Te, as previously described (Br. Heart J. 83, 69, 1995). NO-donors were tested alone (BQ158, 1μM) and (ii) substance P (SubP) 0.1μM, agonists that release NO from coronary vascular endothelium. Both NO and SubP enhanced early LV relaxation without altering systolic parameters e.g. LVpmax or dPV/dmax, similar to previous findings with SNP. These effects were inhibited in the absence of hemoglobin (Hb; 1μM) which inactivates NO.

<table>
<thead>
<tr>
<th>Change NO Peak CF</th>
<th>LVpmax</th>
<th>dPV/dmax</th>
<th>Te</th>
</tr>
</thead>
<tbody>
<tr>
<td>BQ158</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SubP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>63.0±3.1*</td>
<td>-2.3±0.3</td>
<td>-3.8±1.2</td>
</tr>
<tr>
<td>9</td>
<td>74.6±2.9</td>
<td>-3.7±0.2</td>
<td>-4.6±1.1</td>
</tr>
<tr>
<td>6</td>
<td>19.9±2.2</td>
<td>-3.7±0.2</td>
<td>-3.8±1.2</td>
</tr>
<tr>
<td>1</td>
<td>11.4±0.7</td>
<td>-3.7±0.2</td>
<td>-3.8±1.2</td>
</tr>
</tbody>
</table>

These data show that [endothelium released NO selectively enhances LV relaxation in the isolated ejecting heart, in the same way as exogenous NO donors, without affecting 'systolic' performance. These LV relaxant effects could benefit pump performance during tachycardia, when elevated coronary flow increases NO release, by aiding early LV filling and increasing the diastolic interval for coronary perfusion.
(41) POSTER

THE EFFECTS OF HEAT STRESS ON CARDIAC ANTI-OXIDANTS AND RESISTANCE TO OXIDANT STRESS.
S E Seare and D M Yellon.
The Hunter Institute for Cardiovascular Studies, Division of Cardiology, University College London Hospitals, London.

Heat stress (HS) protects the heart against subsequent ischaemia-reperfusion injury. It has been proposed that the associated elevation of endogenous cardiac antioxidant activity after HS plays a major role in this protection. We have explored further the potential for HS to protect the rat heart against oxidant injury by examining (i) the effects of heat stress on myocardial glutathione levels and antioxidant activity (ii) whether changes in antioxidant status after HS can protect the heart against the oxidant stress of exogenous hydrogen peroxide (H2O2).

Twenty four hours after HS or control treatment (C), hearts (n=6 in each group) were excised and refrigerated perfused with Krebs-Henseleit buffer. An isovolumic intraventricular balloon was used to assess ventricular function. After stabilization hearts were perfused with 75 μM H2O2 at 80 minutes. Myocardial catalase activity and glutathione levels were also measured 24 hours after HS or C (n=6 in each group) using spectrophotometric assays.

Prior HS increased myocardial catalase activity by 49% (HS 26.9±2.0, C 18.1±2.6 U/gww, p<0.05), however myocardial total and reduced glutathione were both depleted by 12% (Total: HS 1.45±0.05, C 1.64±0.05, p<0.05, and GSH: HS 1.41±0.03, C 1.59±0.05, p<0.05 (μmol GSH equivalents/gww)). Administration of H2O2 resulted in a progressive decline in ventricular function after 40 minutes of perfusion in both HS and C hearts, but the HS hearts were less resistant to injury in comparison to C (p<0.05).

These results demonstrate that the rat heart is more vulnerable to the oxidant stress of exogenous H2O2 after HS. This may be a result of depletion of myocardial glutathione levels, which may be more important than the concurrent rise in catalase activity. This raises doubts concerning the relevance of enhanced catalase activity as a major component of the protection of the ischaemic/reperfused myocardium afforded by HS.

(42) POSTER

ANGIOTENSIN II DOES NOT AFFECT CARDIOMYOCYTE CONTRACTION
DC Lefroy, F del Monte, T Crake, S Harding, PA Poole-Wilson
Department of Cardiac Medicine, National Heart and Lung Institute, London.

The responses of isolated cardiac myocytes to angiotensin II (All) were measured to evaluate the direct effects of All on cardiac contraction. Ventricular myocytes were isolated by enzymatic digestion from rat and guinea pig hearts, and from failing human hearts (HV) obtained at cardiac transplantation. Human atrial (HA) myocytes were isolated from tissue obtained at routine cardiac surgery. Myocytes were electrically stimulated at 0.5Hz (rat, guinea pig and HA myocytes) or 0.2Hz (HV myocytes) and the contraction amplitudes (% decrease in cell length, mean(SD)) were measured using a video edge detection system. Measurements were made at baseline and during superfusion with 10-4, 10-5 M All. In addition, increasing concentrations of calcium (1-20 mM) were added to rat, guinea pig and HV myocytes, and 10-6 M isoprenaline was added to HA myocytes in order to determine the maximum contraction amplitude (Cmax); *p<0.05, compared to:

Baseline: 10^(-6) M All

Rat
Guinea pig
HA
HV

Baseline: 10^(-6) M All

10 5.7(3.3)% 5.6(3.3)% 14.7(2.3)%
11.8(3.1)% 1.6(1.0)% 8.5(2.6)%
12 1.7(2.1)% 2.4(1.9)% 11.2(3.8)%
1.2(1.4)% 2.2(1.6)% 8.5(2.8)%

All did not change the velocities of shortening or relaxation in any of the groups of myocytes studied. Thus, there was no significant isotropic response to All at concentrations up to 10^-5 M in rat, guinea pig, HV or HA myocytes. These results indicate that All does not have an important direct effect on cardiac contractile function in these three species.

(43) POSTER

PHOSPHOLEMMAN CHLORIDE CURRENTS ARE INCREASED BY CO-INJECTION OF PROTEIN KINASE A mRNA IN XENOPUS OOCYTES.
JP Mooney, LT Horne, JE John, KP Lu, LR Jones, JR Moorman. Indiana University and University of Virginia, USA.

Phospholemman (PLM), a 72-amino acid cardiac membrane protein, is the major substrate for phosphorylation by protein kinases in heart and is therefore of importance in the cardiac response to adrenergic stimulation. When expressed in Xenopus oocytes reconstituted in lipid bilayers, it induces a chloride current (ICl,M). To test the idea that PLM phosphorylation by protein kinase A (PKA) affects ICl,M, we compared currents in Xenopus oocytes injected with PLM mRNA alone to those recorded in oocytes co-injected with mRNA for the catalytic subunit of PKA. The figure shows leak corrected currents during voltage clamp steps from -10mV to -150mV. We found that coinjection of PKA mRNA resulted in a 17 fold increase in ICl,M. Thus, we suggest the amplitude of ICl,M is modulated by phosphorylation by protein kinase A at one or more of the 4 potential phosphorylation sites. Western blots of the membrane fraction of oocytes from each of the experimental groups suggest that the mechanism of this effect is an increase in PLM expression.

(44) POSTER

INHIBITION OF INTIMAL HYPERPLASIA BY PHOTODYNAMIC THERAPY IN THE RAT CAROTID MODEL OF ANGIOPLASTY RESTENOSIS.
I Nyamekye, S Anglin, S Bown, C Bishop J McEwan
Departments of Cardiology and Surgery, University College London Medical School, London.

Fibrocellular intimal hyperplasia (FCIH) arising from the proliferation and migration of medial vascular smooth muscle cells (SMCs), is the major cause of restenosis after angioplasty. To date no drugs have been clinically effective in its treatment. We have investigated the dose dependent effects of photodynamic therapy (PDT) on the medial SMC of the rat carotid artery. The second generation photosensitizer Aluminium disulphonated phthalocyanine (S2) in four doses (0.5, 1.0, 2.5, 5.0 mg/kg) was administered systemically followed by the local application of 80 J/cm2 of 675 nm laser energy. Cellular depletion of the treated segment occurred in a dose dependent manner 3 days after PDT, with the 2.5 and 5mg/kg doses causing total cellular depletion. 14 days after treatment there was endothelial regeneration but the media remained depleted. Medial repopulation with SMC occurred slowly over three to five months and in a few rats this was associated with minimal FCIH. Further rats underwent PDT (S2: 2.5mg/kg, Energy: 50 J/cm2) immediately following injury of the left common carotid artery with a Fogarty PE2 catheter. 14 days after injury the rats were deeply anaesthetised and then killed by perfusion pressure fixation together with appropriate controls. Using planimetry the ratio of the area of intimal hyperplasia and that enclosed by the internal elastic lamina was measured (IH/IEL) and expressed as a percent (see table below).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>IH/IEL (median+range)</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>76 (71-80)</td>
<td></td>
</tr>
<tr>
<td>S2 only</td>
<td>69 (64-75)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Laser only</td>
<td>36 (28-49)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>PDT</td>
<td>0 (0-00)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

No haemorrhage, thrombosis or aneurysm formation was seen. These results demonstrate that PDT applied at the time of angioplasty effectively inhibits the rat experimental model of FCIH. This may offer a new approach to the prevention or reduction of angioplasty restenosis.
PLATELET ENCAPSULATED ILOPROST INHIBITS INTIMAL THICKENING FOLLOWING BALLOON ANGIOPLASTY
AP Banning, MJ Lewis, H Cheadle, PJ Groves, L Brewer, N Penny, N Crawford*. Department of Cardiology, University Hospital of Wales, Cardiff and Department of Biochemistry*, Royal Free Hospital, London.

Intimal thickening following balloon angioplasty has remained largely refractory to systemic therapy. Local delivery of agents to the site of injury permits a high local drug concentration with minimal systemic side effects. In this study we have exploited natural targeting of platelets to sites of vascular injury, to deliver iloprost (IL) (a stable prostacyclin analogue which inhibits smooth muscle cell proliferation in vitro). IL was encapsulated into the platelet by electroporation, a technique using high voltage discharge pulses to generate transient pores in the platelet surface membrane which allow drug incorporation into the platelet cytosol. Pig (n=30), randomised to receive either IL-loaded or sham-loaded (electroporation alone) platelets, underwent bilateral carotid angioplasty using the proximal balloon of a 4-lumen-dual-balloon catheter with intervening delivery ports. The site of injury, isolated by inflation of both balloons at low pressure for 10 minutes, received 0.8ml of autologous platelets. Carotid arteries were removed at 7 days (n=10 sham, 10 IL) or 21 days (n=20 sham, 20 IL) and sections taken for histology (n=6 each artery Van Giesen stain) and planimetric analysis. Rupture of the internal elastic lamina (IEL) is associated with increased intimal thickening and arteries were therefore classified as either intact IEL or ruptured IEL. In arteries with intact IEL, morphometric parameters were similar in the 2 groups at 7 days; however at 21 days, IL significantly reduced both intimal area (0.115±0.01 vs 0.16±0.02mm², mean±SEM p<0.05) and intimal/media ratio (0.029±0.003 vs 0.04±0.005, p<0.05). In arteries with ruptured IEL, no significant differences were observed between the 2 groups. We conclude 1) that intimal thickening following balloon angioplasty is reduced by locally delivered IL, 2) that these beneficial effects are overwhelmed in the presence of severe balloon injury, and 3) that drugs can be applied locally to the site of injury in vivo using electroporated platelets.

REGIONAL LEFT VENTRICULAR FUNCTION DURING DOBUTAMINE INFUSION IN PATIENTS WITH ISCHAEMIC HEART DISEASE PRE AND POST ANGIOPLASTY
SP Karwatowski, NA Chronos, SM Fuhr, RH Mohiuddin, GZ Yang, DN Firmin, NP Buller, SR Underwood. Royal Brompton National Heart and Lung Hospital, London.

In patients with ischaemic heart disease increased myocardial workload may exacerbate rest abnormalities of ventricular wall motion and induce new ones. We used magnetic resonance velocity mapping (MR) to study regional ventricular long axis function at rest and during symptom limited dobutamine infusion. Twenty five patients with ischaemic heart disease (7 with prior infarction) were studied. MR cine velocity information was acquired through a basal short axis plane and during "low" (5 or 7.5 μg/kg/min) and "high" (10 or 15 μg/kg/min) dose dobutamine infusion. The resulting velocity data was divided into 16 sectors providing regional long axis ventricular wall velocity. Maximal early diastolic long axis wall motion was measured and standardised to the baseline value allowing comparison between stages of stress. Velocity profiles in controls during dobutamine infusion were ranked and a regional reduction of 30% from baseline was defined as abnormal. Five patient studies were unusable due to artefact. Patients without effort angina did not develop reductions in long axis velocity. Of 15 patients with effort angina 8 developed reductions in mean peak long axis velocity during stress, 2 more developed abnormal regional reductions, 1 patient developed improved wall motion in an area proximal at rest. Regional abnormalities was significantly more likely to be detected in patients with anterior ischaemia than inferior ischaemia (χ² statistic 4.5 p<0.05). Eight patients had a repeat study after angioplasty. 4 out of 5 patients with improved exercise tolerance did not develop further deterioration during dobutamine infusion, the others showed no change in their response. MR velocity mapping with dobutamine infusion is a useful technique for studying the effects of increased myocardial workload on regional and global ventricular function.
POSTER

ISCHAEMIC CHANGES DURING CORONARY ANGIOPLASTY USING PERFUSION AND STANDARD BALLOON CATHERETERS
L K Michalis, M R Thomas, S Thomas, M J Monaghan, D E Jewitt
Cardiac Department, King's College Hospital, London.

It has been suggested that perfusion balloon catheters decrease the ischaemia induced by balloon inflation during coronary angioplasty (PTCA). We have compared the ischaemic effect during the first balloon inflation of a new autoperfusion monorail catheter (Speedflow, Schneider) versus a standard monorail catheter. The ischaemic indicators used were: a) the time to development of ischaemia (chest pain, surface ECG changes, echocardiographic wall motion abnormalities) and b) the degree of ischaemia (echo index wall motion abnormalities score). Fifty consecutive patients with proximal coronary artery stenoses and neither resting echo wall motion abnormalities nor angiographic collateral circulation were randomly allocated to PTCA using either the perfusion (25 patients / 27 lesion [Group A]) or a standard balloon (25 patients / 30 lesions [Group B]). In Group A the guide wire was withdrawn proximally during the inflation, thereby optimising distal blood flow. Group A and Group B were compared during the balloon inflation for the time (mean +/-SD): to: chest pain (64.5 +/-83.5 vs 78.1 +/-55.8), surface ECG changes (79.1 +/-84.1 vs 30.4 +/-5.7), echo wall motion abnormalities (30.0 +/-18.7 vs 28.5 +/-20.4) and echo index score (1.6 +/-0.8 vs 1.8 +/-0.7). None of these ischaemic indicators were significantly different in the 2 groups. In conclusion the monorail perfusion balloon catheter does not reduce the myocardial ischaemic burden and therefore does not offer any myocardial protection during PTCA.

POSTER

CORONARY ANGIOPLASTY IN PATIENTS 70 YEARS OF AGE OR OLDER: TWELVE YEARS EXPERIENCE
Department of Cardiology, Guy's Hospital, London.

Surgical revascularization in the elderly is associated with a higher mortality and morbidity, and previous reports on the efficacy of coronary angioplasty have shown conflicting results. We report on the acute and long-term results in 163 consecutive patients aged 70 years and older (mean age 73, 63% male) who were treated over a 12 year period. Angiographic success was achieved in 86% and clinical success in 82%. Complications included 4 deaths (2.4%), 3 myocardial infarctions (1.8%), and 5 (3.1%) emergency bypass surgery. Patients with impaired left ventricular function had a significantly lower clinical success rate (70% versus 91%, p<0.001) and a trend towards a higher complication rate (12% versus 4%, p=0.06).

Complete follow-up data was available (median 35 months, range 2 to 146 months). During follow-up 16 patients (10%) died, 2 (1%) had myocardial infarction, 12 (7%) underwent elective bypass surgery, and 24 (15%) had repeat angioplasty. Although revascularization was only complete in 43%, the cumulative probability of survival was 90.7% (SE 2.4%) and 83.4% (SE 3.7%) at one and five years, respectively. The one and five year freedom from death, myocardial infarction, bypass surgery, and repeat angioplasty were 68.2% and 56%, respectively.

Multiple proportional hazards regression analysis identified incomplete revascularization as the only independent predictor of poorer overall survival (p=0.005) and event free survival (p=0.001). At 1 year, of the 143 survivors 75 (52%) were asymptomatic and only 7% (compared of grade 3/4 angina (p<0.001). Conclusion: Coronary angioplasty can be performed safely in the elderly and provides good symptomatic relief and favourable long-term outcome. Complete revascularization may not be necessary if the primary goal was to achieve symptomatic relief but at the expense of a higher incidence of late cardiac events and a less favourable long-term survival.

POSTER

COMPARISON OF CLINICAL OUTCOME AFTER ELECTIVE AND "BAIL-OUT" CORONARY STENT INSERTION.
N M K Robinson, M R Thomas, D E Jewitt, R J Wainwright.
Department of Cardiology, King's College Hospital, London.

Coronary stents may be used electively or as a "bail out" device during PTCA. We report the clinical outcome of elective and "bail out" stenting in 56 patients (67 Palmaz-Schatz stents). Stents were deployed as "bail out" in 41 patients (abrupt vessel closure [AVC] in 15 and threatened closure [TVC] in 26) and electively in 15 patients. Major in hospital complications were as follows (NB: may be >1 event/patient):

<table>
<thead>
<tr>
<th></th>
<th>Elective</th>
<th>TVC</th>
<th>AVC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0/15 (0%)</td>
<td>0/26 (0%)</td>
<td>2/15 (13.3%)</td>
</tr>
<tr>
<td>CABG</td>
<td>0/15 (0%)</td>
<td>2/26 (7.7%)</td>
<td>6/15 (40%)</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>0/15 (0%)</td>
<td>0/26 (0%)</td>
<td>3/15 (20%)</td>
</tr>
<tr>
<td>MI</td>
<td>1/15 (6.7%)</td>
<td>1/26 (3.8%)</td>
<td>5/15 (33.3%)</td>
</tr>
</tbody>
</table>

Subsequent out of hospital events were infrequent in both groups over a 6 month follow up period. No patients died or had CABG. One patient in the "bail out" group had an MI (late stent thrombosis). Two patients from each group had repeat angiography because of recurrent chest pain (see Kaplan-Meier Event Free Survival Graph below).

In conclusion "bail out" stenting, particularly for abrupt vessel closure, has an increased incidence of in-hospital complications compared to elective procedures. If these short term problems can be overcome, however, the clinical events in the first 6 months after leaving hospital are low and similar to patients undergoing elective procedures.

POSTER

PERCEIVED CHEST SYMPTOMS AFTER ANGIOPLASTY
TY Huehns, S Dubrey, EMS Garcia, KJ Beatt
Academic Medicine, Charing Cross and Westminster Medical School, London.

After coronary artery bypass grafting (CABG), many patients experience chest pains which are atypical for angina. These symptoms may be disabling and may last for years. Most have been attributed to chest wall disruption; some may be related to increased awareness of normal chest feelings. Over a three year period, 365 patients (pts) underwent angioplasty at this centre. Follow-up by questionnaire was undertaken to establish the incidence of chest discomfort at a mean of 20 (range 6-44) months after angioplasty. Patients with chest pain were asked to describe the type of discomfort experienced. Descriptions suggesting ischaemic chest pain were coded by an experienced clinician into Canadian Classification Scores (CCS) and atypical symptoms were also graded. At follow-up, only 0.6% of patients had regular angina (CCS 3), 21% had occasional angina (CCS 1 or 2), and 71 pts (20%) perceived chest symptoms that were considered to be atypical chest pain (ACP). In most cases the chest pain was not disabling (55 pts, 92%) but in 6 it was restricting lifestyle (8%). Nineteen (27%) of the patients with ACP at follow-up had undergone repeat angiography (11 of these had restenosis); seven patients with ACP had CABG during follow-up. Thirty-four patients with ACP had undergone exercise testing (12 positive, 22 negative), the result did not influence whether they subsequently went on to have reangioplasty or CABG. In conclusion, atypical chest pain occurs after coronary angioplasty; in most cases it is not disabling and may be related to increased awareness of normal sensations. Non-invasive tests have limited value in discriminating between atypical chest pain and angina after angioplasty and it may be necessary to perform further invasive study; however, despite reintervention, atypical chest pain commonly persists.
**Post 1**

**EARLY CLINICAL EXPERIENCE WITH A COMBINED CORONARY ANGIOPLASTY AND INTRA-LUMINAL DRUG DELIVERY DEVICE**

J Gunn, D Tsakaditis, A Ahsan, S Arafa, L Rowlands, R Bowes, D Cumberland. Deps of *Haematology and Cardiology, Northern General Hospital NHS Trust, Sheffield*

**Introduction**

The Trans-Coronary balloon/stent/infusion catheter (Cardiovascular Dynamics) comprises an inner conventional angioplasty balloon (2.5-3.5 mm diameter) and an outer porous balloon (36-48 holes 2.5-3.5 mm diameter). The 0.014 inch guidewire compatible, with shaft diameter 2.7F, of ‘over-the-wire’ construction. Fluid may be infused intraluminally, with inner balloon deflated, at 2.5-6.0 ml/min at 1-3 ATM.

**Methods**

We deployed this catheter in 12 patients with lesions suitable for angioplasty. Nine had unstable angina, 5 with angiographic thrombus. In the 9 unstable lesions it was used in its dual role. After premedication with aspirin 300mg and heparin 10,000u, 2-5mg (2-5ml) tissue plasminogen activator (tPA) was infused at the lesion before (6) or between (4) inflations. Peripheral blood mean (SD) fibrinogen (F) and plasminogen (P) pre and post tPA were:

<table>
<thead>
<tr>
<th></th>
<th>Pre 20 min</th>
<th>60 min</th>
<th>240 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>F (g/l)</td>
<td>3.1 (1.0)</td>
<td>3.2 (1.0)</td>
<td>3.1 (1.0)</td>
</tr>
<tr>
<td>P (mg/l)</td>
<td>92 (16)</td>
<td>84 (13)</td>
<td>89 (20)</td>
</tr>
<tr>
<td>T (10^-7)</td>
<td>17 (9)</td>
<td>22 (12)</td>
<td>25 (14)</td>
</tr>
</tbody>
</table>

**Results**

As shown in the table, there was no significant change in these parameters after local delivery of tPA. Also there was no thrombosis, embolism, dissection, perforation, myocardial infarction or death. In four cases needed deployment of balloon stent then only (1) or CAEB (2). All 12 patients left hospital well.

**Conclusion**

Intra-luminal drug delivery and balloon dilation with a combined catheter is safe and feasible. This approach has potential in acute coronary thrombosis. When tPA-2.5mls infused intraluminally peripheral complication parameters are unaltered. The technique may ultimately prove useful in the local delivery of agents to prevent restenosis.

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**Post 2**

**FEASIBILITY OF DAYCASE CORONARY ANGIOPLASTY**

M Shahi, E Skinner, D Hacker, DW Davies, RA Foale Department of Clinical Cardiology, St. Mary's Hospital, London.

With the increasing experience of cardiologists, continued improvement in technology and safety of the technique, we have examined the potential role of daycase coronary angioplasty (PTCA). During a ten month period, all patients who were to undergo emergency angioplasty were considered as potential daycase candidates. The operator was asked before the procedure began whether the patient would be suitable for a daycase PTCA, in the expectation that any patient who considered that all sheaths would be removed in 6 hours and mobilisation commenced 2 hours later. Patients would continue antiplatelet therapy post operatively in order to document whether any late occlusions or complications occurred in this group. The operators were also given the option of changing their decision after the procedure if they felt that heparin should be given overnight. Patients who were not felt to be potential daycases were given heparin overnight and observed for the 24 hour period; operators were also given the option in these patients to change their decision after the PTCA if they felt that heparin was not required overnight. 239 elective PTCA patients were assessed for the study. 137 (57%) patients (mean age 58, range 37-79 years, 119M and 18F) were initially thought to be suitable for daycase PTCA. Of these 106 had single coronary vessel disease (vd) and 31 had two vd. 122 had normal left ventricular (LV) function, 11 had impaired LV function and 3 had poor LV function. Operators changed their decision in 32 (23%) patients and decided to give overnight heparin after the procedure. Of these, 24 patients had a small local dissection at the site of the PTCA and overnight heparin was given to prevent the possibility of an early occlusion. 8 patients had procedures which resulted in extensive dissections. These were successfully treated by coronary stenting in 3 patients and by long perfusion balloon inflations in 5. Of those patients not given heparin overnight, 15% had early occlusion within 6 hours after the procedure and required further PTCA. 102 (43%) patients (mean age 61, range 34-79 years, 47M and 55F) were initially thought to be unsuitable for daycase PTCA. Of these, 36 had local dissections, 17 had vD vd and 17 had 3 vD 85 had normal LV function, 13 had impaired LV function and 4 had poor LV function. The major reasons for their unsuitability were proximal coronary disease, restenosis and patients were considered by the operators as being ‘unstable’. Operators changed their decision in 7 (7%) patients and decided not to give heparin after the procedure, usually because of an uncomplicated PTCA. 5 patients in this group had extensive dissections which were treated by emergency surgery in two, coronary stenting in one and by prolonged balloon inflation in two. There were no occlusions in the 24 hours following PTCA in this group. The results of this feasibility study suggest that with experienced operators and good case selection, daycase PTCA should be possible in a significant number of patients.

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**Post 3**

**IDENTIFICATION OF HIGH RISK PATIENTS AWAITING ROUTINE CORONARY INTERVENTION**

J Chester, N Rowland, D Senerez, JR Welsh, D Ward, J J Costa, Department of Cardiological Sciences, St. George's Hospital Medical School, London.

**Objective**

To determine whether the development of adverse coronary events (AE) in patients awaiting routine PTCA can be predicted by factors identifiable at the time of the initial angiogram.

**Patients and Methods**

119 consecutive patients awaiting angioplasty on the waiting list for routine PTCA who underwent a second comparable angiogram prior to 3 to 24 months later (132). Variables evaluated at the time of first angiography included age, previous history of MI, hypertension, smoking, diabetes mellitus, family history of CAD, clinical presentation as stable, n=97 or unstable angina, n=22) and fasting serum lipids. Lesion morphology (complex or smooth) was assessed and stenosis severity was measured using an automated edge contour detection system (CAAS). MI, unstable angina (UA) and angiographic total coronary occlusion (TDO) during follow up were recorded as AE.

**Results**

Twelve-eight patients (30%) developed one or more AE (MI, n=2, UA, n=23 & silent TCO, n=11). Multiple logistic regression analysis revealed that only raised triglyceride (TG) and UA at initial presentation were significantly associated with the development of AE. Twelve (35%) of the 22 patients with UA at initial diagnosis developed one or more AE at follow up compared to 15 (15%) of the 97 patients with stable angina at angiographic diagnosis (p<0.01), risk ratio 4.5. TG levels over 2.83 mmol/l in the patients with AE compared to 2.0 ±1 in the patients without AE, (p=0.012). Patients with trig above normal (2.21 mmol/l), were 4 times more likely to develop AE than those with normal TG. Total coronary occlusion developed in 11 patients and was strongly associated with raised plasma lipids and unstable angina at presentation. The combination of UA at initial presentation and raised plasma trig was seen in 8 patients and all developed an AE. By comparison, only 2 of 32 patients with stable angina and normal trig developed an event. Ten out of the 11 lesions that developed TCO at follow up were in patients with UA at the diagnosis.

**Conclusions**

This study suggests that 1) adverse coronary events are relatively frequent in patients placed on routine waiting lists for PTCA. 2) Unstable angina with raised basal fasting plasma triglyceride at presentation are at substantially higher risk of an AE whilst awaiting coronary intervention. 3) Complex stenosis associated with the development of TCO. Whether earlier intervention or aggressive lipid lowering therapy would improve overall outcome in these high risk groups remains to be evaluated.

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**Post 4**

**PROGRESSION OF "TARGET" AND "NON-TARGET" CORONARY ARTERY STENOSES IN PATIENTS AWAITING CORONARY ANGIOPLASTY**


Coronary angioplasty (PTCA) is now accepted as effective therapy for patients with coronary artery disease. "Target" lesions (TS) for PTCA are defined as those lesions identified as causing symptoms or as being the most recent lesion responsible for the patient's symptoms. However, myocardial infarction (MI) may occur after successful PTCA, which is not associated with restenosis, suggesting the involvement of other factors such as mild, "non-target" (non-TS), preexisting stenosis. We compared the evolution (10-26 months follow up) of TS and non-TS in 210 consecutive patients who were candidates for PTCA. After diagnostic angiography, TS and non-TS were identified and patients were on a waiting list for routine PTCA and followed up regularly until repeat angiography immediately before or within 12 months after successful PTCA if they felt they would have benefit. If they thought benefit was unlikely, they continued to be on the waiting list as a non-TS lesion. Patients were continuously reassessed. "Target" lesions were defined as 80% stenosis diameter reduction or new total coronary occlusion. 258 TS and 282 non-TS were assessed. Mean % diameter reduction of TS at study entry was 69 ± 12% diameter reduction compared with 44 ± 16% of non-TS (p<0.001). During follow up, 43 pts developed acute coronary events (MI 7 and UA 36). These were associated with progression of TS in 39 pts and of non-TS in 12 pts. Eight further pts had both TS and non-TS progression. Progression occurred in 22 TS (19 to total occlusion) and in 28 non-TS (8 to total occlusion). Seven TS and eight non-TS were lost to follow up. Baseline severity was similar in stenoses that progressed and stenoses which did not progress. Coronary events in progression of TS were similar to those associated with TS progression. Thus, even with successful PTCA to their TS lesion, a sizeable proportion of our pts would have developed serious events associated with progression of their non-TS PTCA lesions. Prevention of coronary events after successful PTCA may require measures aimed at preventing or slowing down the process that leads to disease progression.
EXERCISE ECHOCARDIOGRAPHY IS THE OPTIMAL NON-INVASIVE TEST FOR THE PREDICTION OF CORONARY ARTERY DISEASE IN WOMEN.

J Williams, D O'Gorman, R Foale, T Marwick, St Mary's Hospital London UK, and Cleveland Clinic Foundation, Cleveland, OH.

Women with chest discomfort and positive exercise tests are found to have normal coronary arteries in up to 50% of cases. A multivariate exercise score (MV) derived from ST response, heart rate and workload has been proposed to improve diagnostic accuracy in this group. The purpose of this study was to compare exercise ECG (ST), MV and exercise echo (ExE) for both the diagnosis of CAD, and ability to stratify patients for optimal use of angiography. Maximal symptom limited bicycle exercise using a 20W/min protocol was undertaken by 70 women without prior myocardial infarction (age 60±9 y). CAD was predicted by ST depression >1mm, a negative MV score, or development of new or worsening wall motion. Patients achieved 86±13% of age predicted maximum heart-rate, and an exercise capacity of 108±22Watts. Significant coronary stenoses (quantised >50%) were present in 33 pts, the sensitivity of ExE (88%) exceeded MV (61%, p<0.05) and (ST 67%, p<0.05). In 37 pts without CAD, the specificity of ExE (84%) was comparable to MV (73%, p=NS) but exceeded ST (51%, p<0.01). Pre-test probability derived from age and symptomatic status classified patients into high (HP), intermediate (IP, 20-80%) and low probability (LP, <20%) groups, with post-test probability calculated in the standard manner.

Conclusion, ExE is superior to MV and ST for the diagnosis of CAD in women. ExE appropriately and effectively stratifies patients into LP and HP groups in order to streamline selection for angiography.

ARE WOMEN WITH ACUTE MYOCARDIAL INFARCTION TREATED AS WELL AS MENS?

KW Clarke, D Gray, JR Hampton.
Cardiovascular Medicine, University Hospital, Nottingham.

Cardiovascular disease is the commonest cause of mortality in the UK and in 1991 accounted for some 68,500 female deaths. We decided to investigate whether women in our health district with acute MI differ from men. We looked at admissions with suspected MI for the years 1982-84 (pre-thrombolysis) and 1989/90 (when thrombolytic therapy was a standard part of management of acute MI). 30% of admissions in 1982-84 and 38% in 1989/90 were female; 24% (1982-84) and 33% (1989/90) of the patients with confirmed MI were women. 71% (1982-84) and 56% (1989/90) of men were admitted to CCU whereas only 48% (1982-84) and 41% (1989/90) were (p<0.001). Women were more likely to delay presentation for more than twelve hours (p<0.001) and to have a higher Killip score on admission (p<0.003). They were less likely to receive thrombolytic therapy (p<0.001), more likely to be treated with intravenous nitrates (p<0.001) and more likely to die within the first 24 hours (p<0.001). There were no sex differences in the number of patients who required temporary pacing, central haemodynamic monitoring or inotropic support.

Women are less likely to be cared for in CCU and to receive thrombolytic therapy. We appear to be putting women at a disadvantage by not giving them the same opportunity of admission to CCU as men.
(61) POSTER


GJ Clesham, S Livingstone, CM Oakley, KM Taylor. Cardiac Surgery and Cardiology, Hammersmith Hospital, London.

The UK Heart Valve Registry was set up in 1986 to establish a computerised database of all heart valve replacement operations performed in NHS hospitals. The aim of this present study was to examine the use of mechanical (MECH) and bioprosthetic (BIO) replacements in women aged between 16-40 years from Jan 1986 to Dec 1992. The use in women (F) was compared with valves used in men (M) within the same age range.

Year F-MECH(n) F-BIO(n, %) M-MECH(n) M-BIO(n, %) 1986 97 45 (32%) 166 58 (35%) 1987 90 28 (24%) 178 34 (16%) 1988 101 18 (15%) 179 26 (13%) 1989 101 15 (13%) 170 27 (14%) 1990 86 19 (18%) 166 18 (10%) 1991 79 11 (12%) 154 9 (8%) 1992 75 6 (7%) 164 9 (5%)

(equal and highly signific trend in M and F, log regression)

Age range F-MECH(n),F-BIO(n, %) M-MECH(n),M-BIO(n, %) 16-23 65 25 (28%) 208 19 (9%) 24-31 145 42 (22%) 364 44 (11%) 32-40 419 75 (15%) 605 118 (16%)

(significant and opposite trend for M and F, log regress)

Conclusions: 1) The proportion of patients aged 16-40 receiving a bioprosthetic valve has fallen in both men and women.
2) There was a greater proportional use of bioprosthetic valves in younger women, probably because of anticipated pregnancy, whereas in men aged 16-40 bioprosthetic valves were more commonly used in the older men.

(64) POSTER

REDUCED UPTAKE AND WASH-OUT OF THALLIUM IN PATIENTS WITH SYNDROME X


Patients (pts) with Syndrome X (SX) may have normal scintigraphic perfusion scans despite symptoms and reduced coronary vasodilator reserve (CVR). To assess thallium uptake and wash-out 25 pts with SX (mean age 54±7 years) and 15 sex and age matched controls (CO) were studied. Four SX pts had reversible defects and were therefore excluded. Total and mean uptake of thallium was normalized for the lung uptake and assessed from the anterior planar image acquired during tomographic acquisition. Wash-out of thallium was expressed as (Stress-Redistribution/Stress). The level of exercise, the total dose of thallium and the time elapsed between the 2 scans were similar in SX and CO.

<table>
<thead>
<tr>
<th>Syndrome X</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Stress Counts (per pixel)</td>
<td>86±20</td>
</tr>
<tr>
<td>Mean Redistribution counts</td>
<td>64.5±16</td>
</tr>
<tr>
<td>Wash-out (total heart counts)</td>
<td>0.23±0.12</td>
</tr>
<tr>
<td>Wash-out (mean heart counts)</td>
<td>0.24±0.17</td>
</tr>
</tbody>
</table>

*P<0.01 syndrome X vs controls

In conclusion, the incidence of reversible perfusion defects (16%) in pts with SX is low. SX pts with normal-appearing scintigraphic perfusion scans, however, have significantly reduced uptake and wash-out of thallium after exercise than CO. This may be the result of a reduced vasodilator reserve (or an abnormality of the myocyte potassium pump). Thallium uptake and wash-out analysis may be of value in the investigation of patients with Syndrome X.

(63) POSTER

REDUCED FREQUENCY OF CHEST PAIN IN RESPONSE TO 170-OESTRADIOL IN WOMEN WITH SYNDROME X

DC Lefroy, GMC Rosano, NS Peters, DC Lindsay, P Sarrel, P Collins, PA Poole-Wilson.

Department of Cardiac Medicine, National Heart and Lung Institute, London.

Syndrome X is the triad of anginal chest pain, a positive exercise ECG, and angiographically normal coronary arteries. The syndrome is associated with abnormal vasomotion of the coronary microvasculature in some patients. Syndrome X occurs more commonly in women and the onset is frequently around the time of the menopause. Oestrogens modulate vascular reactivity, and we have therefore tested the hypothesis that oestrogen deficiency may contribute to the pathophysiology of syndrome X in women. A double-blind, randomised, placebo-controlled, crossover trial was undertaken in 25 women (aged 57±6 years, mean±S.D.) with syndrome X. All cardiovascularly active medication was stopped, and after an initial run-in period of 4 weeks all subjects underwent two 8 week treatment periods with either placebo or transdermal 17β-oestradiol. Symptoms were recorded and maximal exercise testing was performed initially and at the end of each treatment period. The levels of circulating 17β-oestradiol during the active treatment period compared to the placebo period were 386±229 and 53±51 pm respectively. 17β-oestradiol compared with placebo caused a significant reduction in the reported frequency of chest pain (-3.6 episodes per 10 days, 95% CI 0.0 to -6.6, P = 0.045). There was no significant difference in the maximum exercise duration on treatment with 17beta-oestradiol (6.6±2.8 min) compared with placebo (6.8±2.4 min). These results indicate that 17β-oestradiol reduces the frequency of chest pain, but does not increase the maximal exercise capacity in menopausal women with syndrome X. The mechanism could relate to a differential effect of oestrogen replacement on the structural and functional coronary microvascular abnormalities in syndrome X.

(65) POSTER

CORRELATIONS BETWEEN RESTING ELECTROCARDIOGRAPHIC ABNORMALITIES AND VENTRICULAR LONG AXIS FUNCTION IN SYNDROME X.

M Y Henein, H B Xiao, X Y Jin, P A Poole-Wilson, D G Gibson. The Royal Brompton National Heart and Lung Hospital, London.

The function of the left ventricular long axis, representing the subendocardium, may be abnormal in syndrome X (SX) as in coronary artery disease. To investigate possible relations between these disturbances and the ECG in SX, we recorded 2D guided LV long axis M-frames with phonocardiograms in 50 patients (age 57±7) with chest pain, positive exercise stress tests and normal coronary arteriograms, and 21 normals (age 51±11). Long axis function was abnormal in 40/50 and the ECG abnormal in 20 SX pts. In 20 pts (type I), the onset of diastolic lengthening was delayed by >90 ms (upper 95% normal limit): 10 of these pts had reduced T wave amplitude in lateral leads. In 15 pts (type II) systolic shortening either started >135 ms after Q wave or had a component of >1 mm after A2, 7 of these pts lacked septal Q waves. 9 pts had late diastolic abnormalities only: 2 had absent septal Q waves and none had T wave changes. ECG and long axis were both normal in 10. The increased incidence of T wave changes in type I and absent septal Q waves in type II disturbances were highly significant (p<0.001 for both).

Thus: the resting ECG is closely correlated to long axis motion in syndrome X: delayed onset of relaxation with T wave changes and delayed systolic shortening with absent septal Q waves. Changes in late diastole were not associated with ECG abnormality. These so-called 'non-specific' ECG abnormalities may, in fact, provide significant pathophysiological data in syndrome X.
PSYCHOLOGICAL ASSESSMENT OF SYNDROME X PATIENTS
S D Rosen, A P Corlando and P G Camici
MRC Cyclotron Unit and Royal Postgraduate Medical School, Hammersmith Hospital, London

Syndrome X is a disorder characterised by a combination of anginal pain and ischaemic-like changes in the stress ECG despite angiographically normal coronary arteries. To investigate whether these patients have a greater psychological disposition towards the reporting of symptoms and to evaluate the contribution of fatigue and hypertension to these symptoms, 26 patients (18 female, 10 male) and 17 age matched controls (12 female and 5 male) completed the following series of psychological questionnaires:

Self-reported Stress and Arousal (S&A); Vital exhaustion (Manschzh); Hypertension (Nijmegen). Anxiety (Taylor) and the Symptom Rating Test (SRT). Significant differences between patients and controls were found for: Arousal (S&A) - patients reported less than controls (6.1±4.4 vs 10.0±6.2; p=0.002).

Patients scored higher than controls for: vital exhaustion (18.7±5.9 vs 10.8±5.3, p=0.006); hypertention (13.2±6.0 vs 6.3±5.9, p<0.001); somatisation (SRT, 6.0±3.2 vs 1.9±4.2, p<0.001) and total SRT score (19.3±8.26 vs 12.21±7.32, p=0.004). There was a tendency to depression (from the SRT) in the patient group (4.5±2.6 vs 3.0±2.4, p=0.05).

No significant differences were found for assertivity, anxiety or inadequacy and re-analysis with stratification according to sex revealed no differences between male and female patients. Patients with syndrome X are more likely than controls to be exhausted, to hyperventilate and to somatise, suggesting that patients with this condition differ from controls in terms of the quality of their mental states.

Ischaemic preconditioning protects hypertrophied myocardium
M E Specchick-Dick, G F Baxter, D M Yellon
Harzer Institute for Cardiovascular Studies, University College London Hospitals, London

Research into ischaemic preconditioning has so far focused on normal myocardium. This study was designed to explore whether preconditioning (PC) could confer protection in hypotrophy (H). Hypotrophic preconditioning was induced in Sprague-Dawley rats by 4 weeks administration of saline and subcuteaneous deoxycoorticosterone acetate. Preconditioning was produced by 5 min coronary occlusion and 10 min reperfusion in a bolus fashion and normotensive rats. These rats and controls (non-PC) then underwent a 45 minute coronary occlusion, and 3 hr of refepusion. Infarct and risk volumes were determined by tetrazolium staining and fluorescent microspheres respectively. Infarct size was expressed as a percentage of the volume at risk (I/R%).

Heart weight in hypertensive rats was significantly greater than in normotensive rats (1.7±0.06 g vs 1.3±0.04g, p<0.05). Both infarct size and I/R were significantly lower in the preconditioned groups when compared with their respective controls. Interestingly, the reduction in I/R was significantly greater in the hypertrophied preconditioned group than the normotensive preconditioned group.

Thus we have demonstrated that preconditioning protects hypertrophied myocardium and that the protection conferred is more marked than in normal myocardium. Since hypertrophy in humans is associated with a greatly increased risk of ischaemic heart disease, infarction, arrhythmia and heart failure the manipulation of preconditioning in the clinical setting of hypotrophy is of particular interest.

Does Depletion of Endogenous Catecholamines Play a Role in the Mechanism of Ischaemic Preconditioning?
CS Leweke, J Frederic, Departments of Cardiovascular Research and Cardiology, St Thomas' Hospital, Lambeth Palace Road, London SE1

The mechanism by which ischaemic preconditioning (PC) affords protection has yet to be determined. It has been suggested that the brief episodes of ischaemia used to precondition the heart might result in depletion of endogenous catecholamines and thereby render the tissue resistant to ischaemia-induced necrosis and arrhythmias. To address this issue, isolated rat hearts were perfused with whole blood and underneath episodes of regional ischaemia and reperfusion induced with a snare around the left coronary artery. Control hearts (Group C, n=12) were subjected to 40 min aerobic perfusion, 30 min ischaemia and 10 min reperfusion. Preconditioned hearts (Group PC, n=12) were subjected to 10 min aerobic perfusion, 3 cycles of ischaemia and reperfusion (5 min each), 30 min ischaemia and 10 min reperfusion. Cardiovascular rhythm was recorded continuously, and at the end of the experiment, samples of right ventricular (RV; non-ischaemic) and left ventricular (LV; ischaemic) tissue were taken for analysis of catecholamine content. In 5 additional groups (n=group) tissue samples were taken: (i) after 10 min aerobic perfusion, (ii) after 10 min aerobic perfusion followed by 1, 2 or 3 preconditioning cycles, and (iii) after 40 min aerobic perfusion. PC resulted in reductions in the incidences of ischaemia-induced VF (from 67% in Group C to 8% in Group PC; p<0.05) and VT (from 100% to 17%, p<0.05), and the number of ischaemia-induced VPBs (from 240±25 to 5±12; p<0.08). The mean content of noradrenaline and adrenaline was higher in RV than LV tissue in all groups. Within the LV, however, neither PC nor prolonged ischaemia had any significant effect upon the tissue catecholamine content. The significant content of noradrenaline (pmol/g) was 4.1±1.1 prior to PC, 4.5±2.0 following PC and 4.8±2.0 following PC and prolonged ischaemia. These results indicate that, in the presence of blood-perfused rat hearts, the mechanism of ischaemic preconditioning is unlikely to involve depletion of tissue catecholamines.

INCREASED EXPRESSION OF CONNEXIN43 GAP-JUNCTIONAL MEMBRANE BY CARDIAC MYOCYTES IN EARLY RENOVASCULAR HYPERTENSION
S N Peters, F del Monte, K T MacLeod, N J Severs, C R Green, P A Poole-Wilson. National Heart & Lung Institute and University College, London

Ventricular hypotrophy in response to hypertension is associated with alterations in myocardial electrophysiology that cannot be explained entirely by changes in the action potential. The purpose of this study was to investigate changes in gap junction intercellular coupling as a possible factor contributing to altered myocardial electrophysiology in renovascular hypotension. The distribution and quantity of gap-junctional membrane was determined using a 2 kidney, 1 clip model in the guinea pig. At 20±7±0.9 days (mean±SD), the clipped animals (n=6) were hypertensive (blood pressure 141±12±92±9 mmHg) compared with controls (108±11±66±7; p<0.001). The heart/body weight ratio showed no significant alteration. Enzymatically-isolated ventricular myocytes were immunolabeled for the principal cardiac gap-junctional protein, connexin43. Laser scanning confocal microscopy was used to determine the volume and gap-junctional area of 6 randomly-selected cardiac myocytes per animal. The cell volumes of the hypertensive animals were not significantly greater than controls (31422±5778 vs. 25764±3695 µm3; p=0.08). Although the pattern of gap junction distribution was normal, the junctional area was substantially increased in the myocytes from the hypertensive animals (146±11 vs. 92±17 µm2; p<0.001), and remained increased when expressed per myocyte volume (0.0049±0.0008 vs. 0.0037±0.0009 µm2/µm3; p=0.03). This increase in connexin43 gap-junctional membrane area was expected to enhance intercellular coupling, reducing myocardial resistivity, and contributing to the electrophysiologic changes that occur in the early phase of the myocardial hypertrophic response.
(70) POSTER

CORONARY FLOW RESERVE IN PRIMARY AND SECONDARY LEFT VENTRICULAR HYPERTROPHY

L Choudhury, D Patel, P Nibbyanopoulos, P G Camici
MRC Cyclotron Unit and RPMS, Hammersmith Hospital, London.

Reduced coronary flow reserve (CFR), despite angiographically normal coronaries, has been documented in patients with the primary hypertrophy of hypertrophic cardiomyopathy (HCM), as well as in those with left ventricular hypertrophy (LVH) secondary to hypertension or aortic stenosis. To compare CFR and myocardial blood flow (MBF) between primary and secondary LVH, we studied 11 patients with HCM (mean age 34±11 years) and 16 with secondary LVH (mean age 64±18 years). Myocardial blood flow (MBF) was measured by positron emission tomography and H215O at baseline and following i.v. dipyridamole (Dip, 0.56 mg/kg over 4 minutes). CFR was calculated as MBF/dipyridamole/MBF-baseline. The results were compared with those obtained in a group of 21 normal controls (mean age 52±24 years; range 21-66). Results are mean±SD.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Dip MBF</th>
<th>CFR</th>
<th>Resistance (Arbitrary Units)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MBF (m/min/g)</td>
<td>MBF (m/min/g)</td>
<td>CFR</td>
<td></td>
</tr>
<tr>
<td>HCM</td>
<td>0.98±0.35</td>
<td>1.69±0.42</td>
<td>1.69±0.49</td>
<td>55±14</td>
</tr>
<tr>
<td>LVH</td>
<td>1.18±0.27</td>
<td>2.27±0.60</td>
<td>2.18±0.59</td>
<td>46±17</td>
</tr>
<tr>
<td>Normal</td>
<td>1.12±0.33</td>
<td>3.38±1.26</td>
<td>3.35±1.62</td>
<td>90±30</td>
</tr>
</tbody>
</table>

In conclusion: 1) Coronary flow reserve is significantly blunted in patients with either primary or secondary LVH compared to controls; 2) There is no difference in the severity of CFR reduction between patients with primary and secondary LVH as indicated by comparable minimal coronary resistance.

(71) POSTER

MYOCARDIAL β-ADRENOCEPTORS AND SYSTOLIC FUNCTION IN HYPERTROPHIC CARDIOMYOPATHY

L Choudhury, D Leefy, W J McKenna, C M Oakley, P Nibbyanopoulos, P G Camici
MRC Cyclotron Unit and Royal Postgraduate Medical School, Hammersmith Hospital, London

Reduced myocardial beta adrenoceptor density (BAR) has been reported in patients with dilated cardiomyopathy and heart failure. We studied 17 patients with hypertrophic cardiomyopathy (HCM), 11 of whom (mean age 37±10) had good left ventricular systolic function (group 1) and 6 (mean age 53±10) had left ventricular systolic dysfunction and heart failure (group 2). Left ventricular fractional shortening measured by echocardiography was 38±5% in group 1 and 17±6% in group 2 (p<0.001). Patients' results were compared with those in 8 normal controls, mean age 28±7 years. In all subjects, myocardial BAR density was measured by positron emission tomography with [123I]labelled CIP-121177 as the ligand. Myocardial BAR density was calculated from tissue time-activity curves of the tracer using a modification of the graphical method described by Dellorfe et al. Myocardial BAR density was 7.7±1.86 pmol/g in group 1, 5.6±0.88 pmol/g in group 2, (p=0.05 vs group 2) 1.5±0.18 pmol/g in normal controls, (p<0.0001 vs both patient groups). There were no significant regional differences in the myocardial BAR density in each of the 3 groups. Furthermore, there was a significant linear relationship (r=0.52, p=0.03) between myocardial BAR density and left ventricular fractional shortening. In conclusion: a) Myocardial BAR density is reduced in patients with hypertrophic cardiomyopathy; b) Heart failure in these patients is associated with further downregulation of myocardial BAR; c) A significant linear relationship between left ventricular function and myocardial BAR could be demonstrated.

(72) POSTER

DOES VERAPAMIL FAVOURABLY ALTER MYOCARDIAL BLOOD FLOW DISTRIBUTION IN HYPERTROPIC CARDIOMYOPATHY?

L Choudhury, M F Ryan, C A Page, H Boyd, W J McKenna and P G Camici
MRC Cyclotron Unit, Hammersmith Hospital, and Department of Cardiological Sciences, St. George's Hospital Medical School, London, UK.

Patients with hypertrophic cardiomyopathy have been shown to have reduced coronary flow reserve, as well as a reduced subendocardial/subepicardial (endo/epi) myocardial blood flow (MBF) ratio following dipyridamole (Dip) infusion. Preliminary work suggests that low doses (2.40 mg) were sufficient but not affecting total MBF and CFR in HCM, may reduce subendocardial underperfusion. We measured regional MBF at baseline and following dipyridamole infusion (0.56 mg/kg over 4 minutes), in 9 male patients with HCM before and after 4 weeks of verapamil treatment (480 mg daily) using 15O-labelled water and positron emission tomography (PET). CFR was calculated as MBF-Dip/MBF-baseline. The resolution of the PET scanner (~4mm) allowed the calculation of MBF values in the subendocardial (endo), and subepicardial (epi) regions in the thickest portion of the left ventricular myocardium, which was the interventricular septum. The endo/epi ratio was used as an index of subendocardial perfusion. The results are expressed as mean±SD.

<table>
<thead>
<tr>
<th></th>
<th>Pre treatment</th>
<th>Post treatment</th>
<th>&quot;y&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBF-baseline</td>
<td>0.79±0.23</td>
<td>0.75±0.27</td>
<td>ns</td>
</tr>
<tr>
<td>MBF-Dip (ml/min/g)</td>
<td>1.5±0.31</td>
<td>1.2±0.4</td>
<td>ns</td>
</tr>
<tr>
<td>CFR</td>
<td>1.65±0.54</td>
<td>1.7±0.51</td>
<td>ns</td>
</tr>
<tr>
<td>Endo/epi Ratio baseline</td>
<td>1.17±0.22</td>
<td>1.15±0.14</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Endo/epi Ratio Dip</td>
<td>0.87±0.22</td>
<td>0.98±0.20</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

In conclusion, while therapy with 480 mg verapamil daily does not alter total MBF and CFR in HCM, it redistributes transmural perfusion to eliminate subendocardial steal during dipyridamole infusion.

(73) POSTER

ST segment depression during ambulatory electrocardiographic monitoring in patients with hypertrophic cardiomyopathy.

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Department of Cardiological Sciences, St. George's Hospital, London.

SW17 OQT

Recent publications have highlighted ST segment depression preceding sudden death in young patients with hypertrophic cardiomyopathy (HCM). Myocardial changes suggestive of ischaemia are often present at postmortem and are considered to be of clinical and prognostic importance. Many patients with HCM have resting abnormalities on the standard 12 lead ECG and interpretation of ST segment changes is considered difficult. ST segment analysis was performed on 24-48 hour Holter recordings in 137 consecutive patients aged 65 years or less (71 male, 42 female, mean age 38±14 years). ST segment depression during normal daily activities was related to clinical features. Episodes of ST segment depression were coded as positive if ≥ 1 mm from the baseline at 60 milliseconds after the J point; ≥ 1 minute in duration and separated from other episodes by ≥ 1 minute. 92 (81%) tapes were considered suitable for ST segment analysis, 5 tapes were excluded because abnormality of the ST and or PQ segments precluded definition of the J + 60 millisecond and isoelectric points respectively. 104 episodes of ST segment depression were recorded in 16 males and 8 females (mean age 37±13 years, range 15-63 years). 16 patients had at least one episode greater than 2 mm from baseline (total 46 episodes), 14 had more than one episode. In patients aged less than 30, ST segment depression was associated with a history of exertional chest pain (6 of 10 with versus 2 of 22 without pain; p=0.002), and dyspnoea NYHA class II/III (7 of 14 versus 1 of 18; p=0.007). ST segment depression was not associated with markers of increased risk of sudden death (syncope, family history of sudden death or VT on Holter). In summary this study establishes the feasibility of ST segment analysis on ambulatory electrocardiographic monitoring in HCM and demonstrates an association between chest pain and ST segment change in young patients.
COMPARATIVE EFFECTS OF AN ACE-INHIBITOR AND A CALCIUM CHANNEL ANTAGONIST IN TRANSLATIONAL AND TRANSCRIPTIONAL EVENTS OF THE REGRESSED MYOCARDIUM.

Departments of 1Clinical Biochemistry and 2Cardiology, King's College School of Medicine & Dentistry, London.

In this study we examined at the cellular level the effects of the calcium channel antagonist, amiodipine (10 mg/kg/day), and the ACE inhibitor, lisinopril (5 mg/kg/day), in spontaneously hypertensive rats (SHR). Aged-matched, normotensive Wistar-Kyoto rats were also examined. After 8 weeks of treatment rates of protein synthesis were measured and the left ventricles dissected out and subjected to subcellular fractionation and compositional analysis. In normotensive rats left ventricle (LV) weights were reduced by lisinopril (-15%; P<0.01) (all data mean ± SEM, n = 6-9), whilst in SHR's lisinopril reduced LV weights by -26% (P<0.001). Amiodipine had no significant effect on LV weights in either WKY or SHR rats. Lisinopril in SHR rats reduced total RNA and DNA content of the left ventricle (LV), suggestive of regulation by translation (1.22 ± 0.03 mg; P<0.001, and 2.23 ± 0.07 mg; P<0.001 respectively), whereas amiodipine had no effect. Right ventricular RNA and DNA contents remained unchanged in both amiodipine and lisinopril treated SHR rats (P>0.05). Fractional protein synthesis rates (kP), RNA activity (kRNA) and cellular efficiency (kDNA) were unchanged in the LV mixed fraction, of both amiodipine and lisinopril treated SHR rats. In the LV myofibrillar fraction kP was significantly elevated in lisinopril treated SHR rats (+12%; P<0.025), suggestive of compensatory mechanisms; in all other fractions translational rates remained unchanged (P>0.05). Data for the right ventricular mixed protein synthesis rates as follows; neither drug altered kP however in lisinopril treated SHR rats kRNA increased significantly (+12%; P<0.025). Amiodipine increased kDNA rates in SHR rats (+14%; P<0.05). In conclusion, the ACE-inhibitor lisinopril regressed the hypertrophied myocardium while the effects of amiodopine appeared less distinctive.

SERUM ANGIOTENSIN-CONVERTING ENZYME ACTIVITY IN RELATION TO RISK OF PREMATURE CORONARY HEART DISEASE.


Angiotensin-converting enzyme (ACE) has recently been postulated to be involved in the pathogenesis of cardiovascular disease. To investigate the possible association with coronary heart disease (CHD), we measured serum ACE activity in 110 patients (male: 50; mean age 60 ± 10 years) with angiographically documented CHD and in 57 age-matched controls (23 men) with normal epicardial coronary arteries. All subjects were Caucasian and none were diabetic or taking ACE inhibitors. CHD patients had significantly higher serum ACE activity when compared to controls (median 46 vs 36 IU/L respectively, Mann-Whitney: p<0.0002). This association was almost entirely due to differences among subjects aged ≤56 years (n=75, median 48 vs 34 IU/L, p<0.0001). In subjects aged >55 years the association was lost (n=32, median 46 vs 34 IU/L, p=0.4). No significant correlation was found between ACE activity and conventional risk factors or sex to explain these findings. These data suggest a powerful association between serum ACE activity and the risk of premature CHD.

PROTO-ONCOGENE INDUCTION BY PRESSURE AND ANGIOTENSIN II IN THE ISOLATED WORKING RAT HEART.

C Roffe, AR MacDiamid-aod-Gordon*, V O'hian*, AM Hegerty*.
Dept. of Geiatric Medicine, Hope Hospital, University of Manchester, *Dept. of Medicine, Withington Hospital, University of Manchester, Manchester, GB.

The proto-oncogenes c-fos, c-erz and H-ras have been implicated in the development of left ventricular hypertrophy (LVH) in systemic hypertension and rise in a characteristic pattern in the hypertrophying left ventricle (LV) in the coagulation model of experimental hypertension in intact animals. However, in vivo studies do not discriminate between the direct effects of pressure and pressure independent trophic stimuli of circulating hormones like Angiotensin II (AII) on the development of LVH. To examine these influences separately we studied isolated working hearts from normotensive female Wistar rats exposed to varying afterload for 0.5,1,2 and 4h and perfused with a modified Krebs-Henseleit solution with or without the addition of AII (0.20mg/L). Proto-oncogene mRNA induction in the LV was assessed by Northern blot analysis, GADPH was used as internal control. Results: 1. The effect of increasing afterload for 1 h:

<table>
<thead>
<tr>
<th>Afterload (mmHg)</th>
<th>60</th>
<th>80</th>
<th>100</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td>c-fos/act. unit</td>
<td>1.8±0.3</td>
<td>3.9±0.4**</td>
<td>1.7±0.4</td>
<td>2.1±0.3</td>
</tr>
<tr>
<td>c-myc/act. unit</td>
<td>1.2±0.4</td>
<td>2.5±0.4*</td>
<td>1.1±0.2*</td>
<td>1.8±0.4</td>
</tr>
<tr>
<td>H-ras/act. unit</td>
<td>8.4±0.5</td>
<td>5.4±0.6**</td>
<td>8.0±0.4*</td>
<td>5.9±0.4</td>
</tr>
</tbody>
</table>

C-fos levels rose at 30 min and peaked at 1h, c-erz cttinued to rise to 4h, and H-ras was suppressed at 30 min, 1h, 2h and 4h. 2. The results for 110 mmHg afterload were similar to those for 140 mmHg.

Comments: Early molecular signals of LVH can be induced by increased pressure alone, without the mediating effects of trophic hormones. In the isolated perfused heart All does not, unlike in cultured myocytes, induce a hypertrophic partner of response, but contrast, attenuates it.

PLASMA FIBRINOGEN LEVEL AND OTHER RISK FACTOR PROFILES; ASSOCIATION WITH CORONARY ARTERY DISEASE.

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Cardiology Dept, University College Hospital, Galway, Ireland.

To evaluate the association between plasma fibrinogen (Fib) and various risk factors in coronary artery disease and their value in predicting its severity in patients with angina, 809 patients undergoing elective coronary angiography were analysed (438 males and 371 females, mean age 59.99 years). 594 patients had coronary artery disease (CAD) and 215 had normal coronary arteries (VDO). Coronary artery disease was classified as 1,2,3 vessel disease with greater than 50% luminal narrowing. Patients with CAD as opposed to VDO had significantly higher levels of Fib (3.3 ± 2.8, p<0.001) and chl/HDL ratio (7.3 ± 6.02, p<0.001). HDL was inversely related to CAD (r=0.2 ± 1.5, p<0.01). Similarly, smoking (relative risk = 1.72, p<0.001), diabetes mellitus (relative risk = 4.37, p<0.001) and family history of CAD (relative risk = 1.37, p<0.001) were significantly associated with coronary artery disease. However hypertension failed to show any statistically significant association with CAD in this study. In relation to gender, a similar trend was seen in the male subgroup as compared to the total population. In the female subgroup, all except triglycerides were significantly associated with CAD. Patients with 3 vessel disease as opposed to single vessel disease showed increased prevalence of diabetes, smoking, family history, higher levels of cholesterol (>8mmol) and Fib (>3.5gm/l). There was a linear relationship between Fib levels and severity of coronary artery disease. Plasma Fib level was significantly elevated in the presence of diabetes, hypertension and/or history of smoking.

Conclusion: This cross sectional study confirms that plasma, fibrinogen and other standard risk factors are strongly associated with coronary artery disease and can be used to predict both the presence and severity of this disease.
DIFFERENCES IN DIETARY FAT IN WHITES: BLACKS AND ASIANS: IMPACT ON PREVENTION OF CARDIOVASCULAR DISEASE

GYN Lip, I Mallik, C Luscombe, M McCarr, DG Beveridge
University Department of Medicine, Dudley Road Hospital, Birmingham B18 7QH.

The mortality and morbidity from coronary heart disease are higher in people of South Asian descent than in other ethnic groups in the United Kingdom. To investigate whether this may be related to differences in fatty food intake, we conducted a survey of food purchasing habits and food preparation methods amongst white, black and Asian households, in order to assess the average dietary fat consumption. We interviewed 224 housewives (84 white, 76 Afro-Caribbean and 72 Asian. The highest quantity of fat in foods purchased per week was found in the Asian population (median 1400g/week per person (IQR 850-1952)), which was significantly greater than Afro-Caribbean subjects, who had the lowest quantity of fat in foods purchased (1012g/week per person (IQR 835-1386)).

Mann-Whitney test: median difference 300.5, 95% CI 23.3 to 600.4, p=0.029. There was a higher quantity of fat in foods purchased per week in the lower social classes from the white and Asian populations. Butter, ghee and egg and milk consumption was significantly greater in Asians. There was also a significant difference in food preparation methods amongst whites and Asians. The most commonest was grilling, boiling or poaching; whilst amongst Asians, frying was more common (X²=81.25, d.f.4, p=0.0001). Our results indicate that there are ethnic differences in quantities of fat in foods purchased per week and in food preparation methods. This is likely to have implications for ethnic differences in fat consumption and may in part explain the higher prevalence of coronary heart disease and the greater central obesity, diabetes and insulin resistance amongst Asians in Britain. This ethnic group should be targeted for dietary intervention and other preventative measures in reducing the risks of heart disease.

A COMPARISON OF CHOLESTEROL VERSUS NO CHOLESTEROL TESTING IN A CARDIOVASCULAR SCREENING AND LIFESTYLE INTERVENTION PROGRAMME.

P A Wood, L Kinmonth, S D N Pyke and S G Thompson on behalf of the British Family Heart Study Group, Department of Clinical Epidemiology, National Heart and Lung Institute; Primary Medical Care, University of Southampton; Wolfson Research Laboratories, University of Birmingham and Medical Statistics, London School of Hygiene and Tropical Medicine, University of London, London.

The effect of cholesterol (C) versus no cholesterol testing (NC) was evaluated in a national randomised controlled trial evaluating cardiovascular screening and lifestyle intervention in 26 general practices in 13 towns across Britain. 1007 subjects (585 men and 422 women) were randomised to receive cholesterol testing (Reflotron) and 331 (190 men and 141 women) to no cholesterol testing. At one year the overall reduction in CHD risk (95SC) when comparing C with NC was 1.7% (-13.9, 15.1) for men and 0.1% (-19.2, 16.3) for women. Mean cholesterol and the proportions at high risk (≥ 6.5 mmol/l) were not significantly different for either men or women, between the groups. Reported cigarette smoking at one year and mean changes in blood pressure over a year were similar in both groups but body mass index was significantly lower (0.22 kg/m² and -0.23 kg/m² for men and women) in those tested for cholesterol. There is no evidence that cholesterol testing is associated with a greater reduction in total cardiovascular risk, mean cholesterol level or the proportion with hypercholesterolaemia in this cardiovascular prevention programme.

AGGRESSIVE CORONARY RISK FACTOR MODIFICATION CAN REDUCE CARDIOVASCULAR MORTALITY IN THE PRIMARY CARE SETTING: A PROSPECTIVE TWELVE YEAR INTERVENTION STUDY IN A PRACTICE OF 7500 PATIENTS.

J Revill, WE Rodden. Lovelweds & Batemoor Medical Centre and Barnsley District General Hospital, South Yorkshire.

Objective. To see if the long term reduction in the cardiac risk factors of hypertension and hypercholesterolaemia is practical, safe and effective in reducing cardiovascular mortality in general practice.

Methods. From 1978, patients in the practice under the age of 70, with known ischaemic heart disease (IHD), hypertension, diabetes or a strong family history of IHD were offered screening for the major correctable factors for IHD. Particular emphasis was placed on hypertension, hyperlipidaemia and the cessation of smoking. If serum cholesterol was not controlled by diet then drug therapy was introduced. The modified standardised mortality ratio trends of the practice were compared with three separate local control groups. The prevalence of fatal and non-fatal myocardial infarction were assessed as were the mortality rates from malignant disease.

Results. Over the study period, mean systolic blood pressure fell by 13.6% and mean serum cholesterol by 17.1%. By the end of the study, the prevalence of IHD in the practice had fallen to 35% of its 1980 level (p=0.024) and had fallen in comparison with the local control group (p=0.036). No excess mortality from malignant disease was seen.

Conclusions. Active correction of risk factors for IHD in a primary care setting, can significantly reduce the prevalence of fatal and non-fatal myocardial infarction. This can be achieved without any adverse effect on mortality from malignant disease.

WEIGHT CHANGE AND RISK OF MYOCARDIAL INFARCTION IN MIDDLE-AGED BRITISH MEN.

M Walker, G Wannamethee, PH Whincup, AG Shaper Department of Public Health, Royal Free Hospital School of Medicine, London NW3 2PF

Weight reduction has been shown to reduce cardiovascular risk factor levels such as blood pressure and blood cholesterol, but the longer-term consequences of weight loss on coronary heart disease (CHD) morbidity and mortality are less certain. The effect of weight changes over a five-year period on the subsequent risk of myocardial infarction (MI), fatal and non-fatal, during 6.5 years of further follow-up has been examined in a prospective study of 7735 middle-aged men, taking into account the confounding risk factors of age, social class, smoking status at baseline and five years later, blood pressure, blood cholesterol and initial body mass index (BMI), as well as pre-existing hypertension and diabetes. Analyses were restricted to the 6445 men (318 cases) who had no diagnosis of CHD at entry and no new MI event prior to weight change. Over half (56%) showed little weight change, gaining or losing less than 4% of body weight, 31% gained and 13% lost weight. The lowest risk was seen in men who gained 4-10% of body weight. Substantial weight gain (>10%) was associated with a significantly increased risk of MI, even after adjustment for confounding factors (RR = 1.53:95% CI 1.0-2.2). This was also associated with increased risk of an MI, but this increase was reduced to non-significant levels after adjustment for other factors (RR = 1.19:95% CI 0.5-2.2). While these results suggest that considerable weight gain (>10%) increases risk of CHD, they do not provide any evidence that weight loss is beneficial in middle-age and indicate the need for careful evaluation of any new health strategies relating to weight loss.
REDUCED PHYSICAL ACTIVITY IN YOUNG SOUTH ASIAN MALES: A FACTOR IN THEIR FUTURE DEVELOPMENT OF HYPERINSULINAEMIA
N Shaukat, D P de Bono
University Department of Cardiology, Glenfield General Hospital, Leicester
The prevalence of hyperinsulinaemia in the adult South Asian community is well recognised, and is thought to contribute to their excess coronary disease mortality and morbidity compared to white North Europeans. In a previous study we have documented significant differences in insulin concentrations between young (15-30 years) fifth generation South Asian and North European male offspring of patients with coronary artery disease(CAD) disease. To investigate whether community differences in insulin concentrations in this age group existed and possible explanations for such differences, we took a random population sample of 70 young South Asian males (mean(SE) age was 19.14(0.62)), 70 age matched North European males were chosen in a similar basis. In addition to conventional risk factors, physical activity was also assessed using both questionnaire (an amended version of that used in the British Regional Heart Study) and pedometer methods. Significant South Asian v North European differences existed for mean fasting insulin concentrations (13.36(0.47) v 8.31(0.32)pmol/l, p<0.001), alcohol consumption (4.6(3.83) v 10.26(9.49)ml/wk, p<0.001), waist ratio (0.86(0.09) v 0.83(0.06), p=0.01), physical activity index (R=520(0.64), p=0.002) and pedometer scores km/day (1.78(0.15) v 2.39(0.19), p=0.01). There were no significant differences between the two young groups for cholesterol, HDL cholesterol, triglycerides, mean blood pressure, diabetes prevalence and smoking rates. Insulin concentrations in both young communities were strongly correlated with physical activity (R=0.53, p=0.0001 for South Asians and R=0.47, p=0.001 for North Europeans), waist-ratio and body mass index. The development of hyperinsulinaemia seen in the South Asian community starts at a young age and is significantly contributed to by reduced physical activity.

WHO DIES FROM A HEART ATTACK - FACTORS INFLUENCING CASE-FATALITY IN MYOCARDIAL INFARCTION G. Wannamethee, PH Whincup, AG Shaper, M Walker Depuy Public Health, Royal Free Hospital School of Medicine, London
It is well established that age and previous history of a myocardial infarction (MI) are strong risk factors for fatality but little is known about other risk factors related to fatal outcome. The relationship between coronary heart disease risk factors and case-fatality, the proportion of fatal first major IHD events was examined in a prospective study of 7715 middle-aged British men. During a follow-up period of 11.5 years there were 742 major ischaemic heart disease events of which 301 (41%) were fatal. Men with previous definite MI (n=428) had a significantly higher case-fatality rate than those without (56% vs 37%). Men with a previous stroke (n=52) showed markedly higher fatality rates than those without (74% vs 40%). In men with no definite MI or stroke, the factors independently and significantly associated with case-fatality in addition to age were presence of atrial fibrillation on ECG (mainly ectopic beats/atrial fibrillation) and low levels of physical activity. Presence of arrhythmia was associated with a nearly two-fold increase in fatality rate. Moderately-vigorous or vigorous levels of physical activity was associated with a 50% reduction in the risk of death in the event of a heart attack and emphasise the importance potential of physical activity as a modifying factor in the incidence of survival in men without a previous MI or stroke.

A COMPARISON OF RISK FACTORS IN SOUTH ASIAN AND NORTHERN EUROPEAN CORONARY ARTERY DISEASE PATIENTS WITH THEIR YOUNG MALE OFFSPRING
N Shaukat, D P de Bono
University Department of Cardiology, Glenfield General Hospital, Leicester
To study whether risk factors for coronary artery disease (CAD) in patients of different ethnic groups with CAD are mirrored in their respective young male offspring, we investigated 95 consecutive South Asian (SA) male patients (mean age 55.87 years) with angiographically confirmed CAD. Nineteen male Northern European (NE) patients studied over the same period of time were matched with the SA patients for extent of coronary disease and age. Where possible one male offspring between the age of 15-30 was chosen from each SA patient, a total of 85 young South Asians (YSA) were sampled (mean age 21.61 years). Eighty-five age matched male young Northern European offspring (YNE) were also chosen from their respective parent group. There was a significant SA v NE difference for mean(SE) fasting insulin concentrations (24.74(1.48) v 15.56(1.33)pmol/l, p<0.002), triglyceride concentrations (2.07(0.16) v 2.12(0.10)mmol/l, p<0.03). 

CARDIOVASCULAR RISK FACTOR CHANGE FOLLOWING LIFESTYLE INTERVENTION IN FAMILIES
SD Pyke, D A Wood, A L Kinmonth and S G Thompson on behalf of the British Study of Heart Families.
Department of Clinical Epidemiology, National Heart and Lung Institute; Primary Medical Care, University of Southampton; Wolfson Research Laboratories, University of Birmingham and Medical Statistics, London School of Hygiene and Tropical Medicine, University of London, London.
2373 families were recruited to a national randomised controlled trial of cardiovascular screening and lifestyle intervention in 26 general practices in 13 towns across Britain. 2054 (87%) comprised both a male and female partner and amongst these 1477 (72%) were represented at screening by both partners. In line with a number of earlier studies, significant cross-sectional associations between partners were found for baseline reported cigarette smoking habit (odds ratio 6.1, 95% CI 4.6, 8.0), and for body mass index (BMI), systolic blood pressure, blood cholesterol and blood glucose (r>0.21, 0.14, 0.10, 0.13 respectively, all p<0.0001). For the first time, we have established significant longitudinal associations for changes in these risk factors. Where both partners were initially smokers, men were more than 3 times (p<0.0001) more likely to have quit where their partner had also quit. Also, amongst men who initially reported smoking, the reported quit rate was 15% where his partner smoked initially compared to 22% where she did not. The strength of these associations remained after controlling for returner bias and mis-reporting of smoking habit (CO validated). Finally, we found that men who initially stopped were more likely to return for re-screening on follow-up than women (22% vs 11% p=0.001). We conclude that there is considerable scope for cardiovascular intervention programmes to capitalise on the tendency of partners to change together and to intervene most effectively where partners habits are discordant.
(86) POSTER

RADIOThERAPY AND CARDIOVASCULAR MORBIDITY?
NE Goodfellow1, PF Currie1, RA Wright1, MJ Errington2, W Jack3, A Rodger3, U Chetty4, J Reid2, NA Boon1. Departments of Cardiology1 and Radiology2, Royal Infirmary, and Radiation Oncology3 and Surgery4, Western General Hospital, Edinburgh.

Radiotherapy (XRT) for breast cancer causes excess cardiac mortality although little is known about related cardiovascular morbidity. From 1974-9, a group of women undergoing simple mastectomy (SMX) for stage III breast cancer were randomised to receive XRT or not. After a median period of 15 years there was no difference in mortality from the malignancy or other causes. The Rose questionnaire was sent to 192 disease free women and those with symptoms were further assessed by brachial and axillary arterial Doppler studies, exercise tolerance testing (ETT) and risk factor screening. A diagnosis of ischaemic heart disease (IHD) required a positive ETT (>1 mm horizontal or downsloping ST depression analysed by an observer blinded to previous treatment) or a previous MI. Where appropriate, stress thallium testing was also performed.

Results: The age and risk factors were not significantly different.

<table>
<thead>
<tr>
<th></th>
<th>XRT (n=44)</th>
<th>p</th>
<th>XRT (n=32)</th>
<th>( \chi^2 ) TEST</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptoms</td>
<td>44</td>
<td></td>
<td>44</td>
<td>p=0.008</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>32</td>
<td></td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Positive ETT / Thallium</td>
<td>8</td>
<td>p=0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>5</td>
<td></td>
<td>3</td>
<td>(NS=p=1)</td>
</tr>
<tr>
<td>Total IHD</td>
<td>13</td>
<td></td>
<td>3</td>
<td>p=0.044</td>
</tr>
<tr>
<td>Cardiovascular symptoms</td>
<td>19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Investigations negative)</td>
<td>8</td>
<td>(NS=p=0.058)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal arterial flow (arms)</td>
<td>10/26</td>
<td>0/39</td>
<td>p=0.001</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Modern radiotherapy protocols appear to be associated with significant cardiovascular morbidity. This is due to coronary and peripheral arterial damage in the radiotherapy field. There is also evidence of excess cardiovascular symptoms in patients without objective evidence of IHD.

(87) POSTER

PERCEIVED HEALTH STATUS IN THE RANDOMISED INTERVENTION TREATMENT OF ANGINA (RITA) TRIAL.
RA Henderson, P Seed, SJ Pocock and JR Hampton for the RITA Trial Investigators.

The Randomised Intervention Treatment of Angina trial is comparing the long term effects of coronary angioplasty (PTCA) and coronary artery bypass surgery (CABG) in 1011 patients with coronary artery disease. To assess perceived health status patients completed a structured questionnaire, the Nottingham Health Profile (NHP). Part 1 of the NHP assesses six areas of perceived health, with possible scores ranging from 0 (no perceived health problem) to 100. Mean scores for part 1 of the NHP decreased between baseline and six months after revascularisation in both treatment groups, and in all six areas of perceived health:

<table>
<thead>
<tr>
<th>Part 1 NHP scores:</th>
<th>Baseline</th>
<th>Six months</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG</td>
<td>PTCA</td>
<td>CABG</td>
</tr>
<tr>
<td>Energy</td>
<td>44</td>
<td>15</td>
</tr>
<tr>
<td>Pain</td>
<td>21</td>
<td>7</td>
</tr>
<tr>
<td>Emotional reactions</td>
<td>29</td>
<td>12</td>
</tr>
<tr>
<td>Sleep</td>
<td>32</td>
<td>19</td>
</tr>
<tr>
<td>Social isolation</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>Physical mobility</td>
<td>19</td>
<td>7</td>
</tr>
</tbody>
</table>

This improvement in perceived health status was maintained two years after randomisation. Perceived problems with seven aspects of daily living (part 2 of the NHP) were also less frequent during follow-up, with no difference between the two treatment groups. However, at six months 11.2% of CABG patients and 31.5% of PTCA patients complained of angina. The NHP scores did not detect any difference in perceived health status between the two revascularisation strategies. But the NHP is not a disease specific questionnaire and may be of limited value in assessing the effects of myocardial revascularisation procedures.

(88) POSTER

ACUTE IMPROVEMENT IN PERFUSION VENTILATION MATCHING FOLLOWING PERCUSUTANEOUS MITRAL VALVOTOMY
AP Banning, NP Lewis, RJ Hall, AH Henderson. Department of Cardiology, University Hospital of Wales, Cardiff, UK.

The increased ventilatory cost of CO2 excretion on exercise (the linear VE/VCO2 slope) in chronic heart failure (CHF) represents an inadequately understood mismatch of perfusion (Q) and ventilation (V) throughout exercise. This may reflect limitations in cardiac output and pulmonary blood flow in response to exercise and/or dysfunction of the pulmonary microvessels as part of the syndrome of CHF. Mitral stenosis (MS) is a reversible cause of CHF and we have investigated the effect of successful percutaneous mitral valvotomy (PMV). Exercise VE/VCO2 was studied sequentially at 1 day to 10 weeks after PMV (n=20 mean age 58yrs). Before PMV, VE/VCO2 was inversely related to peak oxygen consumption (peak VO2) with the same slope as in CHF from other aetiologies, and to mitral valve area (MVA; Gorlin) (<p=0.01). PMV increased MVA (0.9±0.2 to 1.4±0.4cm²) and at 10 weeks exercise duration had improved (476±223 to 626±228min) with a reduction in VE/VCO2 (37±2 to 33±9, <p=0.01). The time course of this normalisation of VE/VCO2 was measured in 7 patients and shown to occur within 24hrs of PMV (40±4 to 35±2, p=0.05) with no further change thereafter. Thus patients with MS show the characteristic increased exercise VE/VCO2 slope of CHF, and this is reduced acutely by PMV. This immediate response to relief of mitral obstruction suggests that the exercise Q/V mismatch in CHF can be improved directly by improving haemodynamics and it not attributable wholly to the chronic vascular changes of CHF.

(89) POSTER

ALVEOLAR-CAPILLARY MEMBRANE CONDUCTANCE CAN PREDICT MAXIMAL EXERCISE OXYGEN UPTAKE IN PATIENTS WITH LEFT VENTRICULAR DYSFUNCTION
S Puri, B L Baker, C M Oakley, J M Hughes, J G F Cleland. Department of Medicine (Cardiology), Royal Postgraduate Medical School, Hammersmith Hospital, London.

The pulmonary diffusing capacity for carbon monoxide (DLco) is reduced in patients with symptomatic chronic heart failure (CHF), mainly due to a reduced alveolar-capillary conductance (Dm). It has been assumed that impairment of pulmonary gas exchange does not influence exercise performance, but recent reports have suggested otherwise. We measured DLco using a single breath technique, and partitioned it into its two subdivisions: Dm, and reactive conductance (0Vc, where Vc=pulmonary capillary blood volume) using the classic Roughton and Forster of measuring DLco at different inspired oxygen concentrations. 20 male patients with left ventricular dysfunction (LVD; age 58±12 years, ejection fraction 32±12%), 20 had symptomatic CHF and were treated with loop diuretics and ACE inhibitors while 10 were asymptomatic. Results were compared with 15 normal subjects (age 50±13 years). All subjects underwent symptom limited high intensity treadmill based exercise testing with respiratory gas analysis to determine maximal oxygen uptake (MVO2).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DLco</th>
<th>Dm</th>
<th>Vc</th>
<th>MVO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVD</td>
<td>7.3±2.1</td>
<td>12±4</td>
<td>67±30</td>
<td>13±5</td>
</tr>
<tr>
<td>Normals</td>
<td>10.1±2.3</td>
<td>20±6</td>
<td>68±16</td>
<td>30±8</td>
</tr>
<tr>
<td>p</td>
<td>0.0001</td>
<td>ns</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

The significant reduction of Dm in the LVD group compared to normal subjects indicates increased alveolar-capillary membrane resistance to gas exchange. This increase in resistance correlates strongly with MVO2 in our patient population (r=0.84, p=0.0001), but not in normal subjects. We conclude that alveolar-capillary membrane function is impaired and may be a significant determinant of MVO2 in patients with left ventricular dysfunction.
LONGTERM FOLLOW-UP OF PATIENTS WITH UNSTABLE ANGINA TREATED WITH IMMEDIATE PTCA

The strategy of undertaking immediate PTCA in the patient with unstable angina remains controversial. We have therefore studied prospectively a group of 252 consecutive patients with unstable angina treated with IV heparin/nitrates, presenting over a 2.5 year period who underwent diagnostic coronary arteriography followed by immediate PTCA.

Average age of the group was 56.5 (range 32-82) yrs, 196 (77.8%) were male. 51 (20.2%) had received thrombolytic, 50 (19.8%) had undergone previous CABG. A total of 393 (range 1-6, mean 1.6) lesions were dilated, single vessel in 172 (48.3%), multivessel in 54 (21.4%), and occlusions (TIMI grade 0) in 26 (10.3%). Data were analysed on an intention to treat basis. Primary angiographic success of all lesions attempted was achieved in 205 (81.3%) pts, partial success (some lesions) in 24 (9.5%) pts and failure in 23 (9.1%) pts.

Patients were followed up for a total of 667 pt/yrs (mean 2.7 yrs, range 0.3 - 8.0 yrs). Follow-up for the group was 99.6% complete. Data were analysed using the Kaplan-Meier method. Actuarial survival was 96.1 (±1.3%), 95.4 (±2.1%), 91.8 (±2.1%) and 88.7 (±3.6%) at 1, 2, 3 and 4 yrs respectively. Freedom from CABG was 81.4 (±2.6%), 77.7 (±2.6%), 72.0 (±2.6%) and 70.1 (±3.3%) at 1, 2, 3 and 4 yrs respectively. Event free survival (myocardial infarction, redo PTCA, CABG or cardiac death) was 62.5 (±3.1%), 53.5 (±3.0%) and 46.1 (±2.6%) at 1, 2, 3 and 4 yrs respectively.

Thus, these long-term results are similar to the published data relating to elective PTCA (eg CABRI, RITA), supporting our approach of undertaking immediate PTCA in the unstable patient.

CORONARY ANGIOPLASTY AND CORONARY SURGERY IN THE MANAGEMENT OF MULTIVESSEL SYMPTOMATIC CORONARY DISEASE: OUTCOMES AT 1 YEAR FOLLOWING RANDOMISATION IN THE CABRI TRIAL.
A. F. Rickards on behalf of the CABRI Investigators. The Royal Brompton Hospital, London, UK.

1054 patients (in 26 European centres) with multivessel symptomatic CAD were randomised to strategies of primary angioplasty (PTCA) or primary surgery (CABG) for the management of their disease. Patients with poor LV function (EF<35%) or recent infarcts (<10 days) were excluded. The average age of the patients was 61 years with 78% being male. The degree of coronary disease and the state of the LV was the same in both groups but the extent of revascularisation differed with an average of 2.8 grafts per patient in the CABG group and 2.1 segments per patient revascularised in the PTCA group. At one year following randomisation the data were analysed by intention to treat. 97% of the patients were alive and 87% were symptom free (Canadian Cardiovascular Society class 0/1 angina).

Variables which predicted failure of therapy (death) included a history of peripheral or cerebral disease, increasing age and decreasing EF. Negative predictors for success (class 0 angina) included pre-operative angina class and a history of infarction. The strategy of CABG or PTCA had no significant effect on outcome judged either in survival or symptomatic terms.

A QUANTITATIVE ANGIOGRAPHIC ANALYSIS OF RESTENOSIS FOLLOWING SUCCESSFUL CORONARY ANGIOPLASTY OF TOTAL OCCLUSIONS
AG Violater, R Melkert, DF Foley, D Keane, PW Serruys. The Thoraxcenter, Erasmus University Rotterdam, The Netherlands.

The aim of this study was to evaluate the long term restenosis rate following balloon dilation of coronary occlusions using quantitative coronary angiography. The study population comprised 3,081 patients prospectively enrolled into 4 major restenosis trials (MERCATOR, MARCATOR, CARPORT, PARK) (98% quantitative angiographic follow up). As the tested compounds demonstrated no angiographic or clinical benefit, data from the active and placebo groups were pooled. The study population included 244 occlusions (6.8%) and 3,305 stenoses (93.2%). The 6 month angiographic restenosis rate using the categorical approach (≥50% stenoses at follow up) was significantly higher in occlusions (44.67%, 109/244 lesions) than stenoses (32.65%, 1079/3305 lesions) (p<0.001, Relative risk 3.280, CI 2.807-5.200). Similarly the relative loss (mean ±SD) in occlusions, 0.172 ±0.276, was significantly higher than in stenoses 0.121 ±0.205, p<0.001. The higher restenosis following successful dilation of total occlusions was due to increased late occlusions in this group, 18.03% (44/244 lesions) compared to 4.72% (156/3305 lesions) for stenoses (p<0.001). When these were excluded from the analysis the restenosis rate between the two groups was similar using the categorical approach, 32.50% (occlusions) vs 29.31% (stenoses) (p=0.338, Relative risk 1.099, CI 1.002-1.164) and, using the continuous approach, the relative loss was significantly lower in occlusions, 0.066 ±0.172, than stenoses, 0.093 ±0.163, (p=0.023). Conclusion: Our results indicate that successfully dilated occlusions have a higher restenosis rate at 6 months, than stenoses. This is chiefly due to a higher rate of re-occlusion rather than long term luminal narrowing suggesting that the low loss rate in recanalised occlusions may be the result of a population subset with an intrinsic haematological or lesion propensity to acute thrombosis.

SUBCUTANEOUS HEPARIN AND ANGIOPLASTY RESTENOSIS PREVENTION: RESULTS OF A MULTICENTRE RANDOMISED TRIAL EVALUATING UNFRACCTIONATED HEPARIN.

Glycosaminoglycans of which heparin is one, are thought to play an important role in vivo in the control of smooth muscle cell (SMC) growth. We have thus evaluated the effect of unfractionated heparin (12,500 U subcutaneously, twice daily) on angiographic and clinical restenosis after balloon angioplasty. 340 patients (to demonstrate a 35% difference in angiographic restenosis) were randomised to either heparin treatment (167) or no heparin (173) with follow up at 4 months. Angiographic follow-up rate was 88%. Blinded quantitative angiographic measurement was undertaken to determine minimal luminal diameters (MLD) pre PTCA, post PTCA and at follow up. The acute gain for the no heparin group and heparin treated group was 1.08mm (0.48) and 1.05mm (0.49). At follow-up the mean (SD) loss in MLD was -0.54mm (0.59) in the no heparin group and -0.44mm (0.57) in the heparin group (treatment effect 0.13mm 95% CI -0.23 to 0.4 p=0.15. A "loss of 50% of the absolute gain" gave a categorical restenosis rate of 49% in the no heparin group and 37% in the heparin group (p=0.22). The percentage of patients in the two groups complaining of angina at follow-up was similar, no heparin group 35%, heparin group 32%. On exercise testing 60% of the heparin group and 55% of the no heparin group had a positive test (either pain or ST changes).

Despite positive results from in vitro work and animal models, unfractionated heparin at a dose of 12,500 U twice daily for 4 months does not significantly reduce the angiographic or clinical restenosis rate following balloon angioplasty.
RESULTS OF THE BENESTENT STUDY

N P Buller, K A Priestley, U Sigwart on behalf of the Benestent study group
Department of Invasive Cardiology, Royal Brompton National Heart and Lung Hospital, London.

The Benestent study is a multicenter randomised trial comparing stent implantation (Palmez Schatz) versus balloon angioplasty (PTCA) in patients (pts) with stable angina and a de novo lesion in a native coronary artery. Patient enrolment (n=520) was completed in March 1993. The clinical events during follow up (FU) were analysed according to the intention to treat principle and ranked according to the highest category on a scale ranging from death (PTCA 1, stent 2); intracranial haemorrhage (PTCA 2, stent 0); Q and non-Q myocardial infarction (PTCA 4, 6, stent 7 + 4); urgent coronary artery bypass grafting (CABG)/bailout stent (PTCA 4 + 10, stent 5 + 1); elective CABG/PTCA (PTCA 5 + 52, stent 8 + 27). The primary clinical endpoint of the study was the occurrence of any one of these clinical events and included the need for revascularisation actuated by the findings at 6 months FU. A primary clinical endpoint occurred in 84 (33%) of the pts randomised to PTCA and 54 (21%) of the pts randomised to stent implantation (relative risk 0.64, 95% confidence interval: 0.48-0.86). Quantitative coronary angiography at FU was available in 447 (96%) pts. In the per protocol analysis, the median and mean minimal luminal diameter at FU (primary angiographic endpoint) were 1.90 and 1.87 in the stent group versus 1.72 and 1.73 in the PTCA group (p=0.04) which corresponds to a restenosis rate (diameter stenosis>50%) of 20% in the stent group versus 33% in the PTCA group (p<0.002). Peripheral vascular complications necessitating surgery and/or blood transfusion occurred in 14.6% of the pts in the stent group compared to only 2.4% of the pts in the PTCA group. In conclusion stent implantation results in a superior long term clinical and angiographic outcome than PTCA in patients with stable angina. However, this is achieved at the cost of a significantly higher risk of bleeding and vascular complications and longer hospital stay.

CORONARY ANGIOPLASTY VERSUS CORONARY ARTERY BYPASS SURGERY: COST ANALYSIS BASED ON THE RANDOMISED INTERVENTION TREATMENT OF ANGINA (RITA) TRIAL.

RA Henderson, M Sculpher, P Seed, M Buxton, SJP Pocock, J Parker, M Joy and JR Hampton, for the RITA Trial Investigators.

The Randomised Intervention Treatment of Angina (RITA) trial assigned 1011 patients with coronary artery disease to treatment by coronary angioplasty (PTCA) or coronary bypass surgery (CABG). To compare the costs of the two revascularisation strategies we have analysed the use of major health service resources in the trial over two years. The assigned PTCA was done in 96.7% of patients randomised to PTCA, but 7.1% of the PTCA group underwent CABG as part of the initial revascularisation procedure. The assigned CABG was done in 97.8% of patients randomised to CABG, but 1% of the CABG patients were treated by PTCA instead. During two years follow-up the risk of subsequent interventions was:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>PTCA</th>
<th>CABG</th>
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<tbody>
<tr>
<td>Subsequent PTCA</td>
<td>17.3%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Subsequent CABG</td>
<td>12.5%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Coronary arteriography</td>
<td>31.3%</td>
<td>5.9%</td>
</tr>
</tbody>
</table>

The mean number of days in hospital up to two years after randomisation was 11.5 for the PTCA group and 16.8 for the CABG group. The estimated mean number of days on anti-anginal medication was 513 for the PTCA patients and 230 for the CABG patients. We are combining these resource use data with unit cost data from two regional cardiac centres. Preliminary cost data from a single centre demonstrate that in the RITA trial the Initial cost of a revascularisation strategy of CABG is about twice the initial cost of a revascularisation strategy of PTCA. However, over two years this cost difference decreases by approximately 50% because of the greater risk of additional procedures and use of anti-anginal medication amongst the PTCA patients.

INCREASED QT DISPERSION RELATES TO SYNCPE IN PATIENTS WITH IDIOPATHIC VENTRICULAR TACHYCARDIA

JS Gill, O Antтонене, DE Ward, AJ Camm, Cardiological Sciences, St George’s Hospital Medical School, London.

Increased QT interval and QT dispersion are both risk factors for sudden cardiac death, however, importance of QT dispersion in patients with idiopathic ventricular tachycardia (VT) is unknown. This study examines QT dispersion in patients with idiopathic VT in relation to the presence of syncope associated with arrhythmia.

Methods: 60 patients with VT associated with a 'clinically normal' heart were studied (mean age 33±15.3 years, 34 males). The resting 12 lead electrocardiogram was enlarged (x+4) and the QT interval measured in as many leads as possible (Mean 9). The maximum (QTcmax), and minimum (QTcmin) corrected QT intervals ( Bazett’s formula), corrected QT dispersion (QTcD) and adjusted QT dispersion (AQTCD) were calculated.

Results: Patients with a history of syncope associated with VT when compared to those without syncope had a greater QTcmax, QTcD and AQTCD, but the QTcmin did not differ. Patients with syncope had faster clinical VT and more had sustained VT (Table).

<table>
<thead>
<tr>
<th>No Syncope With Syncope</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>QTcmax (SD) ms</td>
<td>439.7 (37.1) vs 470.5 (39.1)</td>
</tr>
<tr>
<td>QTcmin (SD) ms</td>
<td>378.2 (29.3) vs 378.0 (28.5)</td>
</tr>
<tr>
<td>QTcD (SD) ms</td>
<td>61.6 (26.0) vs 92.5 (47.2)</td>
</tr>
<tr>
<td>AQTCD (SD) ms</td>
<td>12.4 (8.4) vs 30.4 (15.5)</td>
</tr>
</tbody>
</table>

Conclusions: We conclude that patients with syncope associated with idiopathic VT have increased QT dispersion, faster tachycardia and more patients have sustained arrhythmia. Increased QT dispersion may be a fundamental mechanism in the genesis of rapid VT in a subset of these patients.

PREDICTORS OF SUCCESSFUL RADIOFREQUENCY ABLATION FOR RIGHT VENTRICULAR OUTFLOW TRACT (RVOT) TACHYCARDIA

P A Boreham, R A Leather, G D Young, J Yeung-Lai-Wah, C R Kerr, University of British Columbia, Vancouver, Canada.

Radiofrequency (RF) catheter ablation is an effective therapy for RVOT VT. Two techniques, earliest endocardial activation (EA) and pace mapping (PM) were used to guide the delivery of RF energy. In this study, we report the various aspects of EA and PM that predicted success of RF ablation for RVOT VT in 14 consecutive patients.

Methods: At sites of RF delivery a 12 lead ECG was recorded during pacing from the distal electrode of the map/ablation catheter. This was compared with the ECG of clinical VT for concordance of: i) QRS vector in all leads, ii) amplitude of positive/negative deflections in standard leads, iii) morphology of QRS complex in all leads, iv) preordial transition. Timing of local EA recorded by the ablation catheter was compared with onset of QRS complex of the surface ECG.

Results: 13 of 14 pts were successfully ablated. The 13 successful (sucess) sites were compared to 38 unsuccessful (unsucess) sites. At least 3 PM criteria were met at all suc succ sites vs 4/38 unsucc sites. All suc succ sites had 100% concordance for both QRS vector and preordial transition. Non identical QRS morphology of the PM was present at 2 suc succ sites. EA of ≥25msec pre-QRS was seen in 9/13 succ vs 6/38 unsucc sites (p<0.01). Mean EA was 24±10 msec at suc succ sites vs. 9±13 msec at unsucc sites (p<0.05). A combination of ≥4 PM criteria and EA of ≥25msec pre QRS was seen only at succ sites. There was no difference between the energy used at succ sites (725±415 watt.sec) vs. unsucc sites (857±330 watt.sec) (p=0.47).

Conclusion: Identification of earliest EA or PM alone can predict successful ablation of RVOT VT. The combination of EA plus PM results in a high rate of successful ablation.
CATHETER ABLATION FOR SUCCESSFUL MANAGEMENT OF LEFT POSTERIOR FASCICULAR TACHYCARDIA. AN APPROACH GUIDED BY RECORDING OF FASCICULAR POTENTIALS

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Department of Cardiological Sciences, St George's Hospital Medical School, London

Six consecutive patients (mean age 27 years, range 16 to 39 years) with ventricular tachycardia originating from the left posterior fascicle, underwent electrophysiology study and detailed mapping of endocardial activation. They were successfully treated with low-energy DC current or radiofrequency current ablation. The selection of ablation sites in five of the patients was based on the recording, during left posterior fascicular tachycardia and sinus rhythm, of a descrete potential preceding the earliest ventricular tachycardia and which was thought to represent conduction through the posterior fascicle. The average fluoroscopy and procedure times were 21 min (range 6 to 32 min) and 116 min (range 50 to 176 min) respectively. In a follow-up period of 2 to 8 months, five of the patients were asymptomatic and the remaining had minor symptoms. No patient had any change in intraventricular conduction.

These data suggest a specific anatomical substrate in the mechanism of left posterior fascicular tachycardia. Fascicular potentials can be reproducibly recorded in left posterior fascicular tachycardia and may serve as a reliable marker for successful ablation procedures.

ASSESSMENT OF HEART RATE VARIABILITY IMMEDIATELY BEFORE THE ONSET OF SPONTANEOUS IDIOPATHIC VENTRICULAR TACHYCARDIA

L Fei, DJ Statters, M Malik, AJ Camm
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It has been shown that decreased heart rate variability may be associated with a propensity to ventricular tachyarrhythmias. However, it is still disputed whether there is an abrupt change in heart rate variability before the onset of ventricular tachyarrhythmias. This study aims to assess heart rate variability immediately before the onset of episodes of spontaneous ventricular tachycardia. In this study twenty three patients with symptomatic idiopathic ventricular tachycardia underwent 2 channel 24 hour Holter monitoring in a drug free state. Spectral heart rate variability was computed as low (LF, 0.04 - 0.15 Hz) and high (HF, 0.15 - 0.40 Hz) frequency components at 2 minute intervals over a one hour period immediately prior to the onset of ventricular tachycardia and over the total 24 hour recordings.

Seventy one episodes of ventricular tachycardia were studied in 23 patients. There were no significant differences in the LF, HF or LF/HF ratio for the hour immediately prior to the onset of ventricular tachycardia compared with the averaged values for the 24 hour period. However, the LF/HF ratio was significantly higher during the last few minutes (7.22 ± 4.07 minutes) prior to the onset of ventricular tachycardia than for the whole 24 hours (1.67 ± 0.63 vs 1.24 ± 0.60, p < 0.001). This increase in the LF/HF ratio was largely due to a decrease in the HF value (4.70 ± 1.15 vs 5.10 ± 1.06 in [ms²], p = 0.001) since there was no significant change in the LF value (6.37 ± 1.20 vs 6.34 ± 0.91 in [ms²], NS) compared with the averaged values for the entire 24 hour period. During the last few minutes prior to the onset of ventricular tachycardia, the differences in the LF, HF and LF/HF ratio were not statistically significant between sustained and non-sustained ventricular tachycardia nor between patients with ventricular tachycardia inducible by programmed electrical stimulation and those with non-inducible ventricular tachycardia.

We conclude that there is an abnormal autonomic influence on the heart during the last few minutes preceding the onset of episodes of idiopathic ventricular tachycardia. This seems to result mainly from impaired vagal activity rather than enhanced sympathetic input to the heart.

INITIATION OF EXERCISE-INDUCED ARRHYTHMIA IN PATIENTS WITH IDIOPATHIC VENTRICULAR TACHYCARDIA

Cardiological Sciences, St George's Hospital Medical School, London.

Initiating sequences for ventricular tachycardia (VT) can suggest the underlying arrhythmogenic mechanisms. Initiating sequences for exercise-induced idiopathic VT were examined in thirty two pts (18 males, mean age 33 ± 3.2 (SD) years, with exercise-induced VT in the absence of clinical cardiac abnormality. Patients were divided into 2 groups on the basis of the VT initiating sequence: 1) the long-short sequence of RR intervals prior to the onset of VT (initiating/pre-initiating cycle length ≤0.76) and 2) absence of cycle length changes prior to VT.

Results: VT axis was inferior in all patients of group 2 (p=0.02), and in patients with VT on Holter monitoring, no patient had sustained VT in group 1. Sustained (sust) monomorphic VT could not be initiated by programmed ventricular stimulation (PVS) in any of the patients in group1.

Conclusions: The results demonstrate that at least two different arrhythmogenic mechanisms exist in patients with idiopathic VT suggesting that these form a heterogenous group.

COMPLEX VENTRICULAR ARRHYTHMIAS IN ELITE ATHLETES

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A number of athletes who die suddenly have findings of only concentric left ventricular hypertrophy (LVH) at post mortem examination. It has been postulated that this physiological hypertrophy, a result of prolonged training may cause an increase in ventricular arrhythmias, as LVH does in hypertensives. In order to investigate this we have examined 18 male athletes likely to have the biggest hearts: endurance athletes, including rowers who have reached the highest competitive standard (international, the majority being olympic representatives). They each underwent 2D guided M-mode echocardiography and 24 hour Holter monitoring. These were compared with 18 untreated male hypertensives matched for left ventricular mass index (LVM) and also 11 male normotensive controls.

<table>
<thead>
<tr>
<th>Table: MeanSD</th>
<th>Athletes</th>
<th>Hypertensives</th>
<th>Normotensives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>28±8</td>
<td>39±12*</td>
<td>38±11*</td>
</tr>
<tr>
<td>LVM (g/m²)</td>
<td>158±44</td>
<td>152±47</td>
<td>103±32*</td>
</tr>
<tr>
<td>LVID (cm)</td>
<td>5.7±0.6</td>
<td>5.1±0.5*</td>
<td>4.9±0.5*</td>
</tr>
<tr>
<td>PWT (cm)</td>
<td>1.1±0.2</td>
<td>1.2±0.2</td>
<td>0.9±0.2</td>
</tr>
<tr>
<td>BP (mmHg)</td>
<td>118±17/77±6</td>
<td>160±13/95±72</td>
<td>118±17/73±6</td>
</tr>
<tr>
<td>24hr VE total</td>
<td>10±20</td>
<td>19±51</td>
<td>30±76</td>
</tr>
<tr>
<td>Lown Score</td>
<td>5/0/0/0/0/0</td>
<td>11/0/0/1/1*</td>
<td>6/0/0/0/0/0*</td>
</tr>
</tbody>
</table>

*p<0.01 compared with athlete group

Although total 24 hr ventricular ectopic (VE) count was similar in all 3 groups, arrhythmia complexity was greater in the athletes than the other 2 groups. This is due to the relatively large number with multifocal (grade 3) VEs. No athlete had a VE pair or ventricular tachycardia. Whether complex arrhythmias in athletes are significant is as yet unknown.
THE IMPLICATIONS OF SCREENING FOR ATRIAL FIBRILLATION IN GENERAL PRACTICE.
E Southall, C M Carey, N G Dewhurst.
Mayfield Medical Centre, Paignton.
Torbay Hospital, Torquay.

Atrial Fibrillation (AF) considerably increases the risk of stroke and accounts for 7-31% of strokes in patients over the age of 60 years. Recent studies have provided new evidence concerning the risk-benefit ratio of anticoagulant therapy in patients with AF. To examine the prevalence, underlying cause and potential implications of the diagnosis of AF we embarked on a screening programme using an echocardiographic test in patients aged 65-75 in a general practice population. Those patients found in AF underwent subsequent 12 lead echocardiography and case note review to determine any underlying cause and the potential need for anticoagulant therapy. 888 patients were invited for screening. 764 (86%) attended and of these 26 (3.4%) were found to have AF, 4 had paced rhythm (without background AF) and the remainder (764) were in sinus rhythm. Of the 26 patients, 20 had previously been documented as having AF and 6 of these patients were already taking long term warfarin. 25 patients underwent echocardiography. 12 had abnormality of the mitral valve (previously undiagnosed severe mitral stenosis in 1). 21 had left atrial dimension greater than 4cm and 10 had left ventricular dilatation. 11 patients had evidence of significant impairment of left ventricular function. The small number of patients who were found to have AF and previously not identified would not suggest it is worthwhile to embark on screening for AF in general practice. The frequency of abnormalities on echocardiography would suggest a policy of routine echocardiography for patients with AF. A case for anticoagulation could be made in at least 80% of patients. Such a policy would involve 625 echocardiographic examinations per District General Hospital with a population of 250,000 and could potentially prevent 19 strokes per year.

THE EFFECT OF PSYCHOLOGICAL DEPRESSION ON FUNCTIONAL CAPACITY.
T A McDonagh, B S Davison, J D Norrie, C E Morrison, C A Brown, J McMurray, J T Tunstall-Pedoe, H J Dargie, Dept. of Cardiology, Western Infirmary, Glasgow. *MONICA PROJECT, Glasgow Royal Infirmary, Cardiovascular Epidemiology Unit, Ninewells Hospital and Medical School, Dundee. Scotland. UK.

Depressive symptomatology is common. We aimed to examine the effect of its presence on functional capacity measured by exercise test duration.

We studied 1417 subjects (868 males), aged 25-74 years. They originated from a random sample of 2000 people from a geographical population in North Glasgow (divided into five 10 year age bands of 200 men and 200 women per band.). All 2000 were characterised for standard cardiovascular risk factors at the Third Glasgow MONICA Risk Factor Survey. 1417 were exercised maximally using the STEEP protocol. Non attenders and those with a contraindication to exercise testing were excluded. 1268 of these had also completed quality of life questionnaires allowing depressive symptoms to be scored categorically on an incremental scale from 0-12 (higher numbers reflecting increasing levels of depressive symptoms)

Increasing levels of depression score correlated strongly with a reduction in exercise time. (p<0.01)

Depression score Exercise time (secs)
0-4 697.9 (n=706)
4-8 661.4 (n=440)
8-12 643.0 (n=119)

A multiple regression of exercise time on depression score with the covariates: current smoking, social deprivation class (Decapac score derived from the Carstairs category), female sex and increasing age, showed all of these to be significantly associated with a reduction in functional capacity (p<0.001) for all covariates and in their presence an increased depression score emerged as strongly significant. (p<0.01)

The influence of depression on functional capacity should be borne in mind when using this measurement clinically or in the research setting.

THE BRITISH FAMILY HEART STUDY: PRINCIPAL RESULTS OF A RANDOMISED CONTROLLED TRIAL OF CARDIOVASCULAR SCREENING AND LIFESTYLE INTERVENTION IN PRIMARY CARE.
DA Wood, A L Elsmore, S E M Pyke and S G Thompson on behalf of the British Family Heart Study Group. Department of Clinical Biostatistics, National Heart and Lung Institute; Primary Medical Care, University of Southampton; Wolfson Research Laboratories, University of Birmingham and Medical Statistics, London School of Hygiene and Tropical Medicine, University of London, London.

In a randomised comparison of a nurse led cardiovascular screening and lifestyle intervention programme in 15,427 middle aged men and women in 26 general practices in 13 towns across Britain there was an overall 14% (95% CI 11.2-17.1%) lower coronary (Dundee) risk score in men in the intervention practices at one year as compared to the comparison practices. This was partitioned between systolic blood pressure (7%), smoking (5%) and blood cholesterol (4%). The coronary risk score reduction in women was similar. For both men and women reported cigarette smoking at one year was lower by about 4%, systolic blood pressure by 7 mmHg, diastolic by 3 mmHg, weight by 1kg and cholesterol by 0.1 mmol/l, but there was no shift in glucose. After taking account of the higher baseline prevalence of cigarette smoking amongst those in the intervention group who did not return after one year, and the acclimatisation of repeated blood pressure measurements, the difference in risk factors achieved would, if maintained long term, translate into a 12% reduction in coronary events.

CASE FATALITY IN ASIANS AFTER ACUTE MYOCARDIAL INFARCTION
P Wilkinson, K Lai, K Ranjadayalan, B Marchant, P Kopelman AD Timmis
London Chest and Newham General Hospitals

The risk of death from coronary heart disease is substantially higher for Asians living in this country than for Whites. Ethnic differences in the prevalence of coronary heart disease are generally assumed to account for this but it is not known whether differences in case fatality rates after acute myocardial infarction make an additional contribution. We have followed up 474 patients aged under 65 who were admitted to the coronary care unit with acute myocardial infarction. 149 of these patients (31%) were Asian, compared with 23% of the local district's population (1991 census data). Although our classification of ethnicity does not correspond exactly to the census definition, and our catchment population is not identical to that of the census district, the age- and sex-standardised admission rate for Asians was approximately 80% higher than for Whites. The crude survival probability (95% CI) in Asian patients was 89.0% (82.6-93.1%) at 30 days and 84.3% (77.1-89.4%) at 6 months. This compares with 92.6% (89.0-95.0%) and 89.9% (85.8-92.7%) in Whites (p=0.10). After adjustment for age, sex, treatment (thrombolysis and/or aspirin) and previous myocardial infarction, the survival of Asians was significantly worse as reflected by a hazard ratio 2.05 (1.16-3.60), p<0.015. A much higher proportion of Asian patients were diabetic (38 vs 11%, p=0.001) and this may account for much of their excess risk. Thus, additional adjustment for diabetes reduced the hazard ratio in Asians to 1.28 (0.69-2.37). In conclusion, Asians are over-represented in our coronary care unit, consistent with national data which show an increased risk of coronary heart disease in this ethnic group. Moreover, Asians have a higher case fatality in the first 6 months after acute myocardial infarction. This is due largely to a higher prevalence of diabetes and may contribute to the increased risk of death from coronary heart disease in Asians living in this country.
MORTALITY FROM ISCHAEMIC HEART DISEASE (IHD) OUTSIDE AND INSIDE HOSPITAL: THE BRIGHTON HEART ATTACK STUDY
R M Senior, S E Senior, G P Dixon, D A Chamberlain, R Vincent, Cardiac Dept, Royal Sussex County Hospital, Brighton

It was reported that 25 years ago 60-73% of deaths from IHD occurred outside hospital. To discover whether this has changed we have been recording all cardiac deaths, cardiac arrests, and non fatal myocardial infarcts in the Brighton Health District (population 301,000) in people under 76 years of age since January 1993. Cases are identified from death certificates and hospital records and details checked with general practitioners and bereaved relatives. So far, 407 events have been recorded of which 217 (53%) have been fatal. Successful resuscitation from cardiac arrest has occurred in 29 patients. Median age at death was 69 years, and at resuscitation arrest was 64 years. If arrest occurred outside hospital and the patient died in hospital, the fatal event was considered to have occurred outside.

RESULTS:

<table>
<thead>
<tr>
<th>Event</th>
<th>Age</th>
<th>n</th>
<th>%Out*</th>
<th>n</th>
<th>%Out</th>
<th>n</th>
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<tr>
<td>Death</td>
<td>17</td>
<td>72</td>
<td>111</td>
<td>79</td>
<td>106</td>
<td>64*</td>
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<tr>
<td>RA</td>
<td>245</td>
<td>69</td>
<td>132</td>
<td>73</td>
<td>114</td>
<td>64</td>
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*RA = Reuscucitated Arrest; D + A = Death + Arrest; Out = Out of Hospital

*p < 0.02 35-69 vs 70-75

We conclude that about 70% of deaths from IHD still occur outside hospital, although preliminary results suggest that the absolute number of deaths may have fallen. The proportion of out of hospital deaths appears to be greater in younger than in older patients.

THE PREVALENCE OF HEART FAILURE ESTIMATED FROM PRESCRIPTION DATA.
KW Clarke, D Gray, JR Hampton. Cardiovascular Medicine, University Hospital, Nottingham.

Heart failure is recognised to be a common condition and previous studies in the UK have estimated its prevalence to be between 0.4% and 0.8% of the general population. We set out to determine the prevalence of heart failure in our health district.

Most patients with heart failure receive a loop diuretic (frusemide or bumetanide) as first line therapy. From Prescribing Analysis and Cost (PACT) data we calculated the total amount of frusemide prescribed on a daily basis in Nottinghamshire, and the proportion of loop diuretic prescriptions which were for bumetanide. We then examined the notes of 398 patients in a random sample of General Practices to determine the mean and median prescribed daily doses of frusemide.

To determine the proportion of patients taking diuretics for heart failure rather than for other indications we examined the notes of 505 patients prescribed loop diuretics by their GPs and determined the number of patients who fulfilled pre-determined diagnostic criteria for heart failure.

1,048,566mg of frusemide (the equivalent of 26,200 40mg tablets) were prescribed on a daily basis. The mean prescribed daily dose of frusemide per patient was 60mg and the median dose 40mg. 56% of patients fulfilled diagnostic criteria for heart failure and were therefore assumed to have had diuretics prescribed for this reason. 8.6% of all loop diuretic prescriptions are for bumetanide rather than frusemide.

We estimate that there are therefore between 10,630 and 15,946 patients in Nottinghamshire prescribed loop diuretics for heart failure. The prevalence of heart failure is our health district estimated from PACT data is between 1% and 1.6%.

The age-specific prevalence varies between 1/1000 in patients aged 70-79 years, 5.5/1000 in those aged 50-59 years and 42/1000 in 70-79 year olds.

SYNGEUSTIC VALUE OF SIMULTANEOUS STRESS DOBUTAMINE SESTAMI SPECT AND ECHOCARDIOGRAPHY IN THE DETECTION OF CORONARY ARTERY DISEASE
R Senior, J C Smith, S Sridhara, E Anagnostou, U Raval, C E Hendler, E B Raftery, A Lahiri, Northwick Park Hospital, Harrow, Middlesex

To assess the relative value of simultaneousdobutamine stress sestamibi SPECT (MIIBI) and echocardiography (Echo) for the detection of coronary artery disease (CAD) 61 consecutive patients with chest pain referred for diagnostic coronary angiography were evaluated. Incremental doses of dobutamine (5-40mcg/kg/min) was infused until standard end-points were achieved. Echo was performed at basal, low and peak doses of dobutamine and during recovery. On-line digital Echo was acquired in a quad screen display. MIIBI (120Ci) was injected at peak dose and a rest study was performed on a separate day. Images were interpreted by 3 blinded panels for each modality. A coronary artery lesion of >50% was considered significant. There were 17 patients with normal coronary arteries. Forty-four had CAD, of whom 30 had multi-vessel disease. Both MIIBI and Echo individually were highly significant in predicting CAD for any vessel, for multivessel and for diseases in individual coronary arteries (p<.001). Using logistic regression, the combined techniques significantly increased the prediction of CAD for any vessel (p<.001), for multivessel disease (p<.001), for left anterior descending (p<.001), for right coronary (p<.001) and for left circumflex arteries (p<0.01), compared to either MIIBI or Echo alone. Combining MIIBI and Echo during dobutamine stress improves the detection of CAD compared to any single imaging modality, suggesting a synergistic value of these tests.

SCINTIGRAPHIC ASSESSMENT OF REINNERVATION OF THE TRANSPLANTED HUMAN HEART.
JM McComb, T Hawkins, G Parry, JH Dark. Freeman Hospital, Newcastle upon Tyne.

Radio labelled [123] meta-iodobenzyl-guanidine (MIBG) has an affinity for adrenergic nerves and has been used to image the heart. Imaging depends on uptake and storage of MIBG by intact myocaridal adrenergic nerves. Orthotopic cardiac transplantation results in cardiac denervation, which will prevent uptake of [123]MIBG and so imaging. To assess the possibility of cardiac reinnervation, '5 term' recipients, who had undergone orthotopic cardiac transplantation 2 or 3 years previously and 5 'recent' recipients (within 6-10 weeks) were studied. Two otherwise healthy patients undergoing [123]MIBG imaging for suspected phaeochromocytoma were studied as controls. Because of anticipated difficulties in localising small levels of [123]MIBG uptake in a possibly rotated transplanted heart, the cardiac blood pool of each recipient was initially imaged using 60MBq Tc99 labelled pyrophosphate. One week later imaging with 148MBq [123]MIBG was performed after blocking free iodine uptake by the thyroid by administration of stable potassium iodide orally. The heart, outlined by the blood pool scan, was superimposed on the MIBG image. Images were reviewed qualitatively, and scored as positive (definite uptake) or negative (no discernible uptake). Site of uptake was determined with reference to the cardiac outline in right and left oblique views. Scintigraphic uptake was strongly positive in both normal controls, and was positive in 9/15 'long term' recipients. No uptake was detected in all 5 'recent' recipients and in 3/15 'long term' recipients. The pattern of uptake was similar in all 9 transplant recipients, being confined to the basal septum and basal left ventricular free wall. [123]MIBG imaging therefore suggests that sympathetic reinnervation occurs in the majority of patients 2 or 3 years after cardiac transplantation. The pattern of innervation suggests that sympathetic nerves regrow from base to apex, as anticipated, from the anastomosis.
REVERSE REDISTRIBUTION ON THALLIUM-201 IMAGING IN POST-MYOCARDIAL INFARCTION : SUGGESTS SUCCESSFUL THROMBOLYSIS

B S Sridhara, E Dudicu, S Basu, R Senior, A Lahiri Northwick Park Hospital, Harrow, Middlesex

The clinical significance of reverse redistribution (RR) on TI-201 imaging is not clearly understood. We have evaluated the significance of RR on TI-201 imaging in patients (pts) following myocardial infarction (MI) who have undergone thrombolysis. Sixty-two pts with an age range of 35-79 yrs were studied 6 weeks post MI; 34 had anterior and 28 had inferior MI and all had undergone thrombolytic therapy. Stress and 4 hour redistribution TI-201 imaging and separate day rest TI-201 study following sublingual nitroglycerine were performed. Planar images were acquired and semiquantitative segment analysis was performed using the unprocessed images. All pts had radionuclide ventriculography for the assessment of left ventricular ejection fraction (LVEF) and regional wall motion abnormality (RWM). Thirty-two patients had coronary angiography. Fixed defects were noted in 19, reversible defects in 22, and RR in 21 pts. Those with RR had significantly higher exercise capacity (p<0.01). LVEF was similar in all 3 groups [Mean (SD)-46(12)%]. Patients with RR had significantly less regional RWM (p<0.01) compared to those with fixed or reversible defects. Fifteen out of 21 pts also had enhanced TI-201 uptake in the RR segment, after nitroglycerine when imaging was performed on a separate day; this suggests retained viability. Mean (SD) patency of infarct related artery was more in the RR group when compared to those with fixed or reversible defects (4.6(8.4)). Thus, the finding of RR in the post-infarct patient may imply successful thrombolytic therapy in infarct-related arteries, improved wall motion at the infarct site and retained myocardial viability in that segment.

A COMPARISON OF CLINICAL, ECHOCARDIOGRAPHIC, RADIONUCLIDE AND NEUROHORMONAL METHODS IN DETECTING LEFT VENTRICULAR DYSFUNCTION POST MYOCARDIAL INFARCTION

D Darbar, A M Choy, C C Lang, T Pringle, G P McNeill, N Kennedy, A D Struthers

Departments of Cardiology, Clinical Pharmacology and Medical Physics, Ninewells Hospital and Medical School, Dundee

The recent SAVE trial shows that an angiotensin-converting enzyme (ACE) inhibitor produces a 19% improvement in mortality when given to patients whose left ventricular ejection fractions (LVEF) were ≤ 40% in the 1-2 weeks post myocardial infarction (MI). The challenge now for physicians and cardiologists is to identify this select group since clinically overt heart failure is absent in the majority of them. The available ways to identify these patients are: 1) by radionuclide ventriculography (RNV) 2) echocardiographically by algorithm derived LVEF (Echo LVEF) and by a quick qualitative assessment of LV function (Eyeball echo) 3) clinical assessment using a formalised PEEL score or; 4) measurement of plasma levels of brain natriuretic peptide (BNP, BNP%). We compared the accuracy of these 4 techniques in 75 patients admitted to the coronary care unit of Ninewells Hospital. They were aged 40-88 years old and were studied 2-8 days post MI. Echo LVEF was possible in 57 (76%) patients which correlated well with RNV-LVEF (r=0.8, p<0.05). Eyeball echo was possible in most (97%) and was sensitive (82%) but lacked specificity (62%) in the detection of LV dysfunction. Clinical assessment underestimated the number of patients with LV dysfunction (sensitivity 64%, specificity 86%). Plasma ANP and BNP were elevated in patients compared to controls. The correlation between LVEF and plasma BNP (r=0.5, p<10^-3) but less so with ANP (r=0.3, p<10^-2). We conclude that LV dysfunction is easily and reliably detected by Echo LVEF and Eyeball echo but is likely to be missed by clinical assessment alone. Elevated plasma BNP levels may be a useful indicator of LV dysfunction where echocardiographic and radionuclide services are too limited to cope with screening all post MI patients.

PHARMACOLOGIC VARIABILITY IN THE TIMING OF PEAK CORONARY FLOW RESPONSE TO DIPYRIDAMOLE IN MAN.

J Radvan, J Williams, T Marwick, DJ O'Gorman, N Uren, R Foale, DJ Sheridan and PG Camici St Mary's Hospital and *MRC Cyclotron Unit, RPHS Hammersmith Hospital, London, UK.

Clinical stress imaging and assessments of coronary flow reserve (CFR) using dipyridamole (DIP) rely on the assumption that peak coronary flow response occurs at 8 minutes. Transoesophageal echocardiography (TE) allows the instantaneous assessment of coronary blood flow velocity in the left anterior descending coronary artery (LAD) using pulsed-wve Doppler in the transverse plane view. We have investigated the timing of the peak flow changes from rest following DIP (0.56mg/kg iv) at minute intervals using TE in healthy males aged 30-41 years (mean±SD). The results were compared to measurements of absolute myocardial flow in the LAD territory using positron emission tomography (PET) and oxygen-15 labelled water. After rest, recovery period, stress, stress values were obtained for DIP, 2.5, 5, 8 minutes. After the last PET scan, the PET and TE were performed on different days. Resting and perfusion measurements were corrected to a standard cardiac workload to compensate for heterogeneity in baseline hemodynamics. PET-CFR was calculated as the ratio of DIP/resting flow. To correspond with the timing of the PET flow, coronary blood flow velocity reserve was calculated as the ratio of diastolic LAD flow/resting value at 8 minutes (CBFVR8) as well as maximum recorded LAD flow/resting (CBFVR-max). Mean PET-CFR was 2.35±0.7. CBFVR8 was 2.53±0.8 and correlated with PET-CFR with an R-value of 0.8 (p<0.001). Mean difference between the two was 0.175±0.5. Time to maximum flow was 2.9-12.2 minutes (range 2.9-12.2). CBFVR-max was 2.96±1, significantly more than CBFVR8 (p<0.01). The correlation with PET-CFR was 0.91 (p<0.001), and the mean difference was 0.6±0.4, significantly greater than the difference with the CBFVR8. The biological variability seen in CBFVR measurement may be explained by the time course of response to dipyridamole. Measurements made at 8 minutes may underestimate response.
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<td>Forum</td>
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<td>Papers 141–146</td>
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<td>Overview of stents presently available and prospects for the future</td>
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<td>The cardiologist’s viewpoint (Dr Andrew McLeod)</td>
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<td>Everything you wanted to know about nuclear cardiology and cardiac</td>
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<td>MRI: Teach-in of basics, principles of interpretation and how to use</td>
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<td>Radionuclide ventriculography (Dr John Caplin)</td>
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WEDNESDAY 18 MAY 1994: NURSES’ DAY PROGRAMME

All sessions will be held in the Arena

SESSION ONE – HEART TRANSPLANTATION
Chair:
Carol Walker, London Chest Hospital, London
Dr Nicholas Brooks, Consultant Cardiologist, Wythenshawe Hospital, Manchester

9.30 – 9.55 Patient selection and results
Dr Peter Schofield, Consultant Cardiologist, Papworth Hospital, Cambridge

9.55 – 10.20 Role of the transplant nurse specialist
Jane Griffin, Transplant Nurse Specialist, Wythenshawe Hospital, Manchester

10.20 – 10.45 Heart transplantation – a traumatic event?
Joan Fitzjohn, Transplant Social Worker, Wythenshawe Hospital, Manchester

10.45 – 11.15 Coffee and poster viewing

SESSION TWO – AFTER A MYOCARDIAL INFARCTION
Chair:
Ann Townsend, CCU Freeman Hospital, Newcastle
Dr Nicholas Brooks, Wythenshawe Hospital, Manchester

11.15 – 11.40 Rehabilitation and lifestyle changes
Caroline Carter, London Chest Hospital

11.40 – 12.20 Who needs a coronary angiogram?
Almost everybody
Dr Clive Handler, Consultant Cardiologist, Northwick Park Hospital
Hardly anyone
Prof David de Bono, University of Leicester

12.20 – 12.40 Panel discussion
12.40 – 14.00 Lunch

SESSION THREE – NURSING IN THE 21ST CENTURY
Chair:
Mr Stephen Westaby, Consultant Cardiothoracic Surgeon, John Radcliffe Hospital, Oxford
Carol Walker, London Chest Hospital

14.00 – 14.25 The Cardiac ITU – Do we need one?
Julie Burgess, Queen Elizabeth Hospital, Birmingham

14.25 – 14.50 CCU: The nurse physician assistant
Ann Townsend, CCU, Freeman Hospital, Newcastle

14.50 – 15.10 The catheter laboratory
Dr Raphael Balcon, London Chest Hospital

15.10 – 15.35 The operating theatre
Susanne Holmes, John Radcliffe Hospital, Oxford

15.35 – 15.50 Panel discussion
16.00 Tea (in the Arena)
16.10 ICNS Members’ General Meeting
EFFECT OF VAGAL STIMULATION BY TRANSDERMAL SCOPOLAMINE ON EXERCISE PERFORMANCE AND R-R INTERVAL VariABILITY IN PATIENTS WITH CHRONIC HEART FAILURE

Barbara Casadei
Department of Cardiovascular Medicine, John Radcliffe Hospital, University of Oxford, Oxford

Cardiac vagal tone can be increased in normal subjects by very low doses of muscarinic blocking agents. I studied the effects of transdermal scopolamine (0.5mg delivered over 72 hours) upon the cardiac autonomic balance and the exercise tolerance in 16 patients (age, 58±2 years) with mild to moderate chronic heart failure (left ventricular ejection fraction, 27±6%). Secondary to myocardial infarction in a double blind, randomised, placebo controlled, crossover trial. Scopolamine significantly increased the standard deviation (from 138±32±11.95 to 155±3±14.04 ms, P<0.05) and the percentage of differences >50ms (from 6.5±1.65 to 11.55±2.67%, P<0.005) of all normal R-R intervals in the 24-hour ECG recordings. The baroreflex sensitivity, evaluated by the phenylphrine technique, was increased (from 9.16±1.60 to 15.57±2.5 ms/mmHg, P<0.001), as was the amplitude of respiratory sinus arrhythmia computed by autoregressive spectral analysis of 10-minute ECG recordings (from 177±12±82±02 to 497±09±192±48 ms², P<0.001). The mean 24-hour heart rate was reduced after scopolamine from 77±12±2.8 to 73±5±3.0 bpm (P<0.05) and submaximal exercise heart rate fell from 89±6.53±3 to 84±4.35 bpm (P<0.01). Peak oxygen uptake, minute ventilation and exercise duration did not change.

In conclusion, low doses of scopolamine increased tonic and reflex cardiac vagal activity and improved the time-domain indices of R-R interval variability. This was achieved without affecting exercise tolerance. These results suggest that vagal stimulation could provide a new approach for the management of chronic heart failure.

REDDUCTION IN PLATELET DEPOSITION AND INTIMAL HYPERPLASIA FOLLOWING ARTERIAL INJURY USING A LOCALLY DELIVERED TARGETED ANTIPATELLATE AGENT

Department of Cardiology, Glenfield hospital, Leicester

Potent antiplatelet therapy delivered locally at the site of vascular injury and which remains localised to that site may reduce early local platelet deposition and subsequent intimal hyperplasia. We therefore assessed the activity of a targeted antiplatelet conjugate in vitro and when delivered locally in an experimental rabbit model of angioplasty. The conjugate was developed by cross-linking urokinase to a monoclonal antibody to rabbit platelet glycoproteins IIb/IIIa (AZ-1) and to a monoclonal antibody to damaged endothelium (PI41G1) using N-succinimidyl-3-(2-pyridyldithio)propionate. The conjugate formed ATC(1) had a urokinase activity of 20000U/mg protein. In vitro platelet aggregation studies (using ADP and collagen as agonists) revealed complete inhibition of aggregation by ATC(1) at a mean dose of 8.3 μg/ml, compared to a required dose of 8.8 μg/ml for an AZ-1/Urokinase conjugate and a dose of 23.3 μg/ml for AZ-1 alone. In vivo locally delivered ATC(1) (at a dose of 150μg via a double balloon catheter) significantly reduced local platelet deposition 2 hours post angioplasty (mean(SE) 8.1(8.0) x 10⁶/cm² compared to locally delivered phosphate buffered saline (PBS) 34.5(3.9) x 10⁶/cm², p=0.01), locally delivered AZ-1/Urokinase conjugate (16.6(2.3) x 10⁶/cm², p<0.02) and systemically administered AZ-1 at a dose of 0.2mg/kg 16(3.0)(9) x 10⁶/cm², p=0.01). In a further series of experiments intimal hyperplasia at 1 month post angioplasty was significantly reduced with locally delivered ATC(1) (mean % area reduction compared to PBS control: 80.1%) compared to locally delivered AZ-1/Urokinase conjugate % reduction 32.5%, p=0.05) and systemically administered AZ-1 (% reduction 39.9, p=0.01).

In conclusion we have shown that a locally delivered targeted antiplatelet agent reduces intimal hyperplasia after arterial injury, consequent on platelet deposition. Such agents may have a potential clinical therapeutic niche for reducing the incidence of restenosis following angioplasty.

Monocyte adhesion to human coronary artery smooth muscle and endothelial cells: the role of modified LDL

SA Thorpe, SE Abbot, DR Blake, PG Mills.
Royal London Hospital, London.

Introduction: Oxidatively modified LDL is implicated in atherogenesis; it enhances the binding of monocytes to the endothelium, and has been shown to stimulate foam cell formation. Since focal endothelial denudation occurs early in atherosclerosis, intimal smooth muscle cells are also exposed to the circulation. However, little is known about the ability of intimal smooth muscle cells to support monocyte adhesion.

Aims: The aims of this study were to investigate whether (i) modified LDL and cytokines induce human coronary artery intimal smooth muscle cell-monocyte adhesion mechanisms, and (ii) the role of VCAM-1 and ICAM-1 (vascular cell and intercellular adhesion molecule-1, respectively) in this process.

Methods: Intimal smooth muscle and endothelial cells were cultured from normal human coronary arteries. LDL was isolated from healthy volunteers by ultracentrifugation in the presence of 1mM EDTA. The endotoxin content of 0.1mg/ml LDL was less than 1μg/ml, ensuring no lipopolysaccharide stimulation of adhesion mechanisms. LDL was used in its native state, or after copper oxidation, or minimal modification by prolonged storage. Human peripheral blood mononuclear cells were isolated and labeled with 125I-Chromium.

Adhesion assay: Smooth muscle and endothelial cells were preincubated in medium alone, or with IL-1, TNFa, native or modified LDL (0.1-200μg LDL protein/ml). Cells were then washed before incubating with 125I labeled monocytes. Unattached monocytes were removed. The cells and adherent monocytes were lyed and the number of adherent monocytes determined using a gamma counter. Adhesion molecule ELISA: In parallel experiments, smooth muscle and endothelial cells were stimulated as above, and expression of ICAM-1 and VCAM-1 quantified by an ELISA (monoclonal antibodies provided by D Haskell, Royal Postgraduate Medical School, UK).

Results: Monocyte adhesion to intimal smooth muscle and endothelial cells stimulated by IL-1 and TNFa and by modified, but not native LDL, was significantly enhanced (p<0.01). IL-1 and TNFa induced significant intimal smooth muscle and endothelial cell expression of ICAM-1 and VCAM-1 (p<0.01). Neither native or modified LDL induced intimal smooth muscle or endothelial cell adhesion, although a significant level of adhesion was induced at 10μg/ml LDL. This may reflect the expression of these adhesion molecules induced by the IL-1/TNFa stimulation in these cells.

Conclusions: Human coronary artery intimal smooth muscle and endothelial cells stimulated by modified, but not native LDL, express cytokines and can support the adhesion of unstimulated monocytes. The mechanism by which cytokines induce monocyte binding may involve the expression of ICAM-1 and VCAM-1. However, the expression of these adhesion molecules induced by modified LDL is not trivially related. These studies identify intimal smooth muscle cells as a further cell type which may play an active role in the recruitment of monocytes in atherosclerosis.

PRECONDITIONING IN HUMAN ISOLATED MUSCLE

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Hatter Institute for Cardiovascular Studies, Division of Cardiology, University College London Hospitals, London WC1E 6AU

The mechanism underlying preconditioning (PC) has not been investigated in human myocardium. We have previously demonstrated PC in isolated superfused rabbit heart. Our aim was to extend these observations to investigate PC in human myocardium, using isolated, superfused human right atrial trabeculae (HAT).

HAT were suspended in an organ bath, superfused with modified Tyrode's solution and field stimulated at 1Hz. After a stabilization period of one hour, baseline functional characteristics were recorded and muscles were randomly allocated to control or PC groups. PC was induced by 3 minutes rapid pacing (3Hz) with hypoxic, substrate-free buffer, followed by reoxygenation with substrate for 10 minutes at 1Hz. Subsequently, to simulate ischaemia, muscles were rapidly paced at 3Hz for 90 minutes with hypoxic, substrate-free buffer, followed by 120 minutes reoxygenation at 1Hz with normal Tyrode's. An adenosine antagonist (8-sulphophenyl-theophylline, SPT) and an adenosine A1 agonist (R-phenyl-isopropyl-adenosine, R-PIA) were also used to ascertain whether the observed protection was mediated by adenosine in this model.

<table>
<thead>
<tr>
<th>GROUP</th>
<th>Control</th>
<th>PC</th>
<th>P&lt;0.1</th>
<th>P&lt;0.05</th>
<th>P&lt;0.1</th>
<th>R-PIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>% recovery</td>
<td>24.5</td>
<td>46.5</td>
<td>25.8</td>
<td>22.7</td>
<td>43.8</td>
<td>2.9</td>
</tr>
<tr>
<td>force at 120 mins</td>
<td>2.3</td>
<td>2.4</td>
<td>4.1</td>
<td>2.9</td>
<td>1.5</td>
<td></td>
</tr>
</tbody>
</table>

The results demonstrate that PC can protect isolated human myocardium as seen by improved recovery of developed force (p<0.0001). This protection is abolished by the addition of SPT; and R-PIA protects to a similar degree to PC.

We conclude that PC protects human myocardium by the release of adenosine acting on A1 receptors. This model may be of further use in the elucidation of the exact mechanism of protection.
CARDIAC NORADRENALINE RELEASE: EVIDENCE FOR REINNERVATION OF THE TRANSPLANTED HUMAN HEART.
JM McComb, J Mitchell, RA Peaston, JH Dark.
Freeman Hospital, Newcastle upon Tyne.

Cardiac transplantation leads to cardiac denervation, and thus the transplanted heart does not release noradrenaline into the coronary sinus after sympathetic stimulation of the heart. If reinervation of the left ventricle occurs, noradrenaline will be released. To assess cardiac innervation after transplantation in man, transcatheter noradrenaline gradients were measured in 17 'long term' (2 or 3 years, mean 28 months) transplant recipients. Following routine surveillance coronary angiography, endhole catheters were placed in the ascending aorta and the coronary sinus. Basal blood samples were taken from both, and then tyramine (35 mg/kg) was injected intravenously. Paired blood samples were taken from the aorta and the coronary sinus at 30, 60 and 120 seconds after injection. Blood was rapidly separated and the serum frozen and stored at -70°C. Noradrenaline was subsequently measured in each sample using high performance liquid chromatography. The transcatheter noradrenaline gradient was calculated as the difference in noradrenaline levels between the coronary sinus and the aorta. Noradrenaline release (or uptake) was calculated by subtracting the baseline gradient from the gradient after tyramine. Noradrenaline was released in 9/17 patients, with a mean release of 2.01 mmol/l (range 0.3 - 4.9). Thus, cardiac noradrenaline release was detected in response to sympathetic stimulation with tyramine in 53% of cardiac transplant recipients at 28 months post transplantation, implying sympathetic reinervation of at least the transplanted left ventricle.

CHANGES IN CHRONOTROPIC RESPONSE WITH TIME AFTER CARDIAC TRANSPLANTATION.
CD Scott, JH Dark, JM McComb. Freeman Hospital, Newcastle upon Tyne.

The transplanted human heart is autonomically denervated at the time of surgery and consequently has an abnormal chronotropic response. Bradycardia is universal in the immediate postoperative phase while resting tachycardia is usual in long term survivors. Changes in myocardial catecholamines and beta-receptor responsiveness are probably responsible. The evolution of the exercise response over the first few months has not been adequately investigated. Thirty adult transplant recipients underwent serial symptom limited exercise studies 5, 6, 12 and 24 weeks after surgery using the chronotropic assessment exercise protocol (CAEP). Results were analysed using the concept of heart rate reserve (HRR). Results are expressed as mean (standard error):

<table>
<thead>
<tr>
<th>Week</th>
<th>Week 6</th>
<th>Week 12</th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest HR</td>
<td>86.9(2.3)</td>
<td>94.5(2.5)</td>
<td>98.1(1.9)</td>
</tr>
<tr>
<td>Peak HR</td>
<td>110.2(2.2)</td>
<td>124.4(2.6)</td>
<td>127.2(1.8)</td>
</tr>
<tr>
<td>Ex. time (secs)</td>
<td>485(29)</td>
<td>659(27)</td>
<td>730(23)</td>
</tr>
<tr>
<td>% HRR peak</td>
<td>27.3(1.7)</td>
<td>39.3(2.2)</td>
<td>39.9(2.2)</td>
</tr>
</tbody>
</table>

All these changes were statistically significant by one way analysis of variance. Thus there were consistent increases in exercise time, resting and peak heart rates between 3 and 6 weeks after transplantation. The absolute increase in mean and increased variation in peak % HRR between 12 and 24 weeks was not accompanied by a substantial change in exercise capacity and was attributable to an enhanced response in 5 of 31 subjects (16%) who achieved more than 75% of HRR. 4 of these 5 also exhibited a rapid decline in heart rate during the recovery phase (more than 10 bpm at 3 minutes) compared with 1 of 26 other subjects (p < 0.001). Thus the chronotropic response in cardiac transplant recipients improves over the first 6 weeks in all subjects. Between 12 and 24 weeks further improvement is seen in a minority of subjects (16%). The pattern of this response and the recovery phase is highly suggestive of early sympathetic reinervation.

SINUS NODE FUNCTION IN HEART TRANSPLANT RECIPIENTS.
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Sinus node dysfunction is the commonest cause of clinically significant bradycardiacs after heart transplantation. Previous electrophysiological studies have reported a very high incidence of sinus node dysfunction (approximately 50%). However the incidence of bradycardiacs attributable to sinus node dysfunction in several larger series without electrophysiological data has been much lower. Serial electrophysiological studies have not been previously undertaken. Thus the natural history of sinus node dysfunction after transplantation has not been adequately described. Forty adult heart transplant recipients underwent serial electrophysiological testing of sinus node function 1, 2, 3 and 6 weeks, 1, 2 and 3 months after transplantation. Corrected maximal sinus node recovery time (CSNRT) and sinoatrial conduction time (SACT) were measured using standard techniques. Seven subjects (17.5%) had abnormal CSNRT by standard criteria (> 255 msec) on at least one occasion. CSNRT was abnormal at 1 week in 6 (early sinus node dysfunction) and was first abnormal as 3 months in 1 (late sinus node dysfunction). CSNRT decreased progressively from week 2 in all subjects with early sinus node dysfunction and had returned to normal by week 6. SACT was abnormal (> 250 msec) in 5 subjects all of whom also had sinus node dysfunction. In contrast with CSNRT an abnormal SACT developed late in two subjects with early sinus node dysfunction. Two subjects with abnormal CSNRT at 3 weeks received permanent pacemakers, 1 of these who later developed an abnormal SACT required long term pacing. The incidence of sinus node dysfunction after cardiac transplantation as defined by electrophysiological testing is much lower than has been previously reported. Abnormalities of sinus node automaticity and sinoatrial conduction are usually associated. Whereas sinus node automaticity returns to normal in subjects with early sinus node dysfunction, abnormalities of sinoatrial conduction may develop late and may necessitate long term pacing.

INTRACORONARY ADRENALINE CAUSES CHEST PAIN IN PATIENTS AFTER CARDIAC TRANSPLANTATION.
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Intracoronary adrenaline causes chest pain indistinguishable from angina in normal subjects and patients with coronary artery disease. On this basis it has been proposed that adrenaline may be a messenger in the development of myocardial ischemic pain. After orthotopic cardiac transplantation the heart is denervated but reinervation can occur. There is no simple test for reinervation in these patients. This study examined the effect of bolus intracoronary injections of intracoronary adrenaline in transplant patients versus normal controls. Six transplant patients and two controls were studied. Diagnostic angiography was undertaken via the left femoral artery using a 7F sheath. Intracoronary injections were given as 4ml boluses over ten seconds. These contained either normal saline or adrenaline in normal saline solution (in doses of 0.1875mg, 0.375mg, 0.75mg, 1.5mg, 3.0mg and 6.0mg). The patient was blinded to the timing and content of the injection. The procedure was stopped when the patient developed definite symptoms or developed a significant bradycardia with the previous injection. If the patient developed symptoms they were asked if it's size and nature. Both control patients developed transient central chest pain typical of angina. Their threshold dose was for the first 6 weeks (p < 0.05). Four of the six transplant patients (mean of five years post transplantation) also developed transient central chest pain typical of angina. Their threshold dose was and 0.75mg. Further investigations were stopped because of possible heart block (threshold dose 0.75mg and 3mg). In two of the transplant patients (mean of two years post transplantation) the study was stopped after 24 weeks due to abnormal angina (threshold dose 0.75mg and 3mg). The patients were completely asymptomatic. Intracoronary adrenaline injections are a simple method of testing for functional reinervation at routine cardiac catheterisation of patients after cardiac transplantation.
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TECHNIQUE OF ANASTOMOSIS AND INCIDENCE OF ATRIAL TACHYARRHYTHMIAS FOLLOWING HEART TRANSPLANTATION

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An alternative technique for implantation of the transplanted heart has been described at this institution. The left atrium is anastomosed using an atrial cuff, but on the right side direct anastomoses of the donor and recipient venae cavae are performed. We studied the notes of recipients of 63 consecutive heart transplants performed between January 1991 and May 1993 to determine the incidence of post operative temporary pacing and atrial tachyarrhythmias within the first 30 days, and of subsequent permanent pacing. 7 patients who died within 30 days were excluded (5 standard technique, 1 bicaval technique and 1 hybrid procedure). 25 patients received bicaval anastomoses(B) and 31 received standard(S) anastomoses. Atrial tachyarrhythmias occurred in 2 of the bicaval group compared with 11 in the standard group (p=0.015). In addition fewer patients in the bicaval group required temporary pacing (B 9, S 15) and also permanent pacing (B 0, S 3) although neither of these was statistically significant. Preoperative transmural gradient was slightly higher in the standard group (mean 8.5 mmHg), than in the bicaval group (mean 7 mmHg), p=0.047, but ischaemic times were similar. A difference in the incidence of post operative temporary pacing was observed in those who had been on amiodarone preoperatively compared with those who had not (7/8 vs 11/48 p=0.016), but this factor was equally distributed between the bicaval and standard anastomoses. This study shows that the technique of bicaval anastomasis, in addition to a theoretical advantage of maintaining a more normal atrial configuration, has a lower post operative incidence of atrial arrhythmias, complications, and may reduce the need for pacing.

PREDICTION OF LONG TERM PACING REQUIREMENTS IN RECIPIENTS WITH EARLY SINUS NODE DYSFUNCTION AFTER HEART TRANSPLANTATION.

C D Scott, JH Dark, JM McComb. Freeman Hospital, Newcastle upon Tyne.

Early sinus node dysfunction may complicate orthotopic cardiac transplantation. The indications for permanent pacing are controversial and the ability to predict a need for long term pacing would enable more accurate prescription of appropriate systems. Serial 24 hour ambulatory monitoring was performed 1,2,3 and 6 weeks, 3 and 6 months after transplantation in 40 consecutive adult recipients. The minimum heart rate during each recording was identified by automated rate counts with a sample time of 2 minutes and verified by direct inspection. At 1 week 8 subjects were judged clinically to require permanent pacing at 90 bpm on demand. At other times all temporary and permanent pacing systems were programmed to 50 bpm on demand for the duration of the recording. At 1 week 8 subjects (20%) required temporary pacing at 90 bpm and 6 (15%) paced intermittently at 50 bpm. At 2 weeks only 2 (5%) continued to pace intermittently, both received permanent pacemakers. By week 3 only one subject continued to pace intermittently at 50 bpm, this continued at 6 weeks and 6 months after transplantation. The minimum heart rates in the remaining subjects were 52, 54, 60 and 54 bpm at 3 and 6 weeks, 3 and 6 months respectively, 13 subjects (33%) had a minimum rate of between 50 and 70 bpm at 3 weeks. No subject had atrioventricular block. None suffered adverse effects from the relatively low pacing rates utilised. Thus a minimum heart rate of 50 bpm or less during 24 hour ambulatory monitoring 3 weeks after transplantation predicted a requirement for long term pacing. The selection of a low temporary pacing rate of 50 bpm is crucial to the separation of subjects who require long term pacing from those with clinically unimportant relative bradycardia and a minimum heart rate of 50 to 70 bpm 3 weeks after transplantation.

WHAT PROPORTION OF PATIENTS WITH ACUTE MYOCARDIAL INFARCTION SHOULD RECEIVE THROMBOLYTIC THERAPY?

R M Norris, S Roy, G P Dixon, Cardiac Department, Royal Sussex County Hospital, Brighton

It has been suggested that ideally 70 - 80% of patients with acute myocardial infarction (AMI) should receive intravenous thrombolytic therapy. We investigated this in the Brighton Heart Attack Study in which, since January 1993, details of all cases of acute ischaemic heart disease in patients under 76 years of age in the Brighton Health District (population 301,000) have been obtained from hospital records, transcripts of death certificates, general practitioners and bereaved relatives. In Brighton the importance of thrombolytic therapy is emphasized with fast track administration for patients with definite indications and frequent electrocardiograms (ECG) for detection of possible changes when indications are doubtful. Nevertheless, of the first 232 hospital cases of AMI admitted only 49% received thrombolytic therapy. An atypical ECG at presentation prevented administration in 32% of cases and in the remaining 18% non-administration was about equally due to perceived danger of bleeding or presentation at > 12 hours after the onset. Of the 74 presentations with atypical ECG, primary diagnostic changes on the 12 lead ECG (not a normal ECG) in 21 (28%) was diagnostic, only 3 of these (13%) were treated. During the same period in 31 hospital deaths have shown recent AMI and/or coronary thrombosis, all undiagnosed during life. We conclude that methods for detection of AMI, opportunities for increasing the use of thrombolytic therapy are limited.

PROVISION OF THROMBOLYTIC THERAPY FOR PATIENTS WITH PREVIOUS INFARCTION

J S Birkhead on behalf of the Myocardial Infarction Audit Group, Northampton General Hospital, Northampton, NN1 5RD

The provision of thrombolytic therapy for patients with previous myocardial infarction (MI) was examined from information recorded in a continuing audit of the provision of thrombolytic therapy in 25 hospitals in the UK between November 1989 and October 1992. 1161 patients were admitted with a presumed diagnosis of MI, of whom 5987 (50.9%) had a final diagnosis of MI, 247 (31.4%) of those admitted had a previous MI. Patients with previous MI differed in their response to symptoms when compared with patients having a first MI. The emergency service was called more frequently, 33% vs 27% (difference 5.7%, 95% confidence interval 2.4 to 9.1%) and help was sought slightly earlier, median 53 minutes, (95% confidence intervals 45 to 60) vs 60 minutes (55 to 60). As an result hospital was reached more quickly, 126 minutes (120 to 137) vs 145 minutes (130 to 155). A smaller proportion of patients admitted with previous MI had a final diagnosis of MI, 37.3% vs 50.8% (difference 20.7%, CI 18.4% to 23.0%). A greater proportion received thrombolyis after a delay because of diagnostic uncertainty, 24.8% vs 19.5% (difference 5.3%, CI 1.7% to 8.8%). As a result of diagnostic uncertainty the time from arrival to thrombolytic therapy was prolonged, 75 (72 to 80) vs 66 (62 to 72) minutes. The proportion of patients with previous MI having thrombolytic therapy was 63% vs 75.1% (difference 11.8%, CI 7.3% to 16.2%). Conclusion. Although patients with recurrent MI respond more quickly to symptoms and reach hospital sooner, the rapidly diagnostic uncertainty results in thrombolytic therapy being administered with a greater delay to a small proportion of eligible patients.
ARE GENERAL PRACTITIONERS READY FOR PREHOSPITAL THROMBOLYSIS?
WA McCrea, JPM Foran, RI Wainwright.
Cardiac Unit, Brook General Hospital, Greenwich, London.

Prehospital initiation of thrombolysis by general practitioners (GPs) may reduce delay in providing this therapy to patients with acute myocardial infarction (AMI) but it has been recommended that only GPs skilled at electrocardiogram (ECC) interpretation should prescribe such treatment. Therefore, on account of their possible role in prehospital thrombolysis we decided to determine our local GPs’ (a) access to ECC machines and defibrillators, (b) attitudes to general practitioner initiation of thrombolysis in AMI, (c) willingness to administer thrombolytic therapy, (d) usual responses to calls from patients with possible AMI. This information was obtained by asking all 203 GPs registered in our health district to anonymously complete a questionnaire. In addition, GPs were asked to provide details of their age, postgraduate training, and clinical experience. Questionnaires were returned by 165 doctors (81%). Although 52 respondents (32%) owned ECC machines only 3 routinely carried this equipment while on emergency call and none carried defibrillators. Eighty-seven doctors (53%) were opposed to general practitioner initiation of thrombolysis in AMI and 97 (59%) were unwilling to prescribe such treatment. No differences (p>0.05) in age, postgraduate training, clinical experience or ECC machine ownership could be discerned between those doctors willing and those unwilling to initiate thrombolysis. In response to possible AMI, 134 (81%) would usually attempt to attend the patient, 31 (19%) would only summon an ambulance, 115 (70%) would do both and 90 (55%) would also alert the hospital to the patient’s imminent arrival. No difference (p>0.05) in these patterns of response was observed between GPs who were willing to initiate thrombolysis and their colleagues who were unwilling. In conclusion, although the majority of our local GPs try to attend patients with AMI, most are unwilling to administer thrombolytic agents. If ECC evidence of infarction is a necessary prerequisite for out of hospital thrombolytic administration then even GPs willing to initiate thrombolysis will not be able to do so in the foreseeable future.

CAN A RAPID BIOCHEMICAL MEASUREMENT SERVICE HAVE AN EFFECT ON THE EFFICIENT USE OF CORONARY CARE UNIT BEDS?
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Academic Unit of Cardiac Sciences, *Department of Chemical Pathology, St Mary’s Hospital, **Department of Cardiology, West Middlesex University Hospital, London.

Introduction: As the demand for more efficient use of cardiac resources increases, we decided to evaluate the potential role of changing the timing of cardiac measurement and reporting, as an aid to the management of patients admitted to a busy Coronary Care Unit of a District General Hospital to see if a more efficient use of beds could be achieved. Diagnosis was based on the rate of creatine kinase increase on serial samples obtained over the eight hours following admission. Methods: For an initial three month familiarisation period serial creatine kinase results were made available at the end of the working day to supplement clinical management, supported by the traditional protocol of admission and daily enzyme determinations. Over the next four months, the admission to eight hour serial value results were provided by 11am each day and always within 24 hours of admission.

Results: There was a net reduction in length of stay on the coronary care unit to a median of two days (n=66) compared with three days (n=41) for patients with no further symptoms, p=0.0007 (Mann Whitney). Reversion to the original protocol of daily enzyme estimations resulted in an increase in the length of stay back to a median of three days for this patient group.

Conclusion: In the current climate of financial restraint, rapid diagnostic protocols applied within routine clinical practice have the potential for a real reduction in coronary care unit stay. They are cost effective and will allow a more efficient use of coronary care unit beds.

Value of instantaneous Creatine Kinase-MB in patients with suspected myocardial infarction
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Early and accurate detection of acute myocardial infarction (AMI) may facilitate patient care. We determined the value of instantaneous creatine kinase-MB (CKMB) mass in patients admitted with suspected AMI over a 13-month period. A retrospective analysis was carried out to determine whether CKMB measurement influenced the decision for thrombolysis. CKMB was measured using the Hybritech ICON QSR kit and a positive result was defined as >10ng/ml. Of the 397 patients in whom instantaneous CKMB was measured, the medical records were examined in 249 (63%). Inadequate documentation prevented analysis of the remainder. AMI was confirmed in 103/249 (41%) patients by a rising titre of conventional cardiac enzymes (AST and ALT) over a three-day period. Twenty-two and sixty-three CKMBs were measured in these 249 patients and the mean duration of blood sampling from onset of chest pain was 7 hours (median 5; range 0.5-55). The sensitivity of CKMB was 75%, specificity 78% and positive predictive value (PPV) 69%. Of the 103 patients whose conventional cardiac enzymes were diagnostic of AMI, 85 received thrombolytic therapy. Of these, 43 (66%) had diagnostic ECG changes of AMI on admission (ST segment elevation in >2 leads) while 22 (34%) had non-diagnostic ECG changes. Review of medical notes of the 22 patients who received thrombolysis without diagnostic ECG changes showed that thrombolysis was prescribed because of an elevated CKMB level: all 22 patients had CKMB >10ng/ml. The sensitivity of CKMB >10ng/ml was 65%, specificity 89% and PPV 77%.

Conclusion: Instantaneous CKMB measurement was sensitive and specific for myocardial damage, and levels of >10ng/ml were highly predictive of AMI. Patients who do not have diagnostic ECG changes may subsequently be shown to have myocardial damage by conventional cardiac enzyme measurement, and such damage can be predicted by instantaneous CKMB. Whether such patients would benefit from thrombolysis remains to be determined.

SURVEY OF VENOUS ACCESS FOR TEMPORARY PACING IN THE UK
Murphy JJ, Stephenson C.
Department of Medicine, Darlington Memorial Hospital, Co. Durham.

The British Cardiac Society (BCS) has recently produced guidelines relating to venous access for temporary pacing. We investigated the right internal jugular as the route of first choice for inexperienced operators. We report current clinical practice in the United Kingdom. The survey was performed in April 1993. Eighty randomly selected acute hospitals were telephoned and the "on call" senior House Officer (or Registrar if appropriate) contacted. All agreed to be questioned. 7 of the 80 were teaching hospitals and all 80 had Coronary Care Units. The sample consisted of 60 Senior House Officers (SHO) and 20 Registrars who had been qualified for between 2-23 years (median 3). 55/80 (69%) had no resident on duty cover when "on call". Seventy-seven (96%) were inserting central lines, and 62 (77%) pacing wires without supervision. For central venous cannulation, the median number of procedures observed had been 2 (range 0-10) with one having been performed under supervision (range 0-30) before having being left unsupervised. For temporary pacemaker insertion, the 62 doctors had initially observed a median of two procedures (range 0-10) before performing two under supervision (range 0-6). These procedures had been almost invariably taught at the bedside, usually by a fellow SHO (31%) or Registrar (53%). Only 3 had received any additional tuition. 74/77 (96%) could perform subclavian vein puncture, 30 (39%) had used the external jugular, 21 (27%) the femoral vein but only 19/77 (25%) had used the internal jugular route. 26/77 (34%) could only use the subclavian route. 35/62 (56%) had been required to pace a patient shortly after thrombolysis. Thirty-nine (49%) of doctors questioned were unhappy about the training they had received and 47 (59%) felt they would have been helped by formal training, such as tutorials or videos.

Conclusion. There continues to be strong emphasis on the subclavian route and experience with other forms of venous access is limited. If the BCS guidelines are to be implemented it is necessary to alter teaching and clinical practice. Training should be more structured and could be supported by the use of videos or manuals.
ROTATIONAL SCAN RECONSTRUCTION TECHNIQUES FOR TRANSTHORACIC 3-DIMENSIONAL ECHOCARDIOGRAPHY IN CONGENITAL HEART DISEASE

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Transoesophageal echo systems employing a "breadloaf" or parallel slice technique on images acquired during pullback have been used to generate 3-dimensional images in adults. Paediatric patients, however, have superior precordial echo windows which may allow transthoracic (TT) image acquisition and 3-dimensional reconstruction. In addition, rotational scan techniques may facilitate reconstruction of areas of specific diagnostic importance. The aim of this study was to assess the utility of rotational TT acquisitions in congenital heart disease using a high resolution Interspec ultrasound system interfaced with a Tomtec computer with new higher speed reconstruction algorithms. We studied 13 patients aged 7 days to 19 years (mean 4 years), weighing 3.5-11.5Kg. Diagnoses included: AV canal, DORV, Tric Atr, ASD, VSD, AS, PS, AVR, endocarditis, dextrocardia with ventricular inversion, ventricular septum, sub-aortic stenosis and aortic coarctation. All children under 4 years of age were sedated. Rotational acquisition steps with a probe holder controlled by the computer were programmed to match heart cycle length and respiratory phase. All 13 had subcostal scans and paraaortal, apical and right subclavicular windows were used in 7, 6, and 2 respectively. Acquisition times, depending on heart rate and patient mobility, were as short as 3 minutes. All studies resulted in successful diagnostic quality reconstructions which could be formatted, reviewed and rendered into 3-dimensional moving images within 15 minutes of acquisition. Rotational scanning allowed focusing a large number of steps for reconstruction of specific areas and the pre-selection of optimal single point windows. These techniques particularly facilitated high resolution delineation of aortic arch anatomy, VSD anatomy and semilunar or aortic valve anatomy. The ability to focus on areas of specific diagnostic importance through the unique rotational windows available on young paediatric patients, as well as the ease of TT acquisition with this new combined system should bring 3-dimensional reconstruction closer to clinical application for detailing the complex spatial anatomical relationships present in congenital heart disease.

EARLY RESULTS OF STENT IMPLANTATION FOR PULMONARY ARTERY & RIGHT VENTRICULAR OUTFLOW TRACT STENOSIS

Department of Paediatric Cardiology, Guy's Hospital, London.

Balloon dilatation of both congenital and acquired pulmonary artery branch stenoses is disappointing. Large balloons are needed with the risk of rupture of the pulmonary artery and the success rate is low due to recoiling of the lesions after the balloon is deflated. Metal stents, deployed using high pressure balloons, may be more successful. We have implanted 24 Palmaz-Schatz stents (1.6, 2.0 or 3.0 cm long and 7 -14 mm in diameter) in 15 patients with pulmonary artery stenoses or RVOT obstruction, whose age range was 3 - 36 years (mean 11 years), and weights 12 - 74 (mean 29 Kg). 7 patients had Fallof's tetralogy with previous shunt procedures (multiple in 5) and 4 had undergone complete correction. 1 patient had pulmonary atresia / VSD with a shunt related pulmonary artery stenosis. 7 patients had congenital pulmonary artery stenoses; 4 Alagille's syndrome, 1 a restrictive VSD, 1 infundibular stenosis and 1 multiple peripheral pulmonary artery stenoses. Balloon dilatation had failed previously in 4. Stent implantation increased the stenosis diameter from 5 ± 1.6 to 10 ± 2 and produced a fall in the transstenotic gradient from 48 ± 15 to 11 ± 5 mmHg. The right ventricular pressure fell in those without a ventricular septal defect and there was a rise in the distal pulmonary artery pressure in those with a systemic pressure right ventricle. Proximal displacement of a stent into an associated main pulmonary artery (repaired Fallof's tetralogy) occurred in 1 patient and was removed at surgery 48 hours later. In 1 patient with multiple peripheral pulmonary artery stenoses, guidewire perforation of the distal pulmonary artery produced severe haemoptysis and the distal vessel was occluded with coils. In 1 patient a stent was redilated from 8 to 12 mm, 6 months after the initial implant. In 6 patients with a single source of pulmonary artery blood flow, lung perfusion increased in the stented side from 33 ± 19% to 51 ± 20% of total lung perfusion. 1 patient with Alagille's syndrome had had liver transplantation, 2 were awaiting liver transplantation but 1 died from a variceal haemorrhage before transplantation. Follow up extends to 22 months (mean 5 months). Conclusion: Stent implantation to pulmonary arteries is a useful method of relieving postoperative and congenital pulmonary artery stenoses and may have a limited role in infundibular obstructions.

BALLOON DILATATION OF UNOPERATED COARCTATION OF THE AORTA.

Department of Paediatric Cardiology, Freeman Hospital, Newcastle upon Tyne.

Balloon dilatation (BD) of unoperated coarctation of the aorta (CoA) is the preferred procedure in our institution beyond infancy. It is suggested that there may be a risk of late aneurysm formation because the mechanism of BD results in medial and intimal tears with subsequent cistic medial necrosis. A ratio of balloon size to CoA diameter > 3.5 has been associated with early aneurysm formation, but the true incidence of late aneurysm is uncertain, in part, because of variation in definition and imaging techniques. 42 cases of unoperated CoA were treated by BD between Jan 1985 - Aug 1992. Median age at BD was 14.5 years (range 1-32) with follow-up of 5.4 years (0.2-7.7). The gradient was reduced from 26 mmHg median (range 10-84) to 4 (0-25) after the first BD, 6 patients had a good result following repeat BD (median 6 mmHg (2-11). No patient died as a result of the procedure; 2 had transient local vascular problems, and the first 2 patients had immediate evidence of aneurysm associated with use of oversize balloons. Two others were reported as showing evidence of aneurysmal dilatation on MRI scanning 7 years after BD, and on angiography in another. None of the observed aneurysms has progressed during follow-up and none has required treatment. Balloon dilatation of unoperated CoA is a safe and acceptable method of treatment providing satisfactory and sustained relief.

SELF-EXPANDING STENTS IN CONGENITAL HEART DISEASE.

Department of Paediatric Cardiology and Growth Up Congenital Heart Unit. Royal Brompton Hospital, London.

The use of balloon expandable (B-E) stents in patients with congenital heart disease (CHD) is increasingly reported. To date, there are only isolated case reports of self expanding stents (S-E), despite their potential advantages. They are delivered over a wire and carried on a smaller shaft size, have longitudinal flexibility allowing deployment in tortuous or otherwise inaccessible vessels, and are available in longer lengths than B-E stents. We report their use in 12 patients with CHD, age range 15 days to 32 years. There were 6 patients with pathway stenosis after atrio pulmonary or cavopulmonary anastomosis, 3 with complex pulmonary atresia and stenosed aortopulmonary collaterals, and 1 each with postop pulmonary artery stenosis after repair of truncus, pulmonary vein stenosis and coarctation of the aorta. The reasons for using S-E stents were the need for smaller delivery system (S-E), complex tortuous stenosis (S-E), long or multiple stenosis (S-E), unstable sheath position (S-E), or a combination. The deployed stent size ranged from 6-20mm, length 15-48mm.

In one patient it proved impossible to deploy either B-E or S-E stents because of the severe and angulated orientation of the pathway. Successful deployment was achieved in the remainder. There was no embolisation. Complete relief of stenosis was achieved in all patients, although in 3 a balloon dilatation of the stent was required immediately after deployment. Follow up ranges from 4-16 months, there have been no adverse sequelae. Repeat dilatation in 4, 2-8 months after insertion, showed no change in haemodynamics. Although having disadvantages (eg. inability to 'overdilate' to keep pace with growth) S-E stents should be considered when a smaller delivery system and flexibility would aid deployment or in the treatment of long or multiple stenoses.
(130) A DEVICE FOR ALL LESIONS. THE BUTTON OCLUDER.
KP Walsh, SE Abrams, Royal Liverpool Children’s Hospital, Alder Hey, Liverpool.

We report short term results using a transcatheter adjustable button device to close both atrial septal defects (ASD) and patent arterial ducts (PDA). 16 patients (10f, 6m) were considered for closure. Median age was 4yrs (range 1-11). Median weight was 19kg (range 8-34). 4 PDAs were closed using a 7 French long sheath via the femoral vein. Angiography from the arterial side enabled measurement of the minimum diameter and selection of either a 15mm (n=2) or 20mm (n=2) device. The occluder was opened in the descending aorta and withdrawn to occlude the atrial orifice of the duct. The counter occluder was then buttoned to the occluder. Repeat angiography showed complete occlusion in 3 and partial occlusion in 1 (7.7mm duct). At catheter, 3 ASDs were too large and 1 had right to left shunting and pulmonary hypertension. Therefore we attempted to close 8 ASDs. Closure was performed under fluoroscopy and transoesophageal ultrasound with colour doppler imaging. The balloon occlusion size was measured using a Miller-Edwards septostomy balloon. With a long sheath across the ASD, the device was advanced and opened in the left atrium. Positioning against the atrial septum was optimised before placement of the counter occluder. In 7 cases the ASD was successfully closed. In 1 PDA and 1 ASD the device was inadvertently pulled through. Snaring and removal was successfully performed. This PDA was then successfully closed with a second device. There were no other complications. Median screening time was 20 mins (range 13-88). Transthoracic echocardiography performed before discharge showed complete occlusion in 5 ASDs and 3 PDAs and trivial residual shunts in the remainder. Median hospital stay was 2 nights (range 1-2). We conclude that this adjustable button device is a useful and safe method for closing both PDAs and ASDs.

(131) BALLOON EXPANDABLE STENTS IN THE TREATMENT OF BRANCH PULMONARY ARTERY STENOSIS
N Wilson A Houston F Fadley Royal Hospital For Sick Children Glasgow
12 consecutive patients with branch pulmonary artery stenosis underwent cardiac catheterisation with the intention of balloon expandable Palmaz stent implantation. 7 patients had had previous surgery for Tetralogy of Fallot and one patient had undergone a Fontan operation for Tricuspid atresia. 2 of the Tetralogy patients had had residual ventricular septal defect. 4 patients had congenital branch pulmonary artery stenosis, one of whom also had a ventricular septal defect and anomalous origin of the left coronary artery. Average age was 9 yrs (range 1 to 33), average weight 33.2 kg. In 2 cases an old patient weighing 11 kg it was not possible to achieve a stable septal position and thus the procedure was abandoned early. In the remaining 11 patients, under general anaesthetic an 11 Fr sheath was positioned across the stenosis and either a 30mm or 18 mm long stent was delivered with a heavy duty 12mm diameter balloon angioplasty catheter. Further dilatation to 15mm was performed in eight patients and to 18mm diameter in one patient. 4 patients had bilateral stent implantation. The remaining 7 had unilateral implantation. Haemodynamics were assessed before and after implantation, and isotope perfusion scans were performed in 5 patients. Lesion diameter increased significantly in all patients from a mean of 4.9 to 11.2 mm (range 2 - 17.8mm). Systolic gradient decreased significantly from an average of 41 mmHg to 25 mmHg. Right ventricle to systemic pressure ratio decreased from 0.87 to 0.49, also statistically significant (p<0.005). All patients who had isotope scans showed an increase in perfusion to the stented side when the stenting was unilateral. Complications were relatively frequent. Blood loss requiring transfusion occurred in 4 patients. One patient developed a small pulmonary haemorrhage. Balloon puncture or bursting occurred in 4 patients. One stent, in the smallest patient, was delivered across a lesion in the left pulmonary artery but protruded into the main pulmonary artery, without obvious sequelae. Reinvestigation in 7 patients has shown only trivial neointimal formation, without obstruction, in one patient. Balloon expandable stents are efficacious in the treatment of branch pulmonary artery stenosis in children. The relatively high incidence of potentially serious complications would support pooling of experience throughout cardiological centres.

(132) EXERCISE INDUCED WHITE CELL AGGREGATION
A.C. Tweedle, A.M. McQuiston, L Hutton Royal Infirmary, Glasgow, Scotland.

Leucocytes aggregation has been implicated in the generation of vascular damage in various inflammatory conditions and we have previously shown that following myocardial infarction there are circulating large numbers of high aggregable white cells (wbc). This study aimed to examine the effect of exercise in patients with ischaemic heart disease on wbc aggregability. 32 patients were studied (24 males) undergoing dynamic, symptom limited maximal exercise testing prior to coronary angiography, where all were established as having significant coronary artery disease. White cell aggregation was measured in whole blood, by measuring aggregates formed in response to the aggregating agent N-formyl-methionyl-leucyl-phenylalanine using a Coulter counter. Paired samples were taken for wbc count. At rest, percentage aggregation was 54±2% (mean±SEM) and increased on exercise to 61±2% (p<0.01). WBC count also increased from 6.41±0.53 at rest to 7.51±0.42 (p<0.02) on exercise. In 16 patients exercise was limited by chest pain, aggregation increased from 54±2 to 62±2% and in 16 patients, limited by breathlessness or leg fatigue aggregation increased from 54±2 to 59±3%.

These results would suggest, that in patients with ischaemic heart disease, exercise is associated with increased numbers of aggregable wbc, which potentially may aggravate exercise induced ischaemia.

(133) EXERCISE INDUCED HYPOTENSION IN PATIENTS WITH AUTONOMIC DYSFUNCTION
*R.R.Baliga, L Watson, E Armstrong, CJ Mathias, *Division of Cardiovascular Medicine, St Mary’s Hospital Medical School and The National Hospital for Nervous Diseases, London, UK.

To investigate the role of the sympathetic nervous system on haemodynamic responses to exercise we studied 7 patients with primary (pure) autonomic failure and 5 normal subjects. All patients (with PAF) had postural hypotension and severe sympathetic failure on autonomic function tests. None had anginal symptoms. Measurements were made in the supine position before, during and after bicycle exercise at 3 workloads (25 W, 50 W and 75 W for 2 minutes at each stage). Blood pressure and heart rate responses were measured using an automated sphygmomanometer (Sentron) before and after each period of exercise and blood samples were taken for measurements of plasma noradrenaline (NHL) from an indwelling cannula. Basal systolic and diastolic blood pressure was higher in PAF (152±16 and 82±11 mm Hg) as compared to normals (110±8 and 63±9 mm Hg, p<0.05). After 75 W exercise SBP and DBP fell in PAF (122±33 and 61±17 mm Hg, p<0.05) but rose in normals (122±10 and 73±8 mm Hg, p<0.05). Heart rate rose after exercise in PAF (67±11 to 90±16 min-1, p<0.05) and in normals (71±12 to 101±10 min-1, p<0.05). Basal plasma noradrenaline levels were lower in PAF and did not increase after exercise (105±65 to 90±58 pmol/l, ns) unlike normals (194±53 to 490±225 pmol/l, P<0.05).

In PAF, unlike normals, exercise induces a profound fall in blood pressure even in supine position. This is likely to result from sympathetic dysfunction alone and may be due to a relative lack of vasocostriction in major regional (ie splanchic) vascular beds. Sympathetic dysfunction may contribute to exercise induced hypotension during diagnostic exercise ECG stress testing.
The identification of young patients who are at increased risk of sudden death remains problematic. Exercise hypotension has been reported in up to 20% of consecutive adult patients with hypertrophic cardiomyopathy (HCM). Abnormal blood pressure responses were associated with young age and a family history of frequent sudden death. We studied the blood pressure response during erect exercise in 82 young patients with HCM; they were aged 6-25 years, mean 18 years, 53 were male and 29 female. Symptom-limited treadmill exercise was performed using a Bruce protocol with continuous measurement of the systolic arterial pressure. The blood pressure response was classified as 'normal' (>20 mmHg rise), flat (<20 mmHg rise) or hypotensive (a fall from peak BP of ≥20 mmHg). The blood pressure response was normal in 45 (55%), flat in 8 (9%) and hypotensive in 29 (36%; the fall was 20-50 mean 30 mmHg). The presence of exercise hypotension was associated with a positive family history of death, PR interval >0.24 s and QRS duration >0.12 s. Exercise hypotension was more frequent in patients who showed a hypotensive blood pressure response compared to those who did not (5 of 29 versus 3 of 53; p = 0.05). The high prevalence of exercise hypotension and its strong association with a family history of sudden death and exercise ischaemia suggests that this simple measure is a practical non-invasive marker of risk in the young with HCM.
(139) MODERATED POSTER

CLINICAL VALUE OF GP OPEN ACCESS EXERCISE TESTS
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Cardiac Department, Royal Bournemouth Hospital

A direct access exercise test service for suspected ischaemic heart disease (IHD) was introduced in May 1992. A standard request form was used and by employing appropriate exclusion criteria, the patients booked directly for an exercise test (ET). The test was performed off medication and supervised by a trained clinical assistant. The ET was analysed using fixed criteria for the onset of 1mm ST depression, the heart rate at which this occurred, change in blood pressure and time to recovery of ST changes and then allocated to one of 6 result categories (negative, mildly/moderately/strongly positive, equivocal or non-diagnostic). From May 1992 - July 1993, 416 ETs were performed. 45% of patients were aged > 60 years, 37% > 60 and 18% > 70 years. 58% were male. 48% of ETs were negative, 35% positive (0.5% mildly, 8.5% moderately and 26% strongly) and 17% equivocal or non-diagnostic. The ET result was used in decision-making when comparing the results from each consecutive 100 referrals. There was a higher proportion of positive ETs with age, 48% of ETs were positive in those > 60 years compared to 18% < 60 years (p=0.001). Of the requests, 20% (50% of total) were graded as likely positives - 45% of these generated a positive ET result. Of those thought unlikely to be positive, 25% had a positive ET (p=0.001). The proportion of ETs that were positive was 46% of males and 19% of females (p<0.001). This difference was despite the GPs pre-loading the likelihood of IHD being the same for each sex. (47% of males and 53% of females referred). 146 patients (35%) were made outpatient appointments. Of the 108 patients with strongly positive ETs, 71 were referred for angiography (A). One refused intervention, 17 were awaiting A and 53 had have A (of which 27 had CABG, 7 PTCA, 18 medical management and 1 aortic valve replacement). The second set enabled 72% of patients (85% of the total) to be referred directly back to the GP, with advice when necessary, for further action/reassurance. The projected growth in referral rate to the service 92/93 to 93/94 is 20% and yet there has been no change in the proportion of positive ETs with time suggesting that further demand still needs to be met.

(140) MODERATED POSTER

TRAINING DURATION CORRELATES WITH AN INCREASE IN MINIMAL CORONARY RESISTANCE IN ATHLETES WITH TRAINING-INDUCED LEFT VENTRICULAR HYPERTROPHY.
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*MR3 Cyclotron Unit and RPMS Hammersmith Hospital and the Department of Academic Cardiology, St Mary's Hospital Medical School, London U.K.

Pathological left ventricular hypertrophy (LVH) is associated with an increase in minimal coronary resistance (MCR). The effects of exercise and training-induced LVH on MCR are unknown. We studied 16 male elite rowing athletes (R) aged 26±6 years (mean±SD) with LVH, who had trained for 29±1 hours per week for a mean of 8 years (range 3-19 years), and 12 sedentary normal age-matched male controls (C) aged 25±5 years. LV mass index was defined using 2-D echocardiography. Minimal coronary resistance (MCR), absolute myocardial blood flow, and coronary flow reserve (CFR) were assessed with positron emission tomography, using a standard oxygen-15 labelled water technique following the administration of dipiridamole (0.56mg/kg i.v. over 4 minutes). MCR was expressed as the ratio of mean arterial pressure divided by maximal myocardial blood flow following dipiridamole, and CFR as the ratio of maximal myocardial blood flow/resting flow.

<table>
<thead>
<tr>
<th>LV mass index (g/m²)</th>
<th>150±19</th>
<th>80±15</th>
<th>p&lt;0.001</th>
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<tr>
<td>CFR</td>
<td>3.4±1</td>
<td>3.8±1</td>
<td>ns</td>
</tr>
<tr>
<td>MCR (mmHg/ml/min/g)</td>
<td>37±16</td>
<td>28±10</td>
<td>0.05</td>
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</table>

In rowers, increasing training duration correlated with an increase in minimal coronary resistance, R=0.71, (p<0.005), and an attenuation of CFR, R=0.71, (p<0.005). This effect was independent of age. There was no significant association between LV mass index and MCR, or duration of training. Conclusions: Minimal coronary resistance is increased in rowers compared with controls. Extended intense training at an elite level may increase minimal coronary resistance, and attenuate coronary flow reserve, although CFR remains within the normal range.

(138) MODERATED POSTER

FACTORS INFLUENCING INTER-OBSERVER AGREEMENT IN STRESS ECHOCARDIOGRAPHY: COMPARISON WITH EXERCISE ELECTROCARDIOGRAPHY
P Mazelka, A Nabazdin, Celia M Oakley
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The subjective nature of wall motion (WM) analysis has been cited as a limitation of stress echocardiography. We studied inter-observer agreement and assessed factors which influence it to explore this issue. Two non-biased and experienced observers independently reported 2 groups of 50 stress echocardiograms (dobutamine stress, n=25; exercise stress, n=25). Between these 2 highly comparable sets (set 1 and 2) they underwent a period of joint reading and developed a uniform approach to WM analysis and interpretation. Studies were reported both qualitatively (as normal, fixed or induced WM abnormality) and semiquantitatively (calculation of a WM score index). All studies were assessed in a slow-motion cine-loop display and then graded as of type A (good), B (moderate) or C (adequate) image quality using established criteria. Inter-rater concordance was unaffected by patient age, gender or body weight, or by type of stress. Qualitative agreement (overall kappa coefficient (k) = 0.67, 95% confidence interval (CI 0.54-0.79) was greater for set 2 (k=0.73, CI 0.57-0.89) than set 1 (k=0.6, CI 0.42-0.79). This was due in part to initial relative over-reading by one observer (p<0.05) and was absent on the second set (p>NS). Rates agreed on 18/19 type A, 47/57 type B and 15/24 type C images (p=0.02, trend p<0.01). Concordance was also influenced by extent of WM abnormality (k=0.90 for 1 segment, 0.86 for 2 segment, 0.78 for 3 segment regional asynergy) (p=0.02, trend p<0.01) but not by its location (for exercise echocardiography) (reported as positive, negative or indeterminate) on these 100 patients k was 0.72 (CI 0.6-0.84). Semiquantitative agreement (minimal SEMS Index of agreement) was −0.22 to 0.34 was better for set 2 (−0.26 to 0.24) than set 1 (−0.13 to 0.40) (p=0.02) and poorest for type C studies. Minimal SEMS Index (95% limits of agreement) showed no evidence of over-scoring. In conclusion, inter-observer variability in stress echocardiography is affected by image quality and extent of WM abnormality. A period of joint assessment eliminates relative over-reading and improves agreement to the levels seen with exercise ECG.

(141) MODERATED POSTER

PROGRESSION OF CORONARY ARTERY DISEASE FOLLOWING CESSATION OF CIGARETTE SMOKING
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Cigarette (CIG) smoking is an established risk factor for the development of coronary artery disease (CAD), but whether cessation of heavy smoking influences progression of CAD is unclear. This study of 390 patients (167 men, 223 women, 47±5 years) with CAD, 2 coronary angiograms were performed in an interval of 62±23.5 months. Smoking habits were obtained by questionnaires. Progression of CAD was defined as the sum of new stenosis, progression of existing stenoses and new coronary occlusions. Multivariate classification analyses of risk factor profile revealed CIG smoking (amount per day and length of time) as the most relevant factor for progression of CAD. Non-smokers had a progression score of 0.96 (95% confidence interval, 0.63-1.28) over the observation period. Former smokers (20.2±11.8 CIG/day for 19.4±7.6 years) who quit about 10 years before the first angiogram showed a progression of 2.20 (95%: 1.77-2.63; P<0.01) compared to non-smokers. Those smokers (23.8±9.2 CIG/day for 31.3±7.0 years) who quit at the time of the first angiogram had a progression of 2.47 (95%: 1.97-2.97; P<0.001). Current smokers (20.5±9.7 CIG/day for 34.8±8.5 years) had a progression of 3.17 (95%: 2.35-3.99; P<0.001).

The data indicate that former heavy CIG smoking continues to act as a significant risk factor for progression of CAD even after cessation. This does not mean that current CIG smokers should not stop. On the contrary, continuing to smoke further increases progression of CAD.
CORONARY ARTERY STENOSIS: LOCALISATION AND ASSESSMENT OF SEVERITY BY MAGNETIC RESONANCE IMAGING

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Consistent visualisation of the proximal and mid portions of the coronary arteries by magnetic resonance (MR) imaging has recently been described in normal subjects. We used breath-hold segmented gradient echo MR imaging to localise and assess coronary artery stenoses in 17 patients with angina. Imaging of just the relevant artery was performed and analysis was blinded to the X-ray angiography results. Stenosis was identified on the MR images by localised reduction in vessel signal intensity. Stenosis location by MR was assessed by measurement of its distance from a reference vessel, with correlation to the X-ray findings.

X-ray coronary angiography showed 23 stenoses of which 15 (65%) were correctly located by blind assessment of the MR images. Of the 8 remaining stenoses, a further 5 (63%) were correctly located on the MR images after retrospective comparison (overall sensitivity 87%). There were 3 lesions thought to represent stenosis by MR which on review of the X-ray angiogram proved to be a minor stenosis (<50%) (2 cases), or a tortuous vessel (1 case). Greater signal loss was seen in the more severe stenoses. The stenosis length by MRI was greater than by X-ray (8.4 ± 5.1 mm, p<0.001).

There is an important learning phase in the interpretation of coronary MR images. Overestimation of stenosis length may be due to turbulence, an effect described for peripheral MR angiography, or misregistration of signal to the post stenotic area from blood accelerating through the stenosis. Further refinements in image quality may allow a useful clinical examination to be developed.

Vibrational angioplasty is a new approach to recanalise chronic totally occluded coronary arteries.

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We present the first 12 cases of chronic total occlusions treated with a new angioplasty device. This offers a novel approach to coronary intervention termed "vibrational angioplasty" in which lesions are subjected to vibrational energy. The device consists of two parts: a) a motor and gearing system producing a fine oscillation with a vibrational frequency of 100-500 Hz and b) a steerable guide wire. The tip of the wire is vibrated against the lesion for 1-2 minutes before slow passage through the lesion is attempted while vibration continues. Once the lesion is crossed with a wire coronary angioplasty (PTCA) is performed using the minimal pressure required for adequate vessel dilatation. Using "vibrational angioplasty" we treated 12 patients (8 male, 4 female, mean age: 61.8 yrs, age range: 49-73) with symptoms of stable angina and total coronary occlusions (left anterior descending: 4, left circumflex: 3, right coronary: 5). In all 12 cases at least two conventional wires used without vibration (high torque floppy, intermediate, standard, Magnum) had failed to cross the lesion. The mean duration of the occlusion was estimated either clinically or by sequential coronary angiograms, was 14.8 months (range: 7-60 months). In seven out of twelve cases the lesion was crossed by vibrating a blunt ended wire while in 5/12 cases additional wires, either a hydrophilic (4/5) or a high torque floppy (1/5) had to be used. In 2/12 cases no balloon could subsequently cross the lesion. In 10/12 the lesion was crossed successfully by a balloon and PTCA was performed with pressure ranging between 2.5 - 6 Atm. The post procedural result was: successful in 7/12 (mild dissection in 1 case), major dissection needed stenting in 1/12, compromised by the evidence of severe diffuse disease distally in 2/12 and failure in 2/12. The total procedural and screening times (mean +/- SD) were 84.0+/−50.17 and 43.2+/-32.32 min respectively. In conclusion "vibrational angioplasty" appears to achieve high primary success rates in the recanalisation of totally occluded arteries. Further studies are needed to clarify the impact of vibrational energy on the

ENDOTHELIUM-DEPENDENT DILATION IN THE ARTERIES OF ASYMPTOMATIC SUBJECTS RELATES TO CORONARY RISK FACTORS AND THEIR INTERACTION

JE Deanfield, DS Celemajer, S Robinson, O Thomas.
Hospital for Sick Children, London.

Endothelial dysfunction has been demonstrated in humans with established atherosclerosis. We postulated that known coronary risk factors (such as older age, male sex, high cholesterol, and smoking) might interact to produce endothelial dysfunction in asymptomatic subjects, earlier in the natural history. Using high resolution ultrasound, we measured systemic arterial diameter at rest, after reactive hyperemia (leading to flow increase; flow mediated dilation, FMD, is endothelium dependent) and after sublingual nitroglycerin (GTN, an endothelium-independent dilator), in 500 clinically well, non-hypertensive children and adults (252 males and 248 females) aged 3-73 (36±15) years, including 179 current and former smokers. As optimal vessel size for response evaluation is 2.06-0.0mm, the superficial femoral was studied in 46 children and the brachial artery in 454 adults. There was a wide range of endothelium-dependent responses (FMD -1 to +17%). All arteries dilated in response to GTN (17±6%), suggesting an abnormality of endothelial function in subjects with impaired FMD. On univariate analysis, reduced FMD was related to hypercholesterolaemia, smoking, higher blood pressure, male gender, older age, positive family history of premature vascular disease and larger vessel size (p<0.01 for all). By multiple stepwise regression analysis, reduced FMD was independently associated with cigarette smoking, ruder age, male gender and larger vessel size (<0.005 for each), but not with cholesterol level. A composite risk factor score was strongly and independently related to FMD, suggesting risk factor interaction. When the smoking/cholesterol interaction was examined, cholesterol level was significantly related to FMD in non- and light smokers only; in heavy smokers, impaired whatever the cholesterol level. Furthermore, light and moderate smoking was more damaging in subjects in the highest compared to the lowest cholesterol quartile. Thus the same risk factors that predispose to atherosclerosis and its complications interact to produce loss of endothelium-dependent dilation in young and middle-aged asymptomatic subjects. This may be an early manifestation of the atherogenic process.

VIBRATIONAL ANGIOPLASTY, A NEW APPROACH TO RECANALISE CHRONIC TOTALLY OCCLUDED CORONARY ARTERIES

School of Medicine, Stanford, California, USA.

Experimental endothelial denudation is associated with proliferation of underlying vascular smooth muscle cells (VSM). This phenomenon is considered to result, in part, from loss of the tonic inhibitory effects of endothelial NO production on VSM growth; restoration, in vivo, of tonic local NO production may therefore have utility in the prevention of restenosis following angioplasty. In this study we describe the successful in vivo transfer of constitutive endothelial-type nitric oxide synthase (eNOS) gene into balloon-injured rat carotid arteries. An expression vector containing the eNOS gene, driven by a β-actin promoter and CMV enhancer, was prepared; the vector without eNOS served as control. Following unilateral balloon carotid injury, in vivo gene transfection was accomplished using the high-efficiency Sendai virus (HVJ)-mediated method previously described; the carotid arteries were removed and studied 4 days after injury. NOS protein was stained histochemically in frozen sections of carotid artery by NADPH diaphorase staining, showing diffuse positive staining within the media of eNOS-transfected but not of control-transfected vessels. Carotid artery NO production was measured as NO (NO+NO2) in vivo and in vitro; levels were lower in injured (eNOS- and control-transfected) vessels incubated with arginine (10M) + Ca2+ (100M) + l-arginine (10M) + A23187 (10M) + L-NMMA (10M) + L-NMMA (10M). NO production was highest in uninjured vessels (31±11 pmol NO/fg wet weight, n=4), and lowest in the injured control-transfected carotid arteries (7±2.1 pmol NO/fg wet weight, n=4). Endothelial nitric oxide production was restored by L-NMMA-transfection to levels similar to those in uninjured vessels (32±11; n=4).

These findings indicate successful in vivo transfection of eNOS in a model of vascular injury, and represent a novel potential strategy in the prevention of restenosis following angioplasty.
Differential Progression of Complex and Smooth Coronary Stenoses Within Individuals With Stable Coronary Artery Disease.

M. Chester, L. Chen, D. Tousoulis, J. C. Kaski. Department of Cardiological Sciences, St. George’s Hospital, London.

Recent evidence has demonstrated that coronary stenosis progression is an important predictor of future coronary events. We and others have shown that complex coronary stenoses are associated with progression to acute coronary syndromes and adverse outcomes in a variety of clinical settings. This study was designed to investigate the influence of clinical factors on the behaviour of morphologically distinct coronary lesions we compared the rates of progression of angiographic complex lesions (CL) and smooth lesions (SL) within the same coronary tree in patients with clinically stable coronary artery disease.

Patients & methods: 98 pts male underwent 2 closely comparable angiographic studies in our institution between Jan 1988 and Jan 1990. We selected all clinically stable pts who had only one of each morphological stenosis type (complex and smooth) in different coronary arteries at the first diagnostic study. Pts with lesions at branching points or with any stenosis >90% severity were excluded from analysis. Automated edge detection (CAAS) was used to determine lumen diameter and % stenosis reduction in 30 pts. Stenosis morphology (complex: overlapping edges, ulceration or thrombus or smooth: no complex features) was determined by previously described techniques.

Results: % stenosis progression of complex, smooth and follow-up

<table>
<thead>
<tr>
<th>Type</th>
<th>Mean (% stenosis)</th>
<th>Median (% stenosis)</th>
<th>Maximum (% stenosis)</th>
<th>Minimum (% stenosis)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complex</td>
<td>40.2 ± 9.6</td>
<td>41 ± 12.7</td>
<td>98.5 ± 12.7</td>
<td>0 ± 12.7</td>
<td>30</td>
</tr>
<tr>
<td>Smooth</td>
<td>41.6 ± 12.3</td>
<td>68.8 ± 14.0</td>
<td>95.3 ± 13.1</td>
<td>0 ± 11.6</td>
<td>30</td>
</tr>
</tbody>
</table>

(mean ±SD) Mean interval 10:36 hrs ± p = 0.03, Mann-Whitney test, 88/90 CL, pooled lesions: progressed >15%. There was no relationship between initial severity and progression.

Conclusion: This study shows for the first time that there is a differential rate of progression of coronary artery lesions. The results suggest that complex coronary stenoses within the same coronary tree in patients with clinically stable coronary artery disease. The increased growth rate in complex stenoses is mainly due to rapid stenosis progression in a small proportion of lesions.

A Functional Role for Proto-Oncogene Proteins in Neonatal Cardiomyocytes.

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Transfection studies allow the functions of specific gene products to be investigated. Protocols for transformed cell lines are well established but few have been performed using primary cultures of cardiac myocytes. We have developed an electroporation transfection method to allow the introduction of proto-oncogene expression vectors directly into neonatal rat ventricular myocytes. Increased proto-oncogene expression has been demonstrated in developing and adult neonatal cardiac hypertrophy, therefore we wished to examine the effects of transfected proto-oncogene expression on cell growth. Myocytes were isolated from 1:2 day old rats, cells were plated in an electroporation cuvette, vector DNA added and the cells subjected to a high voltage pulse of defined magnitude (200V, 960 μF). Increased expression of oncogene expression vector was then confirmed by Northern and Western blotting. After electroporation cell numbers were assessed by haemocytometer counts. The effects of transfected gene expression on DNA, RNA and protein synthesis were measured by the incorporation of tritiated thymidine, uridine and phenylalanine respectively, and the results obtained compared to control cells and cells transfected with the vector PSV0 which contains a viral promoter but lacks proto-oncogene coding sequence. Cell proliferation was observed in control groups demonstrating that neonatal cardiac myocytes in primary culture retain the ability to undergo cell division (con 2d, 25 ± 1.8; con 6d, 50 ± 2.2 × 10^5 cells/ml; con 10d, 5 ± 5.6; con 20d, 156.9 ± 5.6 × 10^4 pm/cell; p < 0.001). By 4 days post-transfection cell numbers were increased in all groups (con 2d, 23 ± 1.8; PSV0 mcyd 2d, 24.8 ± 6.1; con 4d, 34 ± 1.9; PSV0 4d, 22.2 ± 5.1; PSV0 mcyd 4d, 44.8 ± 3.0 × 10^5 cells/ml) however at days post-transfection a significant increase in the number of mcy transfected cells was observed compared to controls or cells transfected with PSV0 (con 6d, 50 ± 2.2; PSV0 6d, 34.7 ± 2.5; p < 0.001). Measurements of DNA synthesis followed a similar pattern, RNA and protein synthesis were also increased. Given the growing body of evidence that endothelin plays an important physiological role in the heart, we have investigated the effect of endothelin-1 on the phosphoinositide signalling system and protein synthesis in neonatal cardiomyocytes. Cardiac myocytes derived from 1-4 day old Wistar rats were cultured in DMEM containing initially 10% fetal calf serum, supplemented with antibiotics and plated at a density of 10^5 cells per well on collagen coated plates. Following pre-labelling with 1 μCi [3H]leucine, endothelin-1 stimulated phosphoinositide hydrolysis in a dose dependent manner (EC50 1nM).

In serum free medium, endothelin-1 (10^-8 M) significantly increased the rate of incorporation of [3H]-phenylalanine into myocardium (see table, mean ± SD, disintegrations per minute per 10^6 cells, n = 5, p < 0.001). The specific protein kinase C inhibitor, Ro 31-8220 (1 μM), significantly reduced phenylalanine incorporation compared with control (p < 0.004) and following endothelin-1 (ET-1) with Ro 31-8220 compared with endothelin-1 alone (p < 0.034).
ADENYLYL PURINES CONTRIBUTE TO THE MYOCARDIAL RELAXANT EFFECT OF BRADYKININ IN THE INTACT HEART

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Endogenous bradykinin (BK) produced by endothelial cells may be involved in the therapeutic response to ACE inhibitors. BK acts via B2 receptors on endothelial cells to cause the release of several factors, eg nitric oxide (NO), prostaglandins. We have previously shown that BK causes myocardial relaxation, in part, via a NO-independent mechanism. Since BK has been reported to release adenosine triphosphate (ATP) from endothelial cells, we investigated whether part of the myocardial relaxant effect of BK is mediated by an adenylyl purine mechanism. We compared the effects of 0.1μM BK alone (n=10) and in the presence of two P2-purinoceptor antagonists a) the P2X2 and P2Y2 antagonist suramin (S; 10μM, n=6) and b) the P2X antagonist PPADS (P; 10μM, n=5) on left ventricular (LV) performance in isolated guinea-pig hearts (constant loading and heart rate; Krebs's buffer; 37°C; 1μM indomethacin). LV pressure (LVP) and dp/dt were measured using a 2F Millar catheter and coronary flow (CF) from timed collections of effluent from the right atrium. LV relaxation was assessed by a mono-exponential time constant (τE). Results: Baseline LV relaxation was 17±5 ms (n=10). BK increased CF and enhanced LV relaxation (ie decreased τE) without affecting systolic performance. BK effects were attenuated by S but not P.

Data show that both the vasodilator and myocardial relaxant effects of BK are mediated in part by adenylyl purines through an action on P2y purinoceptors.

ELEVATED SOLUBLE INTERLEUKIN-2 RECEPTOR IN DILATED CARDIOMYOPATHY: EVIDENCE OF T-CELL ACTIVATION

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Recent evidence suggests that dilated cardiomyopathy (DCM) is an autoimmune disease. The serum level of soluble interleukin-2 receptor (sIL2R) is a marker of T-cell activation and is higher in patients with dilated cardiomyopathy (DCM) compared to healthy controls. However, the effect of heart failure per se and the clinical significance of raised levels of sIL2R in patients with DCM is uncertain. In this study, levels of sIL2R, soluble T-lymphocyte antigen-1 (sTAC-1), and the clinical significance of raised levels of sIL2R in patients with DCM was examined. In a study of 60 patients with DCM (mean age 43±13, 47 male), 66 patients with heart failure secondary to ischaemic heart disease (HHD) and in 34 age-matched healthy controls. DCM was diagnosed using WHO criteria and all patients underwent endomyocardial biopsy and patients with myocarditis (Dallas criteria) were excluded from the study. Patients with DCM had mean symptoms for 37±47 months, 31 were in NYHA class II and 29 III/IV, and 41 had established endomyocardial fibrosis. The normal range for sIL2R has previously been established as <191 U/ml. The level of sIL2R in the 3 groups and the proportion of individuals with an abnormal result were:

<table>
<thead>
<tr>
<th>Group</th>
<th>Level of sIL2R (U/ml)</th>
<th>21 (35%) a</th>
<th>11 (17%) b</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCM</td>
<td>842±583</td>
<td>762±755</td>
<td>544±307</td>
</tr>
<tr>
<td>HHD</td>
<td>21 (35%)</td>
<td>11 (17%)</td>
<td>4 (12%)</td>
</tr>
</tbody>
</table>

Levels of sIL2R were higher in patients with DCM compared to healthy controls (p<0.009). Elevated levels of sIL2R were more common in patients with heart failure secondary to DCM compared to HHD (p=0.03). In patients with DCM high levels of sIL2R were associated functional status (I/II - 709±376, III/IV 984±724 U/ml, p=0.006), impaired systolic function (p=0.11), reduced peak oxygen consumption (p=0.008), and normal endomyocardial histology vs established fibrosis 721±415 U/ml (p=0.001). During follow-up (mean 25±21 months, range 1-101) 21 patients suffered progressive heart failure requiring cardiac transplantation while 10 of the patients who suffered progressive heart failure had higher levels of sIL2R at presentation than those who remained stable (96±733 vs 739±537 U/ml, p=0.12). In conclusion, the finding of raised levels of sIL2R in patients with DCM supports a role for activated T-cells in the pathogenesis of the condition. The higher levels of sIL2R in DCM patients with more severe disease and adverse prognosis may identify a subgroup of patients who may benefit from aggressive immunosuppressive therapy.
Analysis of Genetic Locus Heterogeneity in Hypertrophic Cardiomyopathy.
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Four genetic loci have been identified that are the site of disease genes for familial hypertrophic cardiomyopathy (FHC): CMH1 (the β myosin heavy chain gene) on chromosome 14q1, and three loci without known disease genes - CMH2 on 1q3, CMH3 on 15q2 and CMH4 on 11. Identification of these loci provides a framework for a genetic classification of this disease. To evaluate the contribution of each locus to the prevalence of the disease, ten newly identified families with typical FHC, and three with variants of the phenotype, were tested for linkage. Analyses were performed with intragenic markers for CMH1 and flanking markers for the other loci, with an assumed penetrance of 0.95.

Of the families with typical FHC, one mapped to the β myosin heavy chain gene, two mapped to CMH2, and two to CMH4 (LOD scores > 1.3, equivalent to 95% confidence interval). Of the remaining five families, all could be excluded from CMH1, but three were not sufficiently informative to exclude each of the other loci. Two families, however, were shown to be not linked to any known locus (LOD scores < -2) - implying the existence of at least one further disease locus. Thus multiple disease genes exist, each resulting in typical FHC and each contributing to only a minority of total disease prevalence.

Three families with variant phenotypes (two with apical hypertrophy, one with disarray and no hypertrophy) were unlinked to all known FHC loci, suggesting that such disease entities are genetically distinct.

Prospective Study of Antibodies to Acetaldehyde Adducts of Human Heart Proteins in Patients with Alcoholic Cardiomyopathy
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The mechanism by which ethanol induces alcoholic cardiomyopathy (ACM) is not known. Acetaldehyde is an ethanol metabolite which can reach proteins antigenic. We have previously demonstrated the presence of antibodies to acetaldehyde-modified cardiac proteins in 4 of 14 patients with ACM; studied retrospectively. Patients with ACM were therefore investigated prospectively for these antibodies. Sera were studied from 7 patients with ACM (prolonged consumption of >80 units alcohol weekly; no evidence of ischaemic heart disease, moderate to severe left ventricular dysfunction by echocardiography) and 39 controls, (20 idiopathic dilated cardiomyopathy, 8 ischaemic heart disease and 11 normal individuals) who drank less than 21 units (males) or 14 units (females) weekly. Eight patients with alcoholic liver disease were also studied. Cytoplasmic fractions of normal human myocardium were incubated with or without acetaldehyde in the presence or absence of cyanoborohydride (which stabilises acetaldehyde adducts). Western blots were prepared and were indirectly immunostained with the test sera. All seven patients with ACM had detectable antibodies against acetaldehyde modified cytosolic protein, detected only against samples treated with acetaldehyde and cyanoborohydride. Antibodies were of IgG class in 3 patients, IgA antibody in 3 and IgM antibody was detected in 6. Only one control sample (of 39) had similar antibodies. Thus, patients with ACM possess circulating antibodies against acetaldehyde modified cardiac cytosolic proteins, which are not generally found in the sera of controls.

The presence of these antibodies in all the patients in this prospective study strongly supports a possible role for the humoral immune system in the pathogenesis of ACM.

Dilated Cardiomyopathy: A Familial Disease?
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Recent studies have suggested that familial dilated cardiomyopathy (DCM) is inherited in a dominant manner and that the inheritance of familial DCM in the UK we prospectively screened 254 relatives (mean age 54±17 years, 128 male, 137 1st-degree) of 49 consecutive patients with DCM (WHO criteria). Screening consisted of clinical examination, 12-lead electrocardiogram and 2-D echocardiography. Relatives with systemic hypertension were excluded from the study. All echocardiograms were performed by a dedicated echocardiographer who was blinded to clinical information. Relatives were classified as having DCM, left ventricular enlargement (LVE) by the method of Henry, depressed fractional shortening (DFS; <25%), or as being normal. Relatives with abnormal investigations underwent invasive evaluation where appropriate. Twenty-seven (11%) relatives from 12 families were found to have DCM indicating a familial prevalence of at least 24%. Pedigree analysis in all families was most consistent in autosomal dominant inheritance with incomplete penetrance. Of the remaining apparently healthy relatives, 40 (18%) had LVE and 9 (4%) had DFS. The frequency of LVE and DFS was higher in these relatives than in a healthy control population screened using the same methodology (24/238, 10%; p=0.02 and 1/239, 0.4%; p=0.01, respectively). This demonstrates that familial DCM is common and is transmitted with autosomal dominant inheritance. Prospective follow-up of relatives with mild echocardiographic abnormalities is necessary to determine if these findings represent early DCM.

Cardiac Autoantibodies in Dilated Cardiomyopathy Become Undetectable with Disease Progression

Cardiac antibodies (Abs) are common in patients (pts) with dilated cardiomyopathy (DCM) 30% of the myocardium was detected only to different antibodies and/or to reduction in antibody levels with disease progression. Seventy-three pts (57 M, 16 F, aged 43±14 underwent immunological evaluation at diagnosis and at follow-up (mean 2, range 1-151 months) to determine the relation of antibody and disease status. Cardiological evaluation at diagnosis included: 2-dimensional echocardiography (2D-E), 12 lead ECG, cardiac catheterisation and endomyocardial biopsy. In 50 maximal exercise testing (ET) with maximal oxygen consumption (VO2 max) was performed. Of the 73 DCM pts (WHO criteria), 50 were in NYHA class I/II, 23 in class III/IV. Cardiac Abs were detected by immune/lourescent human heart. Skeletal muscle was used to identify cross-reacting Abs. Sera were tested blindly from clinical data. The following features were assessed in pts with and without Abs at follow-up: age, symptom duration, NYHA class, LV dimension on 2D-Echo, VO2 max expressed as % of predicted value (VO2%). At diagnosis, Abs were detected in 31/73 (16% of the “organ-specific” and 15 of the “cross-reactive 1” type); at follow-up the frequency of these Abs was significantly lower (12/73, 16% p<0.006). The majority of the antibody positive pts (1031, 61%) lost these Abs during follow-up. Conversely, all pts who were negative at diagnosis remained negative at follow-up. The persistence of cardiac Abs at follow-up was not associated with any clinical or diagnostic feature, but pts who remained antibody positive tended to have longer symptom duration and greater exercise capacity compared to those who were antibody negative (19±26 vs 32±45 months, p=0.33, VO2 max 73±14 vs 61±20, p=0.23 respectively. Thus, cardiac Abs in DCM become undetectable with disease progression. The finding of Abs as early markers, which become detectable with disease progression, is recognised in other autoimmune conditions such as insulin-dependent diabetes mellitus. This raises the possibility that absence of these markers in pts at diagnosis may relate to long-standing pre-clinical DCM.
PREDICTING OUTCOME AFTER CARDIAC SURGERY USING PHYSIOLOGICAL VARIABLES

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St George's Hospital, Guy's Hospital, Royal Brompton Heart & Lung Hospital and University College London

In a multi-institutional study, we collected prospectively a range of physiological variables and recorded the therapeutic interventions in cardiac surgical patients with a protracted postoperative course, i.e. in intensive care beyond 48 hours after surgery. During 1992, 2256 adult patients underwent cardiac surgery (excluding transplants) in the 3 collaborating hospitals. 162 patients remained in the intensive care unit (ICU) after 48 hours and of these, 47 died there. The ICU stay ranged from 3 to 90 days (median 6) and the survivors spent between 7 and 111 days in hospital (median 21).

We applied 2 prediction algorithms using a trend analysis method developed by Chang, Jacobs and Lee (Int. Care. Med. 1988 14: 558-66) for general ICU patients. These are based on APACHE II scores and the occurrence of acute organ system failure.

The algorithms for predicting death in the ICU performed as follows:

<table>
<thead>
<tr>
<th>Prediction method</th>
<th>APACHE II Organ Failure</th>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>38 %</td>
</tr>
<tr>
<td>Specificity</td>
<td>98 %</td>
</tr>
<tr>
<td>Positive Predictive Value (PPV)</td>
<td>90 %</td>
</tr>
<tr>
<td>Negative Predictive Value (NPV)</td>
<td>80 %</td>
</tr>
<tr>
<td>Correct</td>
<td>81 %</td>
</tr>
</tbody>
</table>

The high specificity is the crucial component in what is designed to be a conservative estimating tool. The results ran counter to the hypothesis that APACHE II scoring is inadequate for assessing cardiac surgical patients. In addition, if treatment were to be withdrawn in the patients correctly predicted to die, it would only free about 1/3 of ICU bed-days overall (3-4% for the 162 cases).

We are currently refining these predictive tools for our particular clinical context and we regard them as a means to aid rather than override clinical decision making. Our study has institutional approval.

NON-INVASIVE ASSESSMENT OF LEFT ANTERIOR DESCENDING CORONARY ARTERY BLOOD FLOW FOLLOWING GRAFTING WITH THE INTERNAL MAMMARY ARTERY CONDUIT

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Studies have shown that flow in internal mammary artery (IMA) grafts may be transiently reduced post-operatively but the effect on flow in the recipient LAD has not been studied. The distal LAD may be imaged and blood flow velocities recorded by transthoracic Doppler ultrasound. This technique was used to determine the time course and magnitude of improvement in basal recipient LAD flow following IMA grafting. Six male patients, mean age 63 years (57 to 66), undergoing elective IMA grafting to the LAD were studied the day before, and at 5 days and 18 months post-operatively. LAD diameter and flow velocities were recorded and total flow calculated from: cross sectional area x velocity time integral x heart rate.

RESULTS: Blood flow patterns in the recipient LAD were diastolic predominant and directed towards the apex. A significant increase in heart rate reflecting withdrawal of B blockers was observed post-operatively. Total LAD flow was significantly increased 18 months following grafting, <p=0.05, but was not altered in the early post-operative period. LAD diameter and diastolic velocities were unchanged but the LAD systolic flow component was increased at 18 months.

<table>
<thead>
<tr>
<th>Heart rate</th>
<th>Pre</th>
<th>5 days</th>
<th>18 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>L/min</td>
<td>59 ± 7</td>
<td>86 ± 5</td>
<td>85 ± 41</td>
</tr>
<tr>
<td>L/min/m²</td>
<td>55 ± 6</td>
<td>52 ± 6</td>
<td>74 ± 6*</td>
</tr>
<tr>
<td>Peak systolic velocity cm/s</td>
<td>28 ± 7</td>
<td>26 ± 10</td>
<td>40 ± 6*</td>
</tr>
<tr>
<td>Mean systolic velocity cm/s</td>
<td>23 ± 6</td>
<td>21 ± 6</td>
<td>32 ± 10*</td>
</tr>
<tr>
<td>Peak diastolic velocity cm/s</td>
<td>78 ± 9</td>
<td>71 ± 10</td>
<td>77 ± 10</td>
</tr>
<tr>
<td>Mean diastolic velocity cm/s</td>
<td>54 ± 5</td>
<td>50 ± 8</td>
<td>49 ± 7</td>
</tr>
<tr>
<td>LAD diameter min</td>
<td>1.8 ± 0.1</td>
<td>1.8 ± 0.1</td>
<td>1.8 ± 0.07</td>
</tr>
</tbody>
</table>

These studies suggest that IMA grafting may not increase basal LAD flow in the early post-operative period, but improvements occur with time which reflected an increase in the systolic flow component. This may relate to changes in the IMA.

These data are from a larger study that included techniques described should find application in the follow-up of IMA grafts.

MAZE 3 (for atrial fibrillation): two cuts too few?

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The Maze procedure has been developed as a surgical approach to the management of patients with atrial fibrillation refractory to medical treatment. The latest modification (Maze 3) involves four cuts that isolate the roof of the left atrium (LA) including the ostia of the pulmonary veins. We suggest that the very size of this 'block' isolated between the cuts whilst usually leading to good rate control significantly reduces the LA contribution to ventricular filling; the large surface area of erratically contracting LA could also provide a nidus for the development of mural thrombus. The mass of contractile LA and the endocardial surface area contained within the 'block' have been estimated in formalin-fixed hearts obtained from trauma victims with no evidence of cardiac disease (n = 10). In these samples the 'block' constituted ~28% of the weight of the LA (4.3 ± 1.4 g vs. 15.5 ± 5.1 g (mean ± s.d.) and the endocardial surface area of the block was ~35% of the total endocardial surface area of the LA (15.5 ± 3.0 cm² vs. 43.4 ± 10.5 cm²). In an attempt to reduce the size of this redundant component of the LA we have now modified Maze 3 with the incorporation of two additional cuts to isolate each pair of pulmonary veins as they enter the LA. This modification allows the recruitment of the majority of the atrium for the purposes of contraction. The first patient undergoing the modified procedure demonstrated normal sinus rhythm on Holter post-operatively and remained in sinus rhythm following basal atrial pacing at cycle lengths of 200 msec and 140 msec each for 30 seconds. In addition, there was an increment in cardiac output (~36%) with atrial pacing (CO (p=0.001) = 9.3 L/min; CO (p=0.02) = 6.8 L/min where SVR was 580 dyne cm⁻² s⁻¹). Transoesophageal and transthoracic 2D echocardiography showed that the majority of the atrial wall contracted well. We suggest that this modification of Maze 3 has the potential advantage of an augmented cut extending out through the left atrial wall. In addition it reduces the endocardial surface area of the isolated atrial segment which should further lessen the risk of thromboembolic complications.

ENTEROVIRUS RNA IN DILATED CARDIOMYOPATHIC HEARTS

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Polymerase chain reaction (PCR) studies to detect enterovirus RNA within dilated cardiomyopathic hearts have provided conflicting results due to failure to 1) exclude erroneous contamination, 2) confirm sufficient RNA extraction from clinical samples, and 3) provide adequate control data. In this paper, we report an established PCR technique to myocardium taken from 63 patients with DCM and 87 control tissues (5 patients with other cardiac diseases and 30 victims of trauma). In order to verify the presence of sufficient target RNA the constitutionally expressed cellular gene β-actin was co-amplified in each assay. Enteroviral genome was detected in 6 (10%) patients with DCM and 15 (17%) of the controls (p=NS). The presence of enteroviral genome within the myocardium of patients with DCM was not associated with any clinical or histological feature or the presence of Coxackie B virus-specific IgM. Within the control group enteroviral RNA was equally common in patients with cardiac disease and in victims of trauma (3%, 9% and 12, 40%, respectively; p=NS). Direct nucleotide sequencing of the amplified product demonstrated that the positive PCR were unlikely to be result from accidental contamination of clinical samples. Furthermore, 5 of 6 dilated cardiomyopathic hearts contained multiple sequence bands suggesting the presence of multiple enterovirus infection. These results demonstrate that persistent enteroviral infection is rare in DCM. However the finding of multiple PCR bands within enteroviral positive dilated cardiomyopathic hearts warrants further study.
CORONARY ARTERY BYPASS SURGERY: CURRENT PRACTICE IN THE UNITED KINGDOM
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A survey of current clinical practice was carried out among the 120 consultant cardiac surgeons currently performing coronary artery bypass surgery in the United Kingdom. The data was then compared with a similar survey conducted five years ago.

The 104 surgeons who returned the questionnaire (87%) performed an estimated total of 25,234 coronary artery bypass operations in 1992 with an average case load per surgeon similar to that in 1987 (243 vs 214, n.a.). The internal mammary artery was regarded as the conduit of choice by 101 surgeons (97%) and was used in 93% of bypass grafts to the left anterior descending coronary artery compared with 73% in 1987 (p<0.001), but only in 7% of grafts to the circumflex and right coronary systems. There was also a significant increase in the number of surgeons using both internal mammary arteries (88% vs 59% p<0.01) but only a small increase in those using the internal mammary artery as a sequential graft (55% vs 44%, n.a.). Patients' age remains one of the main contraindications to the use of the internal mammary artery (40%), together with insufficient mammary flow (42%), endarterectomy (22%), and unstable angina (17%). The right gastroepiploic and inferior epigastric arteries were used only occasionally (3%) when the internal mammary artery or the saphenous vein were not available.

The majority of surgeons (96%) still advocate the use of Aspirin to enhance graft patency, with 90 surgeons continuing treatment indefinitely, compared with 40 in the previous survey (p<0.001). As for methods of anticoagulation, 72% of surgeons used cardioplegic arrest while 38% preferred intermittent aortic cross clamping and fibrillation.

There is a general consensus of opinion amongst British cardiac surgeons that the internal mammary artery is the graft conduit of choice. Its use has been significantly extended over the last five years (1987-1992) suggesting a quick response to advances in scientific knowledge. The use of alternative arterial conduits is still limited, perhaps due to a lack of information on their long-term performance. The recently advocated technique of retrograde cardiopulmonary and continuous warm cardioplegia does not seem to have gained much popularity at this time.

SINGLE VERSUS BILATERAL INTERNAL MAMMARY ARTERY GRAFTING USING THE FREE RIGHT INTERNAL MAMMARY ARTERY, A COMPARISON OF EARLY MORTALITY AND MORBIDITY
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Some reports have suggested that the use of both mammary arteries compared to the use of a single mammary artery increases early mortality and morbidity, especially cited has been increased bleeding, respiratory and wound complications. To examine this we undertook a carefully matched retrospective study looking at these factors in 300 patients undergoing single and double mammary grafting in our unit. One hundred and fifty consecutive patients undergoing bilateral internal mammary artery (BIMA) grafting between 1989 and 1992 were investigated. They were matched with 150 patients undergoing single internal mammary artery (SIMA) grafting over the same period of time for age, sex, smoking habits, diabetes, severity of coronary disease, left ventricular function and number of grafts performed. Mean(SE) age for the BIMA and SIMA group was 56.56(7.1) and 58.73(6.5) respectively. Operative and early mortality (30 days) was 1.3% and 2% for the BIMA and SIMA groups respectively, no statistical difference. There was a significant BIMA vs SIMA difference for operation duration (223.5±6.4) vs 247.57±3.8) minutes, p<0.02, clamp time (54.20±1.26) vs 59.90±1.28) minutes, p<0.03, ventilation duration (12.06±0.14) vs 14.12±0.79) hours, p<0.02) and postoperative ventricular arrhythmias (2% vs 6%, p<0.025). Despite the prolonged ventilation in the BIMA group chest infection rates and pleural complications were similar in both groups. Blood loss 513±(20.23) and 481±(22.90)mls for BIMA and SIMA patients respectively was not significantly different. Prevalence of wound infection was also similar in both groups (0.7% and 1.3% for BIMA and SIMA respectively).

The fears regarding increased early mortality and morbidity following BIMA surgery are not confirmed by this study.

A CASE FOR MECHANICAL VALVE PROSTHESSES IN THE ELDERLY
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With an ageing population more elderly people will come to cardiac surgery. Many older patients receive a bioprosthetic heart valve on the basis that their life expectancy is shorter than the durability of the mechanical prosthesis and because of the fear of complications with anticoagulation in the elderly. We compared our experience with 131 elderly patients (70-86 yrs) who received a St Jude Medical mechanical prosthesis with 385 younger patients (50-60 yrs) receiving the same valve over an identical 11 year period (1981-1992). All patients received Warfarin. The anatomical distribution of the prostheses and the presence of additional procedures was the same in both groups. The early mortality was not significantly (NS) different in the two groups. Actuarial survival at 6 years was 71% ± 5% (elderly) and 75% ± 3% (younger) - NS. The hinge related risk from embolic events was 4.7/100 pt. yrs. (elderly) and 4.1/100 pt. yrs. (younger) - NS. Anticoagulant related haemorrhage was 3.8/100 pt. yrs. (elderly) and 1.95/100 pt. yrs. (younger) - NS. Freedom from all valve related morbidity and mortality at 6 years was 71% ± 7% (elderly) and 75% ± 3% (younger) - NS. These results, showing no significant difference in the complication rate between an older and younger group of patients who received the St Jude Medical prosthesis, support our clinical practice of using this mechanical valve in the elderly.

INFLUENCE OF DIETARY FATTY ACIDS ON THE COMPOSITION OF HUMAN AORTIC PLAQUES
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The fatty acid composition of human serum, adipose tissue and aortic plaques have been compared in order to assess the degree to which plaque fatty acid content is influenced by long-term dietary intake. Serum and adipose tissue fatty acid concentrations are largely determined by dietary intake. This is true for the essential polyunsaturated fatty acids (EFA), linoleic (18:2n6) and α-linolenic (18:3n3) acid, which cannot be synthesised by man and are obtained solely through diet. Studies involving dietary recall and angiographic analysis have provided conflicting results when comparing the intake of unsaturated fatty acids with the appearance of new coronary lesions, but typically demonstrate that an increased intake of polyunsaturated fatty acids (PUFA) is associated with a decreased incidence of coronary heart disease and saturated fatty acids (SFA) the converse. However, it is unclear whether dietary PUFA have a direct influence on the development of atherosclerotic plaques. To test this we determined the fatty acid composition of human serum, adipose tissue and post-mortem aortic plaques from 8 men. A comparison of ulcerated and non-ulcerated plaques from the same aorta examined these relationships at different stages of plaque development. Positive correlations were found between serum and non-ulcerated plaque ω6-PUFA (r=0.91), monounsaturates (MUFAs) (r=0.91), and also between non-ulcerated plaque and adipose tissue ω6-PUFA (r=0.91). In ulcerated plaques, there were positive correlations between serum and non-ulcerated ω6-PUFA (r=0.68), and adipose tissue ω6-PUFA (r=0.80). No associations were found between SFA in serum, adipose tissue or aortic plaques. This study has demonstrated highly significant correlations between fatty acids in human serum, adipose tissue and aortic plaques suggesting that the long-term dietary intake of ω6- and ω3-PUFA influences the composition of both non-ulcerated and ulcerated lesions. This may have implications with regard to current dietary trends towards increased PUFA intake.
THE EFFECT OF ACE INHIBITION ON VENOUS GRAFT HYPERPLASIA
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Department of Surgery and Department of Medicine
Leicester Royal Infirmary, Leicester, England

Intimal hyperplasia is a major cause of coronary artery bypass graft failure. Treatment with an angiotensin converting enzyme (ACE) inhibitor has been shown to reduce intimal hyperplasia after angioplasty and this study was devised to investigate the effect of ACE inhibition with perindopril on vein graft hyperplasia. New Zealand White rabbits were randomised to receive either perindopril (1 mg/kg) or nothing in their drinking water. One week after starting treatment all rabbits underwent an autogenous jugular vein-carotid artery bypass operation. Treatment was continued after bypass surgery and groups (n = 5) were sacrificed at 1, 4, and 12 weeks. The contralateral jugular vein and the graft were removed for in vitro measurement of the rate of DNA synthesis and histological assessment of the degree of intimal hyperplasia. DNA synthesis was determined by measuring the incorporation of 3H thymidine and expressed as disintegrations per minute (dpm) per mm vessel length per hour incubation. DNA synthesis in perindopril treated and untreated grafts were identical at 1 week (p = 0.39) but greater than their respective ungrafted contralateral veins (p = 0.024 and p = 0.0048 respectively). DNA synthesis in the untreated grafts increased from 1771 dpm (SEM = 389) to 3066 dpm (SEM = 382) by 12 weeks (p = 0.05) but is reversed in the treated grafts. A reduction from 2808 dpm (SEM = 326) at 1 week to 1332 dpm (SEM = 166) at 12 weeks (p = 0.05) was observed. Intimal hyperplasia was assessed using the ratio of intima to media cross sectional area. Perindopril caused a significant reduction of intima to media area ratio of 35% at 4 weeks, from 1.172 (SEM 0.11) to 0.761 (SEM 0.11, p < 0.05). These results suggest that perindopril reduces growth and intimal hyperplasia in vein grafts and treatment with ACE inhibitors may prolong the patency of vein bypass grafts.

INCREASED MONOCYTE TISSUE FACTOR EXPRESSION IN ISCHEMIC HEART DISEASE
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Cardiological Sciences, St George's Hospital Medical School, London.

Introduction: Enhanced procoagulant activity (PCA) related to tissue factor (TF) expression on monocytes has been described in a number of diseases associated with blood hypercoagulability, including septicemia and unstable angina. Previous methods of assessing PCA have measured the thromboplastin activity of isolated monocytes in a purified coagulation system. We have validated a flow-cytometric technique for measuring monocyte TF expression in whole blood. This method was then used to test whether enhanced monocyte TF expression occurs in ischemic heart disease.

Methods: 100 μL of blood was incubated with 2 μg of polyclonal rabbit anti-human TF antibody (raised against recombinant-human TF), for 30 min at 4°C. Red cells were lysed and the cells washed twice. TF antibody samples and negative controls were then incubated with fluorescent-conjugated swine anti-rabbit antibody. Cells were re-washed and fixed in 1% paraformaldehyde. TF expression was measured flow-cytometrically. Monocytes were identified by gating on forward and side scatter. Fluorescence values were converted into molecules of equivalent soluble fluorescent units (MESF) by comparison with standard calibration beads for each experiment. TF expression was compared before and after separation of mononuclear cells on Ficoll-Paque. Ficoll-separated cells were also tested for PCA on a 96 well plate: 30 μL of a 5×105 cell/L suspension were mixed with 50 μL of Chromogen S2222, 100 μL of culture medium (M199) and 100 μL of factor VII (1 Unit/mL). Plates were incubated at 37°C and colour read spectrophotometrically. A standard curve was prepared using a source of reference bovine thromboplastin. Using the above blood technique, monocyte TF expression was investigated in 11 normal subjects (NC), 5 patients with non-cardiac chest pain (NCC), 13 with chronic stable angina (CSA), 17 with unstable angina (UA) and 30 with myocardial infarction (MI).

Results: The proportion of TF+ve monocytes in the circulation was increased in patients with MI, UA, CSA, and NCC. The number of samples positive for TF were 0/11 (0%) in normal subjects, 3 of 5 (60%) in NCC, 5 of 13 (38%) with CSA, 11/17 (64%) in UA and 16/50 (32%) in MI. (Chi-sq = 19.9, p = 0.0027). Monocyte TF expression correlated with PCA (R = 0.999).

Conclusion: Enhanced monocyte expression of TF in CSA, UA and MI may, in part, explain the systemic hypercoagulable state observed in these conditions.

ANGIOTENSIN CONVERTING ENZYME (ACE) ACTIVITY: AORTIC AND ENDOCARDIAL ENDOTHELIELUM COMPARED
D. Lang, A.M. Shah & M.J. Lewis
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Recent studies indicate that endocardial endothelial cells (ECC), though different embryologically origin to vascular endothelial cells (VEC), show some similarities to the latter, eg. their ability to release nitric oxide (NO). In VEC, local ACE activity degrades kinins, eg. bradykinin (BK), thus reducing the NO released in response to these agonists. The role of ACE in EEC however is undefined. This study therefore compared the effects of BK and the ACE inhibitor ramiprilat in cultured bovine EEC (right ventricle) and VEC (aortic) on intracellular Ca2+ (measured by fura-2 fluorescence) and cyclic GMP (cGMP, an indirect measure of NO release).

<table>
<thead>
<tr>
<th>VEC</th>
<th>[Ca2+]i nM</th>
<th>cGMP fmol/μg protein</th>
<th>[Ca2+]i nM</th>
<th>cGMP fmol/μg protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td>95.37±12.60</td>
<td>0.47±0.02</td>
<td>79.125±3.82</td>
<td>0.08±0.01</td>
</tr>
<tr>
<td>BK</td>
<td>510±729.9</td>
<td>1.88±0.22</td>
<td>326±357.7</td>
<td>0.43±0.04</td>
</tr>
<tr>
<td>BK+Ram</td>
<td>568±804.8</td>
<td>0.54±0.03</td>
<td>76.7±14.4</td>
<td>0.15±0.01</td>
</tr>
<tr>
<td>BK+Ram</td>
<td>405±429.6</td>
<td>0.54±0.03</td>
<td>76.7±14.4</td>
<td>0.15±0.01</td>
</tr>
</tbody>
</table>

Data are ± SD. *p<0.01 of VEC. **p<0.001 of Basal. +p<0.01 of BK. # Ram had no effect on BK-induced increases in cGMP.

These data show that in resting cells levels of Ca2+ and cGMP are greater in EEC than VEC. ACE inhibition by ramiprilat increased these levels of cGMP, but not Ca2+. Conversely, ramiprilat augmented the BK-induced increase in Ca2+, but not cGMP, in both cell types. Thus EEC, like VEC, possess endogenous ACE which may modulate the activity of kinins.
LOCAL DRUG DELIVERY IN PORCINE CORONARY ARTERIES USING A NEW BALLOON CATHETER ALLOWING PROLONGED INFLATION

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Introduction: Local drug delivery by perfusion catheters has been proposed as a means of delivering high concentrations of active drug into the vessel wall but pressure mediated trauma and duration of balloon inflation are key limitations of these devices. We investigated a new delivery catheter which promises to overcome both these restrictions. Method: The device has a dual lumens shaft with a distally located polyethylene coil, which, when inflated, divides the vessel lumen into an external compartment allowing local drug delivery to the vessel wall and an internal compartment which allows distal perfusion. Using an over the wire technique the device was positioned in 16 coronary arteries (luminal diameter (mm): 3.2±0.4(SD)) of 11 non-atherosclerotic pigs (25-68kg) and inflated to 9 atmospheres. Coronary flow was estimated before and during device inflation using a doppler flow wire. Infusion of a selection of drugs with incremental molecular weight (Range 0.3-150 kDa) was then performed for 15 mins using infusion rates of 0.2 to 1.0 ml/min. Following device deflation the animals were sacrificed and macroscopic and histological examination of the vessels performed. Results: Infusion duration 19.9±9.7min (Range 3-60 min) did not result in any signs of ischaemia or haemodynamic compromise (Heart Rate: pre-115±22, during-108±26 bpm (p=n)). Mean Aortic Pressure: pre-83±20, during-67±20 mmHg (p=ns)). Furthermore intracoronary infusion of adenosine with the catheter inflated demonstrated coronary flow velocities similar to controls. Macroscopic examination demonstrated that compounds ranging from 0.3-70 kDa could be successfully infused into the coronary wall. Histological examination revealed localised endothelial damage but an intact internal elastic lamina (IEL) and media, although at the higher flow rates the IEL appeared oedematous. Conclusion: Our data suggest that prolonged balloon inflation is feasible with this device and that local drug infusion occurs with minimal trauma to the vessel wall. The device thus has great potential for ameliorating acute occlusion and late restenosis post coronary intervention.

HUMAN CORONARY ARTERIAL RELAXATION BY 17ß-ESTRADIOL IS ENDOTHELIN-DEPENDENT


We have previously reported that 17ß-estradiol (E) causes endothelium-independent relaxation of rabbit coronary arteries in vitro. However, the effects of E on the human coronary artery are unknown. In this study, human epicardial coronary artery rings (1.3-2.5 mm in diameter and 20-40 mm long) were removed from 13 patients undergoing heart transplantation. Segments were suspended in organ baths containing modified Tyrode solution bubbled with 95% O₂ and 5% CO₂ at 37°C, for measuring the changes of isometric tension. A substantial concentration of U46619 induced comparable contraction in endothelium-intact and denuded arteries (P<0.05). E (0.1mM-10μM) caused significant concentration-dependent relaxation compared to vehicle control (n=12; P<0.05). Relaxation responses ranged from 10±3% at 0.1mM to a maximal relaxation of 82±6% (mean±SEM) at 10μM. This response was unaffected by the removal of the endothelium with a maximum relaxation response of 74±2% at 10μM (P>0.05 cf with endothelium). No differences were observed after nitric oxide synthase inhibition with L-NMMA(10μM) or indomethacin (1μM) compared to time matched controls. These results demonstrate that E, at physiological concentrations, induces endothelium-independent relaxation in human coronary arteries in vitro. The possible modulatory role of E on human coronary artery tone may help explain some of the mechanisms underlying the cardiovascular beneficial effects of estrogen replacement therapy.

GENE EXPRESSION IN RAT VASCULAR SMOOTH MUSCLE CELL LESIONS


To identify genes which may be important in normal and pathological vascular smooth muscle cell (VSMC) function we performed a differential screen of a cDNA library derived from differentiated rat VSMCs in culture. Seven genes were preferentially expressed in differentiated cells and were identified by sequence analysis as α- and γ-SM actin, calponin, SM22α, elastin, phospholamban and CHIP28. Two genes, osteopontin (OP) and matrix Gla protein (MGP), were preferentially expressed in proliferating, de-differentiated VSMCs. It has been shown that the VSMCs involved in neointimal proliferation have some of the properties of neonatal VSMCs. We therefore examined the expression of these genes in the adult rat carotid artery following balloon-induced intimal damage using in situ hybridization and in the neonatal rat aorta using Northern analysis. Seven days after injury, when there is active VSMC proliferation, there was high expression of both OP and MGP in the neonatal VSMCs. However, CHIP28, SM22α and phospholamban were also upregulated in these cells. Fourteen days after injury the expression of these genes had returned to basal levels. None of the genes whose expression was up-regulated in the day seven neointima were highly expressed by the neonatal cells during development. These data therefore demonstrate a disparity between the genes expressed by neonatal VSMCs in vitro and those involved in neointima formation following intimal damage.
(174) POSTER

G-PROTEIN LINKED PHOSPHOLIPASE C (PLC) ISOFORMS IN VASCULAR SMOOTH MUSCLE (VSM)
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The inositol phospholipid pathway leading to the formation of IP3 is central to the regulation of contraction in VSM and is attenuated by NO, acting through cGMP. The purpose of our study is to identify the receptor/G-protein/PLC components in VSM and establish how these are integrated and controlled by cGMP. We report here the identification of the PLC isoforms in pig aortic smooth muscle and their activation by the GTP analogue Gpp(NH)p and agonist (histamine). We have developed an assay based on labelling the inositol phospholipids of pig aortic microsomes with [3H]inositol. The membranes containing the receptor/G-protein portion of the agonist signalling pathway, are used as the phospholipid substrates for PLC isoforms, which are separated from the soluble fraction using heparin affinity columns eluted with a NaCl gradient. Thus we have reconstituted in vitro an intact signalling system for PLC and obtained six peaks of soluble PLC activity with different properties of agonist and Gpp(NH)p activation. Using western blotting techniques we have identified three isoforms of PLC (γ1, β1 and δ1).

Peak No. Activated By Inhibited By Isoform
1 - γ1
2 G (G+A) & (per) G +A
3 G + (A) (per) G
4 - β1
5 G - δ1
6 G +A (per) G + A

We conclude from the complex pattern of regulation of PLC activity by Gpp(NH)p (G), agonist (A) and pertussis toxin (per) labelled membranes that different G-protein subunits activate and inhibit these isoforms.

(176) POSTER

NITRIC OXIDE INDUCES EARLIER ONSET OF LEFT VENTRICULAR RELAXATION AND REDUCES DIASTOLIC STIFFNESS IN MAN
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*Department of Cardiology, University of Wales College of Medicine, Cardiff & Cardiovascular Center, Aalst, Belgium.

In isolated myocardial preparations, we have shown that nitric oxide (NO) released from endothelial cells or derived from NO-donor agents induces earlier onset of myocardial relaxation and decreases diastolic stiffness, probably through cyclic GMP dependent reduced end-diastolic volume and calcium response to calcium. We studied the direct myocardial effects of the NO-donor, sodium nitroprusside (SNP), in 13 patients (11 women, 2 men; age 40-70) being investigated for atypical chest pain. None had clinical, echocardiographic or angiographic evidence of cardiovascular disease. SNP was infused simultaneously into both coronary arteries at very low doses (2 µg/min for 5 min), to avoid peripheral vasodilation. Left ventricular pressure (LVP) was monitored using a micromanometer-tipped catheter, and measurements made of peak LVP, LVEDP and dP/dtmax. The interval between the Q wave on the ECG and peak dP/dtmax ( LVP rel) was an index of time to onset of LVP relaxation and the time constant of isovolumic LVP decay (Tc) were calculated before and after SNP infusion. In 7 patients, sequential LV angiograms were obtained from which LV volumes (V) were calculated. Biocorory SNP induced (i) earlier LVP relaxation (t-LVP rel 432±36 to 415±36 ms; mean,SD), (ii) lower peak LVP (161±18 to 146±18 mmHg; both p<0.01), (iii) no change in dP/dtmax (140±52 to 137±510 mmHg/s) or T (365±5 to 356±5 ms; both p=ns). An equal dose of SNP infused into the right atrium did not reproduce these effects (n=5). In the 7 patients in whom diastolic-LV relations were studied, LVEDP fell from 182±5 to 124±3 mmHg and LVEDV increased from 158±34 to 165±40 ml (both p<0.05); the diastolic-F-V relation was shifted down in 5 of the 7. Lower LVEDP at higher LVEDV and the downward shift of individual diastolic F-V relations suggest reduced diastolic stiffness. These data indicate that NO causes direct LV relaxant effects and reduces diastolic stiffness in vivo in man, as previously documented in vitro. Physiologically, this should facilitate coronary perfusion by prolonging diastole and reducing diastolic extravascular compressive forces during tachycardia, when high coronary flow stimulates NO release.

(175) POSTER

IN NORMAL SUBJECTS CONDUIT ARTERY DISTENSIBILITY IS MAINTAINED BY FLOW-RELATED RELEASE OF EDRF.
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Endothelium-derived relaxing factor (EDRF) increases conduit artery distensibility (dD/dP.D where D is diameter and P is pressure) suggesting a role for EDRF in the maintenance of arterial distensibility. Disease states such as atherosclerosis, non-insulin dependent diabetes and hypertension cause endothelial dysfunction as manifest by reduced EDRF activity, and are associated with reduced arterial distensibility. We have investigated the effects of in vivo regional (millar) and in vitro isolated coronary arteries on conduit arterial distensibility in normal subjects (n=10) and subjects with coronary artery disease (n=10). Using a carbon dioxide/helium mixture and multi- channel microelectrode technology, we have demonstrated that the conduit artery distensibility is increased in brachial artery distensibility during reactive hyperaemia together with endothelium-independent responses to sublingual nitroglycerin (GTN 400µg) in 11 normal subjects (3 male, age range 22-61, mean 40yr, blood pressure <130 mmHg systolic, <90 mmHg diastolic).

Arterial distensibility was determined using a non-invasive ultrasonic wall tracking device (AMA Wall Track System Resolution 3 µm) which measured internal brachial artery diameter continuously during the cardiac cycle, blood pressure measured using photo-plottymography (Finapres), and reactive hyperaemia by transcutaneous Doppler, at rest, 1 min of reactive hyperaemia, and 3 mins after sublingual GTN. In normal subjects, reactive hyperaemia (flow-related endothelium-dependent response) and GTN (endothelium-independent) increased arterial distensibility (+55 ± 79% of baseline, p<0.05). Age reduced the response to GTN (p<0.05) but not the hyperemic response. Thus in normal subjects flow-related release of EDRF maintains arterial distensibility, and, by inference, cardiovascular "efficiency" (cardiac workload relative to tissue perfusion).

(177) POSTER

LOAD INDUCED ELECTROMECHANICAL ALTERNANS IN THE ANAESTHETISED PIG HEART
C.F. Murphy, D.J. Dick, S.M. Horner, B.Y. Zhou, F.G. Harrison, M.J. Lab
British Heart Foundation Cardiac Arrhythmia Research Group, Department of Physiology, Charing Cross and Westminster Medical School, London W.6

Changes in myocardial loading, via the presumed process of mechanical-electrical feedback have been shown to produce a wide range of electrophysiological changes that may be involved in the genesis of serious ventricular arrhythmia. These include stretch induced ectopics, early afterdepolarisations, changes in refractory period and changes in action potential duration. Here we report the onset of electrical and mechanical alternans during transient increases in myocardial loading. Eight pigs were anaesthetised with Halothane 1% in a 1:1 mixture of nitrous oxide and oxygen, the chest wall removed, the heart suspended in a pericardial cradle and a pressure monitoring catheter placed into the left ventricle (Millar). Regional monophasic action potentials were recorded in three areas of the left ventricle using suction electrodes. Hearts were right atrially paced at cycle lengths 50ms greater than the threshold for pulsus alternans. A pneumatically driven aortic snare around the proximal aorta was used to produce transient load increases. The data were digitised at 1000Hz and analysed by computer. Monophasic action potential duration was measured at 70% repolarisation. Oscillations that produced ventricular ectopic beats were not considered. This may produce alternans. Partial systolic occlusions lasting between 5-8 seconds (mean 6 seconds) transiently increased peak intraventricular pressure by between 40 and 90% (mean 70±5%) and produced transient pulsus alternans and transient alternans in monophasic action potential duration (electrical alternans). Beat to beat differences in monophasic action potential duration varied between 3-17ms (mean 7ms). There was also a regional variation in the extent of electrical alternans observed during systolic occlusions. Sudden changes in myocardial loading can produce mechanical and electrical alternans. The latter has been linked with the onset of arrhythmia under numerous circumstances.
**DIABETICS WITH PERIPHERAL VASCULAR DISEASE HAVE AN INCREASED MEAN PLATELET VOLUME, PLATELET COUNT AND MEGAKARYOCYTE PLOIDY.**

A S Brown, Y Hong*, A de Belder, M Edmonds*, D Jewitt, J Etraulinsky, J Martin*. Departments of Cardiology and Medicine, King's College School of Medicine and Dentistry, Denmark Hill, London.

Altered platelet function has been reported in diabetics whose excess mortality is predominantly determined by cardiovascular complications. Therefore mean platelet volume (MPV), platelet count and MPK ploidy (DNA content) were measured in 3 groups of age and sex matched patients: 1) Non diabetics with normal coronary arteries and no peripheral vascular disease* (n=6), 2) Non diabetics with coronary artery disease* (CAD) (n=15) and 3) Diabetics with peripheral vascular disease* (PVD) (n=15) *diagnosed on angiography. Platelet measurements were performed on a coulter 2M particle counter. MKs obtained by sampling the posterior iliac crest were isolated by single gradient percoll centrifugation and identified using the FITC GP IIb/IIIa monoclonal antibody. The platelet count (+/- SD) was increased in diabetic patients compared to patients with CAD and controls (336(109.5) vs 272.5(49.4) vs 236.3(83.1) x10^11/L, p<0.05). Similarly, the MPV was significantly increased in diabetics compared with controls. The MPV was also increased in the CAD patients though this was not significant (8.1(1.3) vs 7.0 (0.3) p>0.05, CAD 8.5 (2.1), p=0.06). The MK ploidy distribution was not significantly altered in the CAD disease group compared with controls. In contrast the diabetics exhibited a significant increase in the % of MKs in the 32N class (p=0.007) with a concomitant reduction in MKs in the 2N, 4N and 16N classes. In the steady state platelet count and MPV are inversely related resulting in a near constant platelet mass. In certain circumstances this equilibrium may be perturbed. This study demonstrates that the MKs of diabetics with PVD have an altered ploidy distribution together with a relative thrombocytosis and an increased MPV. These findings may be important aetiological factors in the development of ischaemic syndromes in diabetics.

**EPICARDIAL CORONARY ARTERY DIAMETER CHANGES DURING ATRIAL PACING ARE DEPENDENT ON NITRIC OXIDE SYNTHESIS IN PATIENTS WITH CORONARY DISEASE.**

D Toussoulis, T Crake, DC Lefroy, C Tentolouris, P Toutouzas, G Davies, Cardiology Units, Hammersmith Hospital London, and Athena University Medical School, Greece.

Epicaldical coronary artery dilatation occurs in response to an increase in heart rate by atrial pacing. The effects of an intracoronary (i.c.) infusion of Nω-monomethyl-L-arginine (LNMMA, an inhibitor of nitric oxide synthesis), 40μmol/min for 4 min, was studied in 5 male patients (mean age 60y) with chronic stable angina and angiographically documented coronary artery disease. Only vessels with non-severe coronary stenoses (<60% luminal diameter reduction) were studied. In all patients atrial pacing (AP) 140 beats/min, was performed during normal saline (NS) and during the LNMMA infusion. Coronary angiograms were recorded during the infusions, AP, and after i.c nitrate (N). The diameter of proximal (Pr) (n=8) and distal (D) (n=13) coronary segments were measured by quantitative angiography. The mean diameters [% (SE) and % changes from baseline were:

<table>
<thead>
<tr>
<th></th>
<th>Pr</th>
<th>NS+AP</th>
<th>LNMMA</th>
<th>LNMMA+AP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter</td>
<td>3.13±0.2</td>
<td>3.35±0.2</td>
<td>3.09±0.2</td>
<td>3.19±0.2</td>
</tr>
<tr>
<td>LNMMA+AP</td>
<td>3.46±0.2</td>
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</table>

Thus dilatation of proximal and distal epicardial coronary artery segments during atrial pacing is inhibited by LNMMA. These data indicate that epicardial artery dilatation during atrial pacing is dependent on nitric oxide synthesis.

**PHASE RELATIONSHIPS OF ELECTROMECHANICAL ALTERNANS DURING ACUTE REGIONAL ISCHAEMIA IN THE ANAESTHETISED PIG HEART.**

C.F. Murphy, S.M. Horner, D.J. Dick, B.Y. Zhou, F.G. Harrison, M.J. Lab. British Heart Foundation Cardiac Arhythmia Research Group, Department of Physiology, Charing Cross and Westminster Medical School, London. U.K.

There is growing evidence that abnormal mechanical factors in cardiac contraction may produce electrophysiological disturbances conducive to ventricular arrhythmia and sudden death by the process of mechano-electric feedback. Pulus alternans is an abnormality of myocardial contraction often associated with a dire prognosis. The aim of this study is to assess electrophysiological changes associated with the onset of pulus alternans during acute regional ischaemia.

Eight pigs were anaesthetised with 1% Halothane in a 1:1 mixture of oxygen and nitrous oxide, the chest wall removed, the heart suspended in a pericardial cradle and a pressure monitoring catheter (Millar) inserted into the left ventricle. Regional monophasic action potential (MAP) and regional contraction were measured using suction based devices placed on the left ventricular epicardium. Recordings were taken from a control area and an area made ischaemic by ligation of a diagonal coronary artery. Stepwise increases in pacing rate were used to induce alternans at 5 minute intervals up to 30 minutes after artery ligation. Ischaemia produced a rapid decline in regional contraction such that within 10 seconds segments paradoxically stretched during systole. Pulus alternans could always be induced by sufficiently rapid pacing (minimum cycle length 250ms) and was always associated with the onset of alternation in MAP duration (measured at 70% repolarisation). In the control area alternans was invariably discordant (stronger, higher pressure heat associated with shorter action potential) however in the ischaemic area alternans was concordant or absent. The onset of pulus alternans is associated with alternans in MAP duration. This is an example of 'mechano-electric feedback'. The electrical alternans observed in ischaemic and normal areas were out of phase. This serves to increase regional disparity in MAP duration, an effect which may be pro-arrhythmic.

**THE SKELETAL MUSCLE SIGNAL TO VENTILATION ON EXERCISE IS A FUNCTION OF MUSCLE BULK USED.**

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Background. Patients with chronic heart failure (CHF) have an excessive ventilatory response to exercise. Patients have skeletal muscle abnormalities with both decreased bulk and abnormal muscle function. This study was designed to examine the hypothesis that ventilatory response to exercise is influenced by the muscle group performing an exercise load. Methods. A group of 11 subjects undertook cycle exercise using arms or legs at the same absolute work load during an incremental 9 minute protocol (25 watt increase every 3 minutes). Metabolic gas exchange was measured using mass spectrometry with indicator gas dilution. Results. Arm exercise resulted in the same total oxygen consumption as leg exercise, indicating that the same external work was being performed (6.4 (0.2) vs 5.9 (0.5) litres; p:NS). There was an increase in ventilation at a given work load. The ventilation/carbon dioxide production slope was greater by 25% during arm exercise (from 21.9 (0.9) to 26.3 (0.8) (p<0.001), and the end-tidal carbon dioxide was lower during arm exercise (5.96 (0.10) vs 6.41% (0.20) at the end of stage 3 (p = 0.02). Conclusions. These results indicate that there is a signal to ventilation arising from exercising skeletal muscle which is a function of the muscle group used. Arm exercise at the same level of exercise results in an enhanced ventilatory response, suggesting that the ventilatory stimulus is a function of work per unit muscle rather than total external work. These findings have possible implications for the understanding of the increased ventilatory response to exercise in patients with heart failure, in whom there are both metabolic muscle abnormalities and a reduction in skeletal muscle bulk.
RELATIONSHIP BETWEEN HAEOMODYNAMIC AND NEUROHUMORAL VARIABLES AFTER MYOCARDIAL INFARCTION AND SUBSEQUENT VENTRICULAR REMODELLING

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Factors involved in the progression from ischaemic ventricular damage to the syndrome of chronic heart failure (CHF) remain unclear. Haemodynamic changes and neurohumoral activation are likely to be important. We assessed changes in left ventricular end diastolic volume indices (LVEDVI) measured echocardiographically in 55 patients, mean (SD) age 57 (9) following their first Q wave myocardial infarction (MI). LVEDVI was measured 7 (0.3) days after MI and 6 months later. Neurohumoral (atrial natriuretic peptide (ANF), plasma renin activity (PRA), noradrenaline and adrenaline) and haemodynamic (heart rate, mean arterial pressure (MAP), cardiac index (CI), and systemic vascular resistance (SVR)) variables were measured at rest and at the end of symptom-limited maximal treadmill exercise (designated maximum value) 17 (4) days following MI. Thirty-eight age-matched subjects acted as controls for the echocardiographic data.

Twenty-three (42%) patients showed an increase (122.2 (7.4) ml/m²) at month 6 and 32 (58%) no increase (73.6 (1.9) ml/m²) in LVEDVI compared with the control subjects (71.8 (2.7) ml/m²). Significant correlations were documented between neurohormonal changes in LVEDVI at 6 months following MI and neuroendocrine (ANP at rest r=0.39, p<0.01; ANPmax = 0.33, p<0.05) and haemodynamic (MAPmax r=0.48, p<0.01; cardiac index max r = -0.58, p<0.05; SVRmax r=0.58, p<0.05) variables. Baseline, LVEDVI correlated negatively with changes in LVEDVI (r=-0.65, p<0.01). Haemodynamic and neurohumoral variables measured soon after hospital discharge correlate significantly with changes in ventricular volumes in the six months following MI implicating a role in the pathophysiology of ventricular remodelling.

ADVERSE EFFECTS OF FLUROCORtISONE IN TREATMENT OF VASODEPRESSOR DISORDERS

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9 alpha fluoro corticosterone (F) is a synthetic mineral corticoid which increases pressor sensitivity to circulating catecholamines and angiotensin, alters intravascular concentrations and has central adrenergic effects. It is beneficial in the treatment of hypertensive disorders: vasodpressor carotid sinus syndrome (VD CSS), vasodpressor renovascular syndrome (VD RVSS) and orthostatic orthostatic hypotension (OH) (da Costa D, Brit Heart J 1993; 63: 308-10). The adverse event (AE) profile in these patient groups has not been previously reported.

64 consecutive patients (mean 50 years; 58-98 years; 42F) were contacted on 3 occasions: starting dose 50 mg. Prior to treatment patients had full clinical assessment, 24 hour ambulatory blood pressure (SpaceLab), 24 hour ambulatory heart rate (Oxford), head-up tilt testing for 30 minutes, at 70° (Atrik tilt table), with and without isoprenaline provocation, carotid sinus massing supine and upright (Atrik tilt table) and echocardiography. Phasic blood pressure (Finapres) and continuous surface ECG were recorded throughout. After study inclusion patients were reviewed at 2 monthly intervals during 2 year follow up (mean 1 year). 19 patients had VD CSS, 17 OH and 28 VD RVSS with OH and/or VD CSS.

13 patients died during follow up, 35 reported AE and in 17 medication was withdrawn because of AE (severe hypertension - 200/100 mmHg; n = 4, cardiac failure (n = 7), stroke (n = 1), others (n = 5). 8 required potassium supplementation. Maximum daily dose of F was 50 mg (27%), 100 mg (72%) and 200 mg (15%).

During a two year follow up of patients with hypertensive disorders treated with fluoro cortisone, 5% experienced adverse events related to treatment, and medication was withdrawn in 27%. Fluoro cortisone, even in low doses, is poorly tolerated in patients with hypertensive disorders.

EFFECt OF L- AND D-ARGININE ON THE FOREARM ACETYLCHOLINE RESPONSE IN UNTREATED ESSENTIAL HYPERTENSION. CAN EXCESS SUBSTRATE STIMULATE NITRIC OXIDE PRODUCTION?

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The nitric oxide (NO) pathway is impaired in patients with essential hypertension. Does provision of excess L-arginine substrate increase the response to acetylcholine, a stimulator of NO production, in the forearm arterial bed in these patients? Forearm blood flow (FBF) was measured using venous occlusion plethysmography. Drugs were administered by local brachial artery infusion. The investigation was performed in 7 patients with untreated essential hypertension and 7 age and sex matched healthy controls. The hypertensive patients and their normotensive controls were aged 48.0±4.3 and 45.4±3.6 years respectively. In the hypertensive patients, ACH increased FBF to 292±32% and 308±34% of control. Neither L- nor D-arginine infused alone changed FBF, and co-infusion of either L- or D-arginine with ACH had no significant effect on the ACH response. In the presence of L-arginine, ACH increased FBF to 254±29% and 340±27% of control, in the presence of D-arginine, ACH increased FBF to 256±22% and 314±34% of control. In the normotensives ACH increased FBF to 281±79% and 391±34% of control. Neither L- nor D-arginine infused alone altered FBF. Co-infusion of either L- or D- arginine with ACH had no significant effect on the ACH response. In the presence of L-arginine, ACH increased FBF to 281±94% and 391±108% of control, and in the presence of D-arginine, ACH increased FBF to 212±34% and 308±72% of control. Comparing between groups, there were no significant differences in responses to either infusion of ACH or L- or D-arginine alone, or ACH in the presence of L- or D-arginine. These results show that the forearm ACH response is unaffected by provision of local L-arginine substrate, and suggest that the supply of L-arginine is not rate limiting for NO synthesis in patients with essential hypertension in vivo.

ACTION POTENTIAL SHORTENING DURING ISCHAEMIA IS NOT DUE TO INTRACELLULAR ACIDOSIS

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K* efflux with extracellular accumulation during ischaemia leads to a decrease in cardiac action potential duration (APD). Acidosis causes activation of K* -pore channels in cardiac myocytes because patches and it has been suggested that acidosis, rather than a decline in ATP, may be responsible for the early activation of these channels during ischemia. In this study we investigated the effects of respiratory acidosis and of ischemia on APD using action electrodes with simultaneous measurement of pH, using 9p nuclear magnetic resonance spectroscopy, in perfused heart. Changing solutions from 5%CO2/5%O2 to 15%CO2/60%MCO2 (pH 7.4 both conditions) caused pH to fall from 7.14±0.026 to 6.91±0.035 (p=0.01; t-test) and was associated with ~18% prolongation of APDmax from 245±3 to 295±3 (p<0.01; see fig). Conversely, when pH had fallen to 6.98±0.033 after 7.5 mins of low flow ischaemia APD90 decreased by ~20% from 244±12 to 193±11 (p<0.01; see fig). During low flow ischaemia (ATP) decreased <10% but contraction ceased. These results suggest that the reduction in APD during ischaemia is unlikely to be due to intracellular acidosis but rather this fall in pH may limit decreases in APD.

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Isolated Martynyuk, arrhythmia, of potentials were atrioventricular Adenosine, cells showed spontaneous hyperpolarisation -110 potential inward independent caused equal in the human AV nodal cell, showing a similar density of nerve fibres and fascicles consistent with the conduction system. There was considerable variation in the density of the nerve subpopulations. The dominant subpopulation of nerve fibres and fascicles in the human, porcine and bovine sinus node and atrioventricular node, displayed acetylcholinesterase (ACHE) activity, whereas a larger proportion of tyrosine hydroxylase (TH)-immunoreactive nerves was observed in the guinea pig nodal tissues. Neuropeptide Y (NPY)- and TH-immunoreactive nerves showed a similar distribution pattern in all conduction tissues and represented the main population of peptide-containing nerves in the human, porcine and bovine conduction tissues. The main population of peptide-containing nerves in the guinea pig conduction tissues were immunoreactive for both substance P (SP) and calcitonin gene related peptide (CGRP) (depicting sensory nerves). Non-autonomic intestinal polypeptide somatostatin, SP- and CGRP-immunoreactive nerves represented a relatively small portion of the overall innervation in the human but not in the bovine and porcine conduction tissues. The male population of nerves in the bovine, and especially the porcine ventricular conduction tissues, were ACHE-positive. This is in the direct contrast to the human ventricular conduction system where these nerves are relatively sparse. These variations in nerve subpopulations between species are significant in view of the use of animal hearts for experimental studies and transplantation.

Adenosine increases potassium conductance in isolated rabbit atrioventricular nodal myocytes

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The ionic mechanisms underlying the action of adenosine on the atrioventricular (AV) node, and hence its actions in the management of arrhythmias, were studied in single AV nodal cells, isolated from rabbit hearts by enzymatic dispersion. Electrophysiological recordings were made using a single micro-electrode patch clamp technique from cells isolated from the region of the AV node which showed spontaneous activity. Using current clamp, spontaneous action potentials were recorded, beating at 180 beats per minute at 35°C. Adenosine, 1-50 μM, inhibited this activity, and caused a hyperpolarisation of the membrane potential of 9 ± 3 mV, from a maximum diastolic potential of -43 ± 11 mV (n=13). Voltage clamp recordings showed an adenosine-induced increase in outward time-independent current at the holding potential, -50 mV, and increase in inward current in response to negative voltage steps (e.g. adenosine 10 μM induced a 60% increase in inward current at membrane potential -110 mV). A ramp voltage clamp protocol, from -120 to 60 mV in 10 seconds, was used to obtain "pseudo steady state" currents. The difference between currents in the presence and absence of adenosine demonstrated an adenosine-induced inwardly rectifying current, with a reversal potential of -106 mV, when the extracellular potassium was 2.7 mM. Increase in extracellular potassium to 12.7 mM caused an increase in the adenosine-induced current and a shift of the reversal potential to -63 mV. These reversal potentials were equal to the calculated equilibrium potential of potassium at both concentrations, indicating that the inwardly rectifying adenosine-induced current was carried by potassium ions.

In conclusion, adenosine caused an increase in potassium conductance in AV nodal cells. This may underlie its negative dromotropic action and its use for arrhythmia management.

A novel method of experimental bradycardia applied to hearts with myocardial infarction: effects on capillary supply

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Heart rate reduction is one of the major benefits of β-blockade treatment of myocardial infarction responsible for reducing mortality. Prolonged bradycardia in small mammals has been shown to result in growth of myocardial capillaries and this study reports a method developed to induce bradydrcardia experimentally in the pig model of infarction to assess the effects of chronic heart rate reduction on myocardial capillary supply. Female farm pigs (23-29kg) were used either with or without infarction produced by introduction of a copper coil under fluoroscopic control into the distal third of the left anterior descending coronary artery. At the same time, animals were instrumented with Medtronic dual chamber transcutaneous pacemakers and leads and either atrauimal or ventricular-atrial pacing was used with A-V delays of 150-200ms and rates of 60-80bpm (beats per minute) to reduce heart rate from 112±2±6ms (mean±SEM) to 31±4% in infarcted (n=4) and 30±3% in normal (n=4). Controls were 5 infarcted animals instrumented but not paced. After recovery, heart rates were monitored on a daily basis for 4-6 weeks from ECG recorded by implanted subcutaneous leads. Animals, bradycardia remained stable throughout with heart rates around 40bpm lower than in unpaced animals. At final experiments, heart rates were 79±3bpm in paced infarcted and 77±2bpm in paced normal. Two were significantly different in heart weights between any of the groups. Myocardial capillarity was assessed in non-infarcted myocardium by lecin staining of vascular endothelial and capillary density was significantly increased by pacing in the left ventricular free wall of both infarcted (by 14%) and non-infarcted (by 18%) hearts (p<0.05). These findings demonstrate that long-term bradycardia is able to induce new capillaries in the normal and infarcted pig heart, and that it results in an increase in left ventricular capillarisation. An enlarged capillary bed and possibly better perfusion could explain part of the beneficial effect of post-infarction treatments which involve heart rate reduction.

Endothelial dysfunction contributes to thrombogenesis in chronic atrial fibrillation

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A prospective population-controlled study was performed in patients with chronic atrial fibrillation (AF) to determine possible associations between plasma von Willebrand factor (vWF) (a marker of endothelial dysfunction) and fibrin D-dimer (DD) levels (a marker of intravascular fibrin turnover and thrombus formation). Whether or not such levels are related to treatment with warfarin or aspirin. 85 patients with established AF were studied, with 37 on no anti-thrombotic therapy (Group 1), 31 patients established on warfarin therapy (Group 2) and 17 taking aspirin. Both groups were compared to 158 healthy population controls in sinus rhythm. In Group 1, there was significant elevation of plasma vWF (median difference 65%; 95% c.i. 38 to 89, p<0.0001) and DD levels (median difference 77 ng/ml, 95% c.i. 38 to 122, p<0.01) when compared to population controls. In patients in Group 2, plasma vWF was not significantly different compared to Group 1 (median difference 4%; 95% c.i. 41 to 41), but there was a significant difference in plasma DD levels between the two groups (median difference 90ng/ml, 95% c.i. 39 to 150, p<0.0001). In Group 3, there were no significant differences in plasma vWF (median difference 2%, 95% c.i. 35 to 41) or DD levels (median difference 34 ng/ml,95% c.i. 144 to 21) when compared to Group 1. In patients not on warfarin (Groups 1 and 3) there was a significant correlation between vWF and DD levels (Spearman r=0.52, p<0.01). In conclusion, plasma DD levels were significantly elevated in all groups of patients with AF, irrespective of whether antithrombotic therapy was taken. In patients without any antithrombotic therapy, DD levels were significantly elevated suggesting increased intravascular thrombus formation, which is lowered in patients on warfarin. The elevated vWF levels in AF and positive correlation between vWF and DD in patients not on warfarin indicates a role for endothelial dysfunction in thrombogenesis in patients with AF.
"BILATERAL BUNDLE BRANCH BLOCK" - A COMMON FINDING IN PATIENTS WITH DILATED CARDIOMYOPATHY

Patients with dilated cardiomyopathy (DCM) and left bundle branch block (LBBB) have been shown to have early potentials on signal averaged electrocardiogram (SAECG), which cause early onset of mechanical activity. In order to identify whether early potentials represent activation of the left ventricle from the right, we recorded 12 lead ECGS and SAECGs in 77 pts with DCM. Short and long axis M-mode echocardiograms were used to assess the onset of original wall motion of the ventricles. They were compared to 6 pts with uncomplicated right bundle branch block (RBBB) and 15 normals. 20 pts had LBBB and 29 intraventricular conduction delay (IVCD) on 12 lead ECG. PR interval (186±50 ms vs 150±15, p<0.05) and QRS duration (127±25 ms vs 90±10, p<0.01) were both prolonged compared to normal. Early potential (<40 μV) time was much longer (33±12 ms vs 12±7, p<0.01) in the pts than in normal. The onset of left ventricular free wall motion was similarly delayed beyond 95% of the upper normal limit in all the pts with classical LBBB as well as IVCD with respect to the septum. Right ventricular free wall was also delayed in 12 out of 20 pts with LBBB and 24 out of 29 with IVCD by 65±20 ms, similar to that (75±10 ms) in pts with RBBB. Thus, in the majority of pts with DCM and an ECG pattern of LBBB or IVCD, the onset of mechanical systole is symmetrically delayed in the two ventricles, compatible with "bilateral bundle branch block". Early potentials arise from activation of a small area of myocardium high in the septum directly from the His bundle via "high fibres" originally described by Mahaim and Winston, and not from a normally activated right ventricle.

RESULTS OF RADIOFREQUENCY CATHETERABLATION IN YOUNG CHILDREN
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Although radiofrequency(RF) catheter ablation has become the accepted curative treatment for supraventricular tachycardia in adolescents and adults, its role in infants and young children is unclear. We compared the results of RF ablation in 10 infants and children under 10 years of age (median 5.7, range 0.8 - 9.8 years) (group A) with 20 adolescents and adults (median 16, 10.6 - 19 years) (group B). Group A had 9 accessory pathway and 1 left atrial ectopic tachycardia while group B had 18 accessory pathways and 3 atrioventricular node re-entry tachycardias. One child in group A had Ebstein's anomaly of the tricuspid valve, all others had structurally normal hearts. We achieved a 90% success rate in group A. One child underwent 2 procedures to achieve successful ablation and a left posterior pathway could not be ablated despite 3 separate attempts including a trans-septal approach. We undertook 27 separate procedures in the 20 group B patients to achieve a 75% success rate. The median screening time for group A was 47 (12 -176) min Vs 68 (29 -229) min for group B (NS). The median procedure time for group A was 195 (120 -300) min Vs 270 (150 -450) min for group B (NS). The median number of RF applications for group A was 7 (2 - 63) Vs 18 (3 -56) for group B (NS). The only complication encountered was in a 5 year old with temporary loss of foot pulses which responded to over-night inflation of heparinised balloon. Radiofrequency catheter ablation in younger children appears equally effective and safe to that of older patients. Indications for this curative therapy in younger children should therefore depend on the severity of symptoms and the predicted natural history of their arrhythmia.

IMPACT OF AGE AND SIZE ON OUTCOME AND FEASIBILITY OF RADIOFREQUENCY CATHETER ABLATION OF ACCESSORY PATHWAYS IN INFANTS, CHILDREN, AND ADULTS
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Radiofrequency catheter ablation (RF) is now the procedure of choice for adults with symptomatic supraventricular tachycardia (SVT). Its safety, efficacy and feasibility in infants and children is still in question. We therefore reviewed the outcome (success/failure: S/F) and feasibility/procedural characteristics (procedure time PT, fluoroscopy time FT, and # of RF lesions) in 178 patients (age 1 mo to 67 yrs, mean 15.4 yrs) undergoing their 1st RF for SVT due to an accessory pathway between Mar 91 and June 93. Patients were divided into 5 categories of age and weight. Major complications were seen in only 1 patient with pericardial tamponade needing drainage.

Results:

<table>
<thead>
<tr>
<th>Age (Yrs)</th>
<th>0-5</th>
<th>5-10</th>
<th>10-15</th>
<th>15-20</th>
<th>&gt;20</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of pts</td>
<td>18</td>
<td>24</td>
<td>45</td>
<td>19</td>
<td>23</td>
</tr>
<tr>
<td>S/F</td>
<td>0.72</td>
<td>0.71</td>
<td>0.8</td>
<td>0.74</td>
<td>0.83</td>
</tr>
<tr>
<td>mean PT (min)</td>
<td>345</td>
<td>299</td>
<td>315</td>
<td>322</td>
<td>305</td>
</tr>
<tr>
<td>mean FT (min)</td>
<td>44</td>
<td>46</td>
<td>45</td>
<td>63</td>
<td>35</td>
</tr>
<tr>
<td>mean # lesions</td>
<td>16</td>
<td>23</td>
<td>21</td>
<td>23</td>
<td>17</td>
</tr>
</tbody>
</table>

No variable showed a significant change with age. Analysis by weight categories showed a similar lack of difference. Excluding the failures and analyzing only successful procedures also showed no correlation between age/weight and outcome/feasibility.

Conclusions: The outcome and feasibility of RF for SVT due to an accessory pathway is unaffected by age. There is no evidence to support the view that RF is more risky, less successful or less feasible in children.
MULTIFACTORIAL PREDICTION OF EARLY ARRHYTHMIC EVENTS AND EARLY MORTALITY IN SURVIVORS OF ACUTE MYOCARDIAL INFARCTION

Several factors have been proposed as predictors of risk in survivors of acute myocardial infarction (AMI). However, none of the recognised factors used alone has a clinically useful predictive value. This study investigated the predictive value of different combinations of heart rate variability (HRV), left ventricular ejection fraction (LVEF), signal-averaged electrocardiogram (SAECG), and frequency of ventricular ectopic activity (VPB) for the identification of patients who died or suffered arrhythmic complications during the first year of follow-up after the first AMI. The population of the study consisted of 557 survivors of AMI aged ≤70 years who survived to hospital discharge and who were followed for at least 1 year (range 1–6 years). During follow-up of 1 year, 29 patients died and 28 suffered from arrhythmic complications (sudden death and/or symptomatic sustained ventricular tachycardia). SAECG, HRV and VPB data were obtained pre-discharge (day 5–12). The receiver operator and positive predictive calculations were performed for the calculation of 1-year mortality and 1-year arrhythmic complications based on different combinations of the risk factors. At selected levels of sensitivity, the following values of positive predictive accuracy were achieved [%]:

<table>
<thead>
<tr>
<th>Sensitivity level [%]</th>
<th>Mortality</th>
<th>Arrhythmic Events</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>LVEF</td>
<td>11.2</td>
<td>8.9</td>
</tr>
<tr>
<td>HRV</td>
<td>38.1</td>
<td>33.6</td>
</tr>
<tr>
<td>VPB</td>
<td>14.1</td>
<td>10.2</td>
</tr>
<tr>
<td>HRV+VPB</td>
<td>34.6</td>
<td>18.8</td>
</tr>
<tr>
<td>HRV+VPB+SAECG</td>
<td>31.2</td>
<td>25.9</td>
</tr>
<tr>
<td>LVEF+VPB+SAECG</td>
<td>31.8</td>
<td>20.0</td>
</tr>
<tr>
<td>Combination of all</td>
<td>23.0</td>
<td>20.2</td>
</tr>
</tbody>
</table>

Conclusion: (1) The combinations of risk factors used in this study were more powerful at predicting arrhythmic complications than all cause mortality. (2) A combination of all used risk factors provided clinically applicable risk stratification.

TRENDS IN PACEMAKER IMPLANTATION: IS THE UK THE "POOR MAN OF EUROPE"?
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A survey of European pacing in 1992 has revealed that 50% of the world's pacemaker implants are performed in Europe. There are huge variations across Europe in implantation rate - the new implant rate in the UK in 1992 was 159 per million, considerably lower than Belgium (600), Germany (450), France (425) and all other countries surveyed with the exception of Poland and Serbia. We performed a multifactorial analysis for data from 14 countries performing 117,000 new implants in 1992. One variable proved to be overwhelmingly the best predictor: IMPLANTING CENTRES PER MILLION POPULATION (p=0.00016)

We then performed bivariate analyses on each predictor to examine the UK's position in comparison with other European countries. UK implants were significantly lower than other countries when predicted by % OF POPULATION >60 and when predicted by GROSS DOMESTIC PRODUCT - we implant too few pacemakers for the age of our population and the limiting factor is not the country's wealth. Although the NUMBER OF IMPLANTS PER IMPLANT CENTRE in the UK lies within the predicted range, the low number of IMPLANTING CENTRES is the main reason for the low overall implant rate.

The UK has 2.3 implanting centres/million population, lower than almost all other European countries, and much lower than Belgium (20.3) and Germany (11.3). This is the principal factor responsible for our low pacemaker implantation rate.

MODES OF SPONTANEOUS INITIATION OF ATRIAL FIBRILLATION
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A variety of patterns of initiation of atrial fibrillation (AF) have been described, and it has been suggested that they may be used to guide preventive drug and pacemaker therapy. However, the frequency of these patterns is unknown.

We therefore examined 78 Holter recordings from patients with paroxysmal AF, using automated analysis with manual editing. The precise times of the first and last beats of 1126 episodes of AF were visually identified, and combined with the computerized analysis, yielding a listing of the rhythm and RR interval of every beat on each tape. The cycle lengths preceding the onset of episodes of AF were then analysed. For each episode of AF, the mean heart rate in the 10s (HR10) and in the 30s (HR30) prior to AF was calculated, along with the mean heart rate of all recorded sinus rhythm on the tape (HRμ).

Additionally, the RR intervals in each of the three beats preceding AF were compared with the mean of the 15 RR intervals preceding AF and classified as short (S, <80% of mean), normal (N, 80–120% of mean), and long (L, >120% of mean).

Results: (i) HR30 was <50 bpm in 8.7% of episodes, 50–100 bpm in 82.8% of episodes, and >100 bpm in 8.5% of episodes. (ii) There was very close correlation between HRF and HR30. However, HR30 was greater than HRF in 86.4% of episodes. (iii) The commonest modes of initiation were: N/N-N (40.9%), N-N-S (11.7%), S-L-S (5.2%), S-L-N (5.1%), L-S-L (4.2%), and L-N-S (3.0%).

We conclude that most episodes of atrial fibrillation do not occur at times of bradycardia or tachycardia, but that they do occur at relatively stable heart rates which are slightly above average. Although cycle length irregularity frequently precedes AF, the commonest mode of onset does not involve either a pause or a premature beat.

EARLY COMPLICATIONS AFTER DUAL CHAMBER VERSUS SINGLE CHAMBER PACEMAKER IMPLANTATION
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This study was performed to compare the frequency of early complications after single versus dual chamber permanent pacemaker implantation. Early complication was defined as one occurring in the 6 week period following implantation. We prospectively analysed consecutive pacemaker implantations from 1.1.87 to 30.6.93 at our regional centre which serves a population of ~2 million. All complications were also analysed for the relationship to operator experience, the venous access route and the presence of a temporary pacing wire at the time of the implantation of the permanent system. A total of 2019 new pacemaker units were implanted during this period. 1733 patients (85.9%) received a VVI pacemaker and 286 a DDD unit (14.2%). Wound infection occurred in 11 (0.6%) VVI patients and 6 (2.1%) DDD patients. Lead displacement requiring reoperation occurred in 15 (5.2%) DDD patients [1 (3.8%) atrial and 4 (1.4%) ventricular] and 18 (1.0%) VVI patients. There were 10 (0.6%) pneumothoraces, 9 (0.5%) haematomas requiring drainage, 1 (0.06%) chylothorax, and 2 (0.1%) deaths in the VVI group. There were 2 (0.7%) pneumothoraces, 2 (0.7%) haematomas, and no deaths in the DDD group. A total of 23 (8.0%) DDD patients and 51 (2.9%) VVI patients required a further intervention. There was no significant increase in complications for in frequency implantation (<12 per year). The subclavian approach was associated with a risk of pneumothorax when compared to the cephalic approach. The rate of wound infection was higher in patients who had a temporary pacing wire in place. The early complications in the DDD group were higher than in the VVI group being mainly due to an increased incidence of wound infection and atrial lead displacement.
ACUTE AND EARLY COMPLICATIONS OF PERMANENT PACING: A PROSPECTIVE AUDIT OF 926 CONSECUTIVE PATIENTS FROM A UK CENTRE
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The Cardiothoracic Centre, Liverpool, L14 3PE

We prospectively audited all new endocardial pacemaker implants at our institution, a Regional Centre serving a population of 2.8 million, over an 18 month period from September 1988 to September 1990. The implant data and follow-up to 2 months was available on 926 patients (pts), median age 77 years (range 16-99). Dual chamber units were implanted in 488 pts (53%), single chamber atrial in 51 (6%) and ventricular in 387 (41%). Median implant times were 45 minutes (range 20-170) for dual and 30 min (range 15-135) for single chamber systems. A temporary pacing lead (TPL) was present at implant in 213 pts (23%). 93% of implants were performed by the subclavian route. Prophylactic antibiotics were used in 96 pts (10.4%). Acute complications were rare: 19 pts (2%) developed a pneumothorax; 9 required treatment by aspiration or intercostal drainage. Arterial puncture without serious sequelae was recorded in 25 patients. There were 2 in-hospital deaths (unrelated to pacing) and 9 further deaths within 2 months of implant. Nine generators (0.97%) were removed for pacemaker pocket infection in the first two months of follow-up. Pocket infection was significantly more common in patients with a TPL (p<0.05). Generator erosion required replacement in 5 pts (0.5%), reabsorbed in 3 and explant in 2. Three pts required haemotoma evacuation and 2 pts needed operative drainage of a serious fluid collection. Lead displacement required reoperation in 14 pts (1.5%). Atrial (n=8)/ventricular (n=1) undersensing was successfully treated by reprogramming of sensitivity in all cases. Six pts developed atrial fibrillation (sustained in 3; 1 pt required cardioversion and 2 were reprogrammed from DDD to VVI). Supraventricular wound infection was successfully treated with antibiotics in 8 pts.

In conclusion there is a low acute complication rate related to permanent pacing in a large Regional Centre with experienced operators. Infection rates are low (<1%); the presence of a TPL at implant is associated with a significantly higher infection rate.

THE VALUE OF THE 12 LEAD ELECTROCARDIOGRAM AT HOSPITAL ADMISSION IN PATIENTS WITH ACUTE PULMONARY EMBOLISM

This study was undertaken: (1) to identify retrospectively the electrocardiographic (ECG) features associated with acute pulmonary embolism (PTE); (2) to determine the accuracy of ECG changes following Doppler echocardiographic (CS-DE) indices of right ventricular pressure or volume overload; (4) to determine the accuracy of ECG changes following Doppler echocardiographic (CS-DE) indices of right ventricular pressure or volume overload; (3) the role of serial ECGs in patients with proven PE and a normal ECG at hospital admission.

In 69 consecutive patients with invasive proven PE (27 M, 22 F, age 44-86 years), the diagnosis could be suspected on the admission ECG in 37 cases (76%). ECG features of PE were: (1) incomplete (N=26) or complete (N=7) right bundle branch block, with ST elevation (N=17) in V1; (2) S > 1.5 mm in I and aVL (N=36); (3) transition at V5 or V6 (N=25); (4) Q in III and aVF, but not in lead II (N=24); (5) frontal QRS axis of > 90° (N=16), or indeterminate axis (N=15); (6) QRS of < 5 mm in all limb leads (N=10); (7) negative T waves in III and aVF (N=12), and in V1-V5 (N=9); (8) atrial arrhythmias (N=11). Of 12 patients without diagnostic ECGs (N=4), serial ECGs were diagnostic of PE in only 3 further patients. On CS-DE, all patients had tricuspid valve regurgitation and an increased right ventricular end-diastolic diameter (RVEDD > 27 mm). There was no significant difference in the RV systolic pressure - RVSP - (mean ± SD, 55 ± 13 mm Hg vs. 54 ± 10 mm Hg) or in the RVEDD (41 ± 7 mm vs. 37 ± 6 mm) respectively, between patients with and without ECG evidence of PE at admission. On comparing subgroups of patients with abnormal ECGs (>7 vs 5-6 vs 3-4 abnormalities), there was no relation between the number of positive ECG features, and the RVEDD or RVSP. In conclusion: 1. The ECG at hospital admission suggested the diagnosis of PE in 76% of patients. 2. ECG abnormalities at admission did not correlate with RVEDD or RVSP. 3. In 18% of patients with proven PE, serial ECGs were normal.

CHANGING TRENDS IN PACEMAKER PRESCRIPTION IN PATIENTS AGED 80 AND OVER: A SINGLE CENTRE AUDIT OF 962 PATIENTS
RK Aggarwal, SG Ray, DT Connelly, DS Coulshed, J Ball, RG Charles
The Cardiothoracic Centre, Liverpool, L14 3PE

To assess the impact of the British Pacing and Electrophysiology Group guidelines on pacemaker prescription in elderly patients, we carried out a prospective audit of all new pacemaker implants from 1992. Of 926 consecutive patients, 369 (40%) were aged 80 and over (group 1). For comparison, data was obtained retrospectively on new pacemaker implants at our centre between 1984-1991; of 2622 consecutive patients, 593 (22%) were aged 80 or over (group 2). There was no significant difference in the primary clinical indication for pacing between the two groups. ECG indication was complete AV block in 35% vs 39% (group 1 vs group 2), partial AV block in 13.8% vs 8%, sinus node disease (SND) in 20% vs 24%, chronic AF with AV block in 27% vs 9.2%, bundle branch block in 2.9% vs 1.2% and unspecified in 1% vs 17%.DDD pacing mode was employed in significantly more patients with AV block in group 1 - 95 of 180 (52.8%) vs 43 of 280 (15.4%) in group 2 (p<0.001). AAI or AADR pacing in SND was also significantly more likely to be undertaken in group 1 than in group 2 - 11 of 74 (14.9%) vs 3 of 141 (2.1%) (p<0.001). In contrast there was no significant difference between the two groups in the use of DDD mode for SND - 23 of 74 (31%) vs 28 of 141 (19.9%) or VVIR mode for chronic AF with AV block - 11 of 100 (11%) vs 6 of 54 (11.5%).

We conclude that increasing proportions of patients undergoing permanent pacemaker implantation are aged 80 and over. The development of national guidelines for pacemaker implantation has lead to a substantial change in pacemaker prescription with significantly more physiological pacing being undertaken even in this very elderly age group.

AMBULATORY BLOOD PRESSURE MONITORING FOR 24 OR 48 HOURS?
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Objective: In the assessment of blood pressure (BP) ambulatory blood pressure monitoring (ABPM) aims to eliminate white coat hypertension. Our clinical impression was that BP was higher on the first day of ABPM than on the second day of ABPM and this mainly occurs acutely. The purposes of this study were (a) to compare the first 24 hrs (day 1) with the subsequent 24 hrs (day 2) of ABPM (b) to compare the BP measured at the onset of ABPM on day 1 with the same time on day 2.

Design and Methods: Fifty patients (age 49.8, SEM ± 1.8) with essential hypertension had ABPM with a Spacelabs 90207 monitor for 48 hrs. The device recorded at 15 min intervals during daytime (0600 to 2200 hrs) and at 30 min intervals at nightime (2200 to 0600 hrs). Analysis of variance showed the difference between mean of day 1BP and day 2 BP, dependent on the hour of the day, (cystolic: p = 0.002 diastolic: p < 0.001). Using paired Student t tests, the mean hourly, daytime, nighttime and the 24 hr BP from the first day were compared to the second day; p < 0.05 was considered significant.

Results: The table shows the mean BP difference (95% of interval).

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP difference (mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 hr Sys</td>
<td>+9.96 (+5.1, +14.8)</td>
<td>-7.80 (+4.3, +11.3)</td>
</tr>
<tr>
<td>2 hr Sys</td>
<td>+5.92 (+0.8, +11.1)</td>
<td>-4.88 (+1.6, +8.2)</td>
</tr>
<tr>
<td>24 hr Sys</td>
<td>+1.38 (+0.4, +2.3)</td>
<td>+0.77 (+0.37, +1.9)</td>
</tr>
<tr>
<td></td>
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</tbody>
</table>

No significant difference was seen after the first 2 hrs, daytime or nighttime BP.

Conclusions: BP is significantly higher at the onset of ABPM for 2 hrs and these recordings should be excluded from the mean BP calculations. ABPM for 48 hrs confers no advantage over 24 hrs.

Cardiac involvement in HIV infection is well recognised, but little is known about the pathogenesis of dilated cardiomyopathy (DCM) or ventricular dysfunction in AIDS. In the last 4 years, 280 patients with HIV infection (mean CD4 count 143 cells/mm² (range 0-940)) have taken part in a prospective echocardiographic survey. The echo's were reported by three independent observers and classified as: Normal, DCM (global LV hypokinesia with fractional shortening <25%), borderline left ventricular dyskinesia (LVD) e.g. dilated left ventricle with preserved systolic function or global hypokinesia with disagreement between observers, or RVD (isolated right ventricular dyskinesia with RV larger than LV in 2D images). Each group of DCM (n=14), RVD (n=12) and LVD (n=20) was paired with a separate control group, matched for age, sex, risk factor for HIV infection and stage of disease (CD4 count) but without cardiac involvement. The survival of these groups was closely monitored.

Results: All subjects with DCM, 7 with RVD and 9 with LVD patients died. The median survival time for DCM patients was 125 days (controls 304), LVD 378 days (controls 320) and RVD 395.5 days (controls 678.5). Kaplan-Meier Survival curves were calculated and the log rank test was used to compare the groups.

DCM vs Controls p<0.01
RVD vs Controls p<0.01
LVD vs Controls NS

Conclusion: This study demonstrates for the first time, that the survival of AIDS patients is adversely affected by DCM. Borderline LVD is not associated with a poor prognosis and may be a consequence of primary myocarditis. RVD often occurs in the setting of pulmonary hypertension, secondary to recurrent pulmonary emboli or infection and, the trend towards early death may be due to this rather than primary cardiac pathology.

ENDOTHELIAL MAINTENANCE OF CONDUIT ARTERY DISTENSIBILITY IS IMPAIRED IN PATIENTS WITH DILATED CARDIOMYOPATHY

MW Ramsey, CJH Jones, LA Luddington, MJ Lewis*, AH Henderson. Departments of Cardiology and Pharmacology*, University of Wales College of Medicine, Heath Park, Cardiff, CP4 4XX.

EDRF activity may be depressed in congestive cardiac failure. This could reduce conduit artery distensibility and increase load on the compromised heart. We measured changes in right common iliac artery (RCIA) pulse wave velocity (PWV; inversely related to distensibility) during endothelium-dependent and -independent vasodilatation in 6 patients with dilated cardiomyopathy (DCM; NYHA grades 2-3, EF<40%; 4 male, mean age 50y) and 9 normal subjects (N; 5 male, mean age 49y), all with normal coronary angiograms and no hypertension, diabetes or hypercholesterolaemia.

DCM patients were on stable medication with ACE inhibitors stopped 48 hours before. PWV was determined from the delay of the foot of a pressure pulse arriving at two pressure transducers 5cm apart on a 6F catheter in the RCIA, at rest and during acetylcitrine (ACH; endothelium-dependent) or adenosine (Ado; endothelium-independent) infusions into the proximal RCA. The effects of downstream microvascular dilatation were measured in repeat studies with RCIA infusions distal to the pressure transducers and were subtracted from the proximal effects to derive the local effects of the drugs on the RCIA. Baseline PWV was similar in the two groups (DCM 8.7±1.1 m/s vs N 9.1±1.5 m/s). ACH (10⁻⁷-10⁻⁵ M) induced dose-dependent reductions in RCIA PWV (-5.1-25%) in normals but no changes (+2, +2.3%) in DCM (p<0.05 at each dose); Ado (10⁻⁷-10⁻⁵ M) induced dose-related reductions in PWV both in normals (-5.1-22.4%) and in DCM (-1.1-14.6%; NS at each dose).

These data indicate that endothelium-dependent maintenance of arterial distensibility is impaired in DCM while endothelium-independent maintenance of distensibility is preserved. Thus, cardiac workload relative to tissue perfusion may be improved in DCM by manoeuvres that enhance endothelium-dependent dilatation in conduit arteries.

ECHOCARDIOGRAPHIC FEATURES AND WHOLE BODY AMYLOID LOAD USING 125I LABELLED SERUM AMYLOID P COMPONENT (SAP) CLEARANCE STUDIES

GJ Cleasham, DM Viguslin, PN Hawkins, J Joshi, CM Oakley, MB Pepys, P Nihoyannopoulos. Cardiovascular and Immunological Medicine, Hammersmith Hospital, London.

Cardiac involvement is of prognostic significance in AL amyloidosis and echocardiography may show characteristic left ventricular wall thickening (LWVT) and a shortened deceleration time (DT) of left ventricular inflow. The aim of this study was to compare echocardiographic features of cardiac involvement with quantification of whole body amyloid load using 125I-SAP plasma clearance studies.

26 patients with biopsy proven AL amyloidosis were divided into 3 groups. Group 1 (14 patients) had a LWVT less than 12mm, group 2 (6 patients) had a LWVT of at least 12mm but less than 15mm and group 3 (9 patients) 15mm or greater. DT was measured with pulsed wave doppler. Amyloid load was measured as the percentage of 125I-SAP measured in plasma six hours after dosing. This has previously been shown to be inversely related to whole body amyloid load.

DT (msec,mean±SEM) 125I-SAP (%mean±SEM)

Group 1 208±9.5 45.9±7.7
Group 2 167±12.9 33.8±7.6
Group 3 146±4.2 36.2±6.5 p<0.01

There was no significant correlation between LWVT and 125I-SAP (r²<0.05; p=NS) or between DT and 125I-SAP (r²<0.02; p=NS).

Conclusion: In patients with AL amyloidosis LWVT and DT are unrelated to whole body amyloid load as measured by 125I-SAP plasma clearance. Thus the presence of cardiac amyloidosis by echocardiographic criteria appears to be independent of the total amount of amyloid in the body.

DOES PAPILLARY MUSCLE ISCHAEMIA CAUSE 'DYNAMIC' MITRAL REGURGITATION?

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During acute ischaemia, some patients with coronary artery disease develop transient or 'dynamic' mitral regurgitation (MR), which has been attributed to papillary muscle dysfunction (PMD). The posteroomedial and anterolateral papillary muscles are usually supplied by the right (RCA) and left circumflex (LXC) coronary arteries respectively. Thus occlusion of either artery would be expected to cause PMD resulting in MR, whereas occlusion of the left anterior descending artery (LAD) would not. To investigate this hypothesis, we studied 37 men (mean age 58 years) using transthoracic echocardiography, before and during elective coronary angioplasty.

With the patient lying supine, the optimal echocardiographic window was identified, marked on the patient's chest, and then used throughout the study. The left atrium was interrogated using colour flow mapping. The ratio of the area of the mitral regurgitant jet (MRJ) to the area of the left atrium (LA) was determined by off-line computerised planimetry. Dynamic MR was defined as an increase of ≥10% in the MRJ/LA ratio during ischaemia (ST segment shift ≥1 mm and/or new regional wall motion abnormality). Anulus diameter and the distance from the mitral leaflet coaptation-point to the anulus plane were also measured.

Of the 26 patients who developed ischaemia during angioplasty, 16 (62%) developed dynamic MR. The average MRJ/LA ratio increased from 5.6±5.2(mean ±SD) to 20.7±7.0 (p<0.01). 9 of the 15 (60%) patients undergoing angioplasty to the LAD developed dynamic MR, compared with 3 of 11 (27%) with RCA and LCX lesions (p<0.05). 11 patients had no ischaemia and none of them developed dynamic MR. During ischaemia, patients in dynamic MR, the distance between the mitral leaftlet coaptation point and the anular plane increased from 0.5 ±0.2 to 0.7 ±0.3cm (p<0.05) but the anular diameter did not change (2.95 ±0.6 to 2.92 ±0.9cm). We conclude that dynamic mitral regurgitation is common during acute ischaemia. The coaptation point is displaced apically suggesting incomplete mitral leaflet closure is the mechanism of such regurgitation. MR occurred more frequently with LAD territory ischaemia than with ischaemia in the territories of the RCA and LCX which supply the papillary muscles. This suggests that papillary muscle dysfunction is not the cause of dynamic MR and that this concept is outdated.
(206) POSTER

PULMONARY EMBOLISM AND PARENTERAL NUTRITION: AN UNACCEPTABLE RISK?

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The use of silicone catheters for long term central venous access is widespread. Few data are available on the prevalence of pulmonary thromboembolic complications. 34 consecutive patients aged 2 months to 21 years (mean age 5.1 +/- 0.4 years) who received cyclical parenteral nutrition (CPN) for enteral therapy were followed for two months and studied by echocardiogram and radionuclide lung perfusion scanning. Thrombosis was identified in 12 patients: pulmonary emboli in 10, right atrial thrombi in 5, and superior vena cava thrombosis in one. 4 patients died; 3 of pulmonary embolism. Three patients underwent right atrial thrombus removal, with pulmonary embolectomy in two. Actuarial survival free of thrombosis was 88% at one year and 27% at 8 years. Survival free of pulmonary thromboembolic death was 74% at 4 years. Multivariate analysis identified autoimmune enteropathy (relative risk 33 versus other diagnoses) and frequent episodes of sepsis (relative risk 57 for >4 versus <1 episodes) as risk factors for thrombosis and a high total number of central venous lines (relative risk 0.0004 for >4 versus 0-1) as a protective factor. Prompt removal of blocked or infected catheters, when indicated, was effective. Right atrial thrombus and pulmonary embolism was a common and potentially fatal complication of long term venous access for CPN. Surveillance protocols should therefore, include lung perfusion scanning and echocardiography. The high incidence of thrombosis suggests a prima facie case for anticoagulation.

(207) POSTER

Left ventricular structures in atrioventricular septal defect with right isomerism compared to similar features with usual atrial arrangement

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In some patients with isomerism of the right atrial appendages, we have found critical regurgitation of the common atrioventricular valve requiring surgical treatment, even after reparative repairs such as total cavopulmonary connection. To determine if this reflected different anatomic arrangements within the left ventricle, we investigated 40 specimens with atrioventricular septal defect and biventricular (either ambiguous or concordant) atrioventricular connection; 14 with right isomerism, 5 with left isomerism and 21 with usual atrial arrangement.

We measured the length between crux and apex; apex and aortic valve; apex and so-called "scooped" crest; the distance between two papillary muscles in the left ventricle; the diameter and the length of the papillary muscles; and the circumference of the mural leaflet. For standardization, all parameters except the circumference were divided by the value of the length between the crux and the apex.

The values of both the diameter and the length of the papillary muscles were significantly smaller in the group with right isomerism compared to the usual atrial arrangement, as were the distances between the papillary muscles and the circumference of the mural leaflet. The proportional length between the apex and the aortic valve was significantly longer in the setting of right isomerism compared to the other groups, while the extent of scooping of the septum showed no differences between the three groups.

We conclude that the papillary muscles of the left ventricle are hypoplastic and, at the same time, severely dislocated in atrioventricular septal defect coexisting with isomerism of the right atrial appendages. These features, together with the disproportion in ventricular shape, might be responsible for the regurgitation of the common valve and the ventricular dysfunction.

(208) POSTER

NITRIC OXIDE IS A POTENT ARTERIAL DUCT DILATOR IN NEONATAL LAMBS

SE Abrams, KP Walsh, M Diamond, MJ Clarkson, SJ Coker. Royal Liverpool Childrens Hospital & University of Liverpool, UK

Neonates with duct dependent pulmonary circulations require patenty of the arterial duct (AD) to maintain the underdeveloped circulation before palliative or reparative surgery. High oxygen (NO) has been used in both animals and patients to relax the pulmonary vasculature and hence reduce pulmonary artery pressure and increase pulmonary blood flow. However AD response to NO is unknown. To determine the responses of the AD to NO, we used the NO donor SIN-1, in vitro on freshly removed ADs and aortas from newborn lambs (aged 1-5 days, n=7). Vessels were cut into rings and mounted on tension gauges in 37°C organ baths containing Krebs-Henseleit. After equilibration with 1gm of tension, the rings were tested for smooth muscle responses to oxygen(O2), prostaglandin E2(PGE2), potassium(K+) and SIN-1. K+ constricted the arterial rings in concentrations ranging from 10-70 mmol/L. PGE2 had no effect in concentrations ranging from 10-10 to 10-6. SIN-1 relaxed the K+ preconstricted arterial rings in concentrations ranging from 10-6 to 10-4. K+ constricted the ADs in a similar concentration range to that of arterial rings. Q, constricted the AD rings at tensions over 80mHg. PGE2 had no effect on the post term AD in concentrations ranging from 10-6 to 10-4. With preconstriction using 40nmol/L of K+, the AD relaxed in response to SIN-1 in concentrations ranging from 10-7 to 10-5 in equal proportion to arterial rings from the same animals under identical conditions (p>0.05). Conclusions: 1) Nitric oxide is a potent dilator of the arterial duct in a similar fashion to its effects on other vasculature and may have a role in the management of neonates with duct dependent circulations. 2) Previous exposure of the AD to oxygen abolishes the relaxation response to PGE2.

(209) POSTER

THE REALITY OF TRAINING IN CARDIAC SURGERY

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All cardiac surgical procedures since Jan 1992 have been entered into a computer database that provides information for audit and permits a review of trainee workload and progress. A Parsonnet risk score based on pre-operative information is also produced for each procedure. Of the 1942 operations performed, 680 have been delegated to trainees.

Parsonnet risk groups

<table>
<thead>
<tr>
<th>TOTAL</th>
<th>0-4</th>
<th>5-9</th>
<th>10-14</th>
<th>15-19</th>
<th>20+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultant</td>
<td>1262</td>
<td>449</td>
<td>289</td>
<td>191</td>
<td>146</td>
</tr>
<tr>
<td>Registrar</td>
<td>277</td>
<td>277</td>
<td>53</td>
<td>26</td>
<td>9</td>
</tr>
<tr>
<td>Son Reg.</td>
<td>403</td>
<td>211</td>
<td>110</td>
<td>47</td>
<td>12</td>
</tr>
</tbody>
</table>

The number and ratio of junior and senior trainee delegated procedures varied between surgeons. The in hospital mortality for operations performed by junior staff was 2.21% compared to a rate of 5.51% for consultants (p < 0.05). Trainees had a lower mortality than consultants in all groups. In the Group 0-4 the mortality (and predicted mortality) was 0.5% (1.45) for trainees and 1.78% (1.65) for consultants. The average Parsonnet score for consultant cases was 8.5 compared to 5.3 for trainees. Consultants perform most of the high risk surgery and trainees are delegated low risk cases. The progress of a trainee can be monitored by tracking the Parsonnet score and as more experience is gained, the case mix should reflect increasing Parsonnet risk score. The lower mortality for trainees in the low risk groups may suggest consultant recognition of low risk factors not reflected in Parsonnet scoring.
IF NOTHING GOES WRONG, IS EVERYTHING ALL RIGHT? SEQUENTIAL MONITORING OF THE RESULTS OF TREATMENT
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Hospital for Sick Children, Great Ormond Street, London and MRC Biostatistics Unit, Cambridge.

When do you blame a series of failures on bad luck and when do you become concerned that it represents the beginning of a deterioration in performance? How can you claim an improvement in surgical results knowing that in any treatment series, viewed sequentially, complications cluster? Approaching these questions with serial significance tests answering the question “Is current performance different from x%?” will be misleading and incorrect. The attractions and disadvantages of three unfamiliar statistical methods are explored.

(1) The simplest approach is to plot cumulative failures against patient number in a series. Lines corresponding to target or unacceptable failure rates or failure rates derived from the literature or multicentre databases can be plotted for comparison and actual performance compared by eye to these.

(2) Cusum methodology offers a formal statistical framework by calculating boundaries within which cumulative failures after each intervention can be plotted as each result becomes available. If the graph crosses the boundary, a statistical statement can be made: “I am x% sure that the long run failure rate is above y%”. (3) The concept that recent results have more power to predict the outcome of the next intervention than those remote in the series is embodied in a methodology formally called the exponentially weighted moving average. In estimating current mortality it can be seen that each previous result is systematically discounted at a fixed %, backwards from the point of estimation. Graphed sequentially, these estimates provide an intuitively satisfying summary of trends in mortality, though the method requires the use of programmable calculator or computer to provide each estimate.

These techniques are illustrated using data from surgical series and provide a means of continuous audit of performance and a framework of alerting to the need for a change in protocol.

OUTCOME OF CARDIAC SURGERY IN THE ELDERLY - SURVIVAL AND QUALITY OF LIFE: A PROSPECTIVE STUDY
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Department of Community Medicine, University of Cambridge.

Papworth Hospital, Papworth Everard, Cambridge CB3 8RE, England.

With an increasing number of elderly patients being referred for cardiac surgery it is important to assess outcomes in terms of survival, morbidity and quality of life. A previous survival analysis of 562 patients aged 65 or older, undergoing cardiac surgery between 1973 and 1984, showed 1, 5 and 10 year survival rates of 85%, 74% and 47% respectively. Of the 521 (93%) patients who survived to leave hospital, survival at five years was 82% which compared with a five year life expectancy in the general population in this age group of 80%. Following this analysis, a prospective study of the quality of life of cardiac surgery patients in the 65 and older age group was planned. 147 patients undergoing cardiac surgery (77 coronary artery bypass grafts (CABG), 52 valve repair/replacements and 18 CABG+valve operations), during the period July 1990 to December 1992, are being interviewed at intervals before and after surgery, to determine various aspects of quality of life, including frequency of symptoms, general health status and mood state. Results are presented from the 118 patients who had interviews before and at one year after surgery. Pre-operation, 86 (73%) patients experienced chest pain and 105 (98%) breathlessness; these reduced to 19 (16%) (P<0.001) and 57 (48%) (P<0.001) respectively at 1 year after surgery. Using the Nottingham Health Profile to assess changes in general health status, there were statistically significant differences in the mean scores of five dimensions, indicating improvements 1 year post-op. in energy, sleep, physical mobility, emotional reactions (P<0.001) and social isolation (P<0.01). From the Hospital Anxiety and Depression Scale 49 (43%) patients pre-op. showed an anxiety score above that considered to be normal (p<7) compared to 20 (17%) at 1 year (P<0.001) and for depression 36 (31%) patients were above normal pre-op. compared to 13 (11%) at 1 year (P<0.001). From these preliminary results it can be seen that the quality of life of these patients had improved significantly at one year after surgery.

QUALITY OF SURVIVAL AT THREE AND SIX MONTHS IN LONG TERM CARDIAC SURGICAL INTENSIVE CARE PATIENTS
L Holmes, T Treasure, K Loughhead, D Bihari, C Morgan and S Gallivan
St George’s Hospital and University College, London

In a prospective study we are investigating the quality of survival in cardiac surgical patients who required intensive care for more than 48 hours. During 1992, 2256 adult patients in three collaborating hospitals underwent cardiac surgery (excluding transplantation). 162 (7.2%) met these criteria. Of these, 47 died in the Intensive Care Unit (ICU), 7 died without leaving hospital and 7 before the 6 month follow up. The ICU stay ranged from 3 to 90 days (median 6) and, for the survivors, the hospital stay ranged from 7 to 111 days (median 21). Quality of life assessments using the Nottingham Health Profile (NHP), Hospital Anxiety and Depression scale (HADS), were made at 3 and 6 months following surgery on 79 survivors (99%).

Using the NHP there was an overall trend towards improvement at 3 and 6 months postoperatively.

<table>
<thead>
<tr>
<th>NHP Dimension</th>
<th>3 months median (Interquartile range)</th>
<th>6 months median (Interquartile range)</th>
<th>p value Wilcoxon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy</td>
<td>24 (0-100)</td>
<td>24 (0-61)</td>
<td>0.06</td>
</tr>
<tr>
<td>Pain</td>
<td>12 (3-30)</td>
<td>3 (0-22)</td>
<td>0.007</td>
</tr>
<tr>
<td>Emotion</td>
<td>7 (0-30)</td>
<td>0 (0-17)</td>
<td>0.5</td>
</tr>
<tr>
<td>Sleep</td>
<td>14 (3-66)</td>
<td>13 (3-64)</td>
<td>0.07</td>
</tr>
<tr>
<td>Social</td>
<td>0 (0-23)</td>
<td>0 (0-22)</td>
<td>0.7</td>
</tr>
<tr>
<td>Mobility</td>
<td>22 (5-55)</td>
<td>11 (0-33)</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

At 3 months using the HAD scale 12 patients had some degree of anxiety or depression, 1 patient scored on anxiety alone. By 6 months there were improvements but also deteriorations.

Age and length of stay in ICU did not have a significant effect on 3 or 6 month quality of life outcome. This group of cardiac surgical patients who required and survived a protracted ICU stay (4.4% of all cases) have an impaired quality of life but show continued improvement between 3 and 6 months after operation.

ARE BIOLOGICAL VALVES AN ACCEPTABLE LONG TERM ALTERNATIVE? THE WESSEX EXPERIENCE
T Edwards, S A Livsey, I A Simpson, J L Monro, Sir J K Ross
Wessex Cardiothoracic Centre, Southampton General Hospital, Southampton

In order to assess their long-term performance, we followed 443 biological valves (274 Carpentier Edwards, 134 homograft and 10 Hancock valves) implanted in 415 patients between 1975-79. Averages ranged from 6-7.7 yrs, mean 59 yrs. There was an operative mortality of 2.9%. Total follow-up was 4248 patient years. Overall event free survival was 60% (±1.5% (1SD)) at 10 years, 32% (±1.4%) at 15 years and 16% (±1.9%) at 18 years. 10 year and 15 years event free survival was 72% (±3.4%), 43% (±3.4%) for aortic homografts, 62% (±3%), 39% (±2.1%) for isolated aortic xenografts and 44% (±3.4%), 21% (±2.7%) for isolated mitral xenografts. Freedom from structural valve degeneration was 87% (±1.3%) and 69% (±2.2%) for all patients at 10 and 15 years respectively, 86% (±2.7%), 58% (±4.4%) for aortic homografts, 93% (±1.7%), 87% (±1.9%) for aortic xenografts, and 76% (±3.8%), 5% (±5.3%) for mitral xenografts. Of the 64 remaining xenograft pts, echocardiography has been performed in 22 pts thus far (14 aortic, 5 mitral, 3 tricuspid) between 14 yrs and 17 yrs following implantation. Aortic pts were either NYHA class II (9pts) or III (3pts). Peak aortic velocity ranged from 1.5-3.5 m/s, mean 2.42 m/s. Aortic gradients were 10-51 mmHg, mean 24 mmHg with estimated aortic valve areas of 0.4-1.92 cm², mean 1.08 cm². Aortic regurgitation detected in 9 pts on colour flow mapping was only apparent clinically in 6 pts but of haemodynamic significance in only 1 pt. Mitral pts were either NYHA class I (7pts), II (1pt) or III (2pts). Peak mitral velocity ranged from 1.4-2.7 m/s, mean 1.9 m/s. Pressure half-times ranged from 69-175 msec, with mitral valve areas of 1.3-3.2 cm², mean 2.2 cm². Mitral regurgitation detected clinically and on colour Doppler flow mapping in 4pts, was of haemodynamic significance in only 1 pt. In conclusion, biological valves have good long term results with acceptable haemodynamic profiles well into their second decade.
POSTER

THE EFFECT OF LOCALLY APPLIED tPA ON THE FIBRINOLYTIC ACTIVITY OF VEIN GRAFTS
M J Underwood, GJ Cooper, RS More, C Toner, A Coumbe, DP de Bono
Department of Cardiology, Glenfield Hospital, Leicester and The Royal London Hospital, London

The fibrinolytic system of the vessel wall protects against thrombosis and may play a role in vein graft initial hyperplasia. To prevent graft thrombosis an agent is required which will provide local protection without systemic effects. This study assessed the efficacy of locally applied tissue-plasminogen activator (tPA) Bilateral saphenous vein grafts were placed in the carotid position of pigs (n=6). After distention to 230mmHg, one graft was treated with 1 mg/ml tPA. Grafts were harvested after 2 hours perfusion and extractable tPA and urokinase (uPA) measured in control vein (CV), distended vein (DV), control graft (CG) and treated graft (TG) using chromogenic substrates. Statistical analysis was performed using the Wilcoxon test. Results are presented as Median (Interquartile Range) IU/mg tissue (IU 10^3 for tPA, IU for uPA).

<table>
<thead>
<tr>
<th></th>
<th>CV</th>
<th>DV</th>
<th>CG</th>
<th>TG</th>
</tr>
</thead>
<tbody>
<tr>
<td>tPA</td>
<td>3.2(2.4-3.8)</td>
<td>1.5(0.9-2.3)</td>
<td>4.1(3.5-4.6)</td>
<td>10(5.9-16.8)</td>
</tr>
<tr>
<td>uPA</td>
<td>0.8(0.5-1.6)</td>
<td>0.5(0.3-0.6)</td>
<td>1.3(0.6-2.0)</td>
<td>1.9(0.8-2.3)</td>
</tr>
</tbody>
</table>

Distention reduced both tPA and uPA activity (p<0.05). Pre-treatment with tPA enhanced tPA activity compared to CG (p<0.05). uPA activity did not differ between TG and CG (p=0.094). Both tPA and uPA increased compared to distended vein (p<0.05). This shows that locally applied tPA persists in the vessel wall and enhances local fibrinolytic activity. This method of treating grafts prior to implantation merits further investigation as do the early changes in endogenous graft fibrinolytic activity which may be involved in the development of initial hyperplasia.

POSTER

The Effect of Systemic Vasodilators on Internal Mammary Artery Flow: Implications for Postoperative Treatment After Myocardial Revascularisation
MB Izzat, RR West, and GD Angelini
Department of Cardiac Surgery, University of Bristol, Bristol.

Postoperative spasm of the internal mammary artery graft can cause morbidity and mortality after myocardial revascularisation. The ability of systemic vasodilators to overcome internal mammary artery spasm has not been studied clinically. In 50 patients in whom the left internal mammary artery was used for myocardial revascularisation, we have investigated the effect of five agents on internal mammary artery free flow. The agents investigated were Normal Saline, Dobutamine, Glyceryl Trinitrate, Sodium Nitroprusside and Enoximone. Following the harvesting of the internal mammary artery, free flow was measured under controlled haemodynamic conditions before any pharmacologic intervention (flow 1), and a median of 17.5 minutes after starting a systemic infusion of one of the five agents (flow 2). The increase in free flow expressed as percentage of initial flow for Enoximone 94% (range 46% to 125%) was greater than Normal Saline 18% (1% to 36%), Dobutamine 41% (3% to 92%), and Glyceryl Trinitrate 50% (-4% to 129%), (all p<0.01). The increase in free flow for Sodium Nitroprusside 81% (9% to 125%) was greater than for Normal Saline and Dobutamine (both p<0.05). We therefore recommend the systemic use of Enoximone and Sodium Nitroprusside, in rank order, to enhance flow in the internal mammary artery early after myocardial revascularisation.

POSTER

VASCULAR RESPONSES TO BALLOON CATHETER-INDUCED INJURY IN THE TGR(mRen-2d)27 RAT
HE Montgomery, S Anglin, J Mullins*, JR McElwan. The Hunter Institute for Cardiovascular Studies, University College London Medical School, London, and *AFCRC Centre for Genome Research, University of Edinburgh, UK.

Pharmacological manipulation of the renin-angiotensin system (RAS) by angiotensin converting enzyme inhibitors or angiotensin II receptor antagonists inhibits the formation of fibrocellular intimal hyperplasia (FCIH) after balloon catheter-induced injury in the rat, but the direct role of systemic and local renin-angiotensin systems in FCIH formation is not clear. The transgenic rat TGR(mRen-2d)27 was derived to allow studies of the functional cardiovascular effects of renin. We have examined the effect of balloon catheter-induced vascular injury in this model of genetically induced hypertension which is associated with high circulating pro-renin levels and expression of the renin transgene in vascular tissue.

A distended FG2 Fogarty balloon embolectomy catheter was passed three times along the left common carotid artery of five 300g homozygote TGR(mRen-2d)27 rats and their Sprague Dawley control strain. The rats were allowed to recover for 14 days, then killed and the carotid arteries fixed in situ before retrieval for Araldite embedding and sectioning for morphometric analysis.

There was no intimal thickening seen in the uninjured vessels of either control or transgenic rats despite the hypertensive phenotype of the TGR(mRen-2d)27 rats. Mean intimal area after injury of the TGR(mRen-2d)27 rats was greater (0.068 ± 0.009mm²) than that in the control rats (0.055mm²). Injured neointima/media ratio was also significantly greater (p=0.05) in the TGR(mRen-2d)27 rats than in the controls. The area of the media of the injured left carotid arteries of the TGR(mRen-2d)27 rats (0.158±0.008 mm²) was significantly greater (p=0.002) than that of the control rats (0.060 ± 0.02 mm²) but in each group was similar to that of the corresponding uninjured vessel.

The extent of the fibrocellular intimal hyperplasia generated after injury and the medial hypertrophy in the TGR(mRen-2d)27 rats may reflect either the hypertension or the expression of the vascular renin. We are currently engaged in studies to determine the different influences.

POSTER

PREVENTION OF HUMAN VASCULAR CELL PROLIFERATION BY ANTISENSE OLIGONUCLEOTIDES TO c-MYB mRNA
C M Holt, L Shepherd, S E Francis*, G H Smith
Sections of Cardiac Surgery and Molecular Medicine*, University of Sheffield, Sheffield, UK

Recent animal studies have demonstrated that antisense oligonucleotides may be useful in the prevention of intimal hyperplasia. We have investigated the feasibility of using this approach for the prevention of occlusive proliferative vascular disorders in humans by testing the effect of antisense oligonucleotides to c-myb on the proliferation of human saphenous vein smooth muscle cells (SMC), aortic SMC, internal mammary artery SMC and umbilical vein endothelium (HUVEC). An unmodified 18mer oligonucleotide directed against the human sequence of c-myb significantly inhibited the proliferation of saphenous vein, aortic, internal mammary artery SMC and HUVEC in a dose-dependent manner. Greater than 80% inhibition was observed at 10μM with no effect on cell viability. Following removal of the antisense oligonucleotides, normal proliferation resumed. Sense oligonucleotides did not significantly inhibit cell proliferation at this concentration. Treatment with antisense oligonucleotides to c-myb caused a decrease in specific protein levels detected using an antibody to c-myb. c-myb mRNA was determined by reverse transcription-PCR. Antisense oligos to c-myb caused a fall in levels of mRNA following 72 hours exposure but not at earlier time points.

The results demonstrate that antisense oligonucleotides to c-myb can inhibit the proliferation of several types of human vascular cells in vitro. The kinetics of their action may be important in determining their efficacy in the clinical setting.
NEOINTIMA FORMATION IN VITRO: AN INTIMIAl TO MEDIAL GRADIENT OF PDGF MESSENGER RNA EXPRESSION DETECTED BY IN SITU HYBRIDISATION
SI George, V1 Thurston, AC Newby. Department of Cardiology, University of Wales College of Medicine, Heath Park, Cardiff CF 4 4XN.

Neo-intima formation in atheroma, after angioplasty and in vein grafts involves chemotactic agents as well as growth factors for vascular smooth muscle cells (SMC). Platelet-derived growth factor (PDGF) exhibits chemotactic properties but the cellular source of PDGF responsible for intima formation is defined only for rat carotid angioplasty. We used organ culture segments of human saphenous vein obtained from coronary by-pass patients (n=6) to investigate the location of PDGF messenger RNA (mRNA) expression by in situ hybridization. Antisense 32P-rhodanoprobe specific for PDGF and B chain mRNAs were synthesized by DNA amplification and in vitro translation. Before culture, PDGF and B mRNAs were most prominently expressed in endothelial cells, although medial SMC and adventitial cells also showed hybridization to antisense but not sense probes. After 14 days of culture, the endothelium still expressed high levels of PDGF and B chain mRNA, but similarly high levels were detected in neointimal SMC. By contrast, expression in the medial SMC was decreased. Global expression of PDGF and B mRNA was confirmed after 0, 1, 7 and 14 days of culture by RNAse protection assay using the same probes. These findings were extended to recovered human vein grafts; high levels of PDGF and lower levels of PDGF-B were detected predominantly in neointimal SMC. We found unexpectedly high levels of both PDGF and B mRNA expression in vein segments before culture, perhaps owing to the risk factors for atheroma in these patients. The location of mRNA expression implies that secretion of PDGF from endothelial cells and neointimal SMC establishes an intimal-to-medial chemotactic gradient of PDGF, which contributes to intima formation.

ENDOTHELIAL CELL PROTEIN KINASE C IS DIFFERENTIALLY ACTIVATED BY OXIDISED LOW DENSITY LIPOPROTEIN AND LYSOPHOSPHATIDYL CHOLINE.

*J A Smith, R J Babujii, Cardiovascular Sciences Research Group, Dept of *Cardiology and Pharmacology & Therapeutics, University of Wales College of Medicine, Cardiff.

Oxidized low density lipoprotein (oxLDL) is known to inhibit endothelial cell-derived relaxing factor activity in vascular preparations. It has been suggested that this effect is mediated via protein kinase C (PKC), which can act to inhibit agonist-induced nitric oxide (NO) release, and that lysophosphatidyl choline (LPC) is the component of oxLDL responsible for these effects. To test this hypothesis we directly measured the effects of copper-oxidised human LDL and LPC on porcine cultured aortic endothelial cell PKC activity measured by radioenzymatic assay (Amersham International).

OxLDL (0.1mg protein/ml) resulted in prolonged activation of both cytosolic (cyto) and particulate (part) endothelial cell PKC. whereas LPC (20μM) produced only a brief activation (Table 1).

Table 1. Results (pmol of 32P-phosphate transferred to substrate /min) are expressed as mean±SEM, *=p<0.05, #p<0.01 of time zero, n=6.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>0</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>5</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>oxLDL cyto</td>
<td>0.17±0.04</td>
<td>0.35±0.05</td>
<td>0.31±0.05</td>
<td>0.44±0.05</td>
<td>0.58±0.05</td>
<td>0.35±0.05</td>
</tr>
<tr>
<td>oxLDL part</td>
<td>0.17±0.02</td>
<td>0.32±0.02</td>
<td>0.17±0.02</td>
<td>0.32±0.02</td>
<td>0.27±0.02</td>
<td>0.27±0.02</td>
</tr>
<tr>
<td>LPC cyto</td>
<td>0.3±0.1</td>
<td>0.45±0.1</td>
<td>1.08±0.2</td>
<td>0.54±0.2</td>
<td>0.47±0.2</td>
<td>0.37±0.2</td>
</tr>
<tr>
<td>LPC part</td>
<td>0.21±0.07</td>
<td>0.76±0.07</td>
<td>0.86±0.07</td>
<td>0.45±0.07</td>
<td>0.44±0.07</td>
<td>0.25±0.07</td>
</tr>
</tbody>
</table>

Agonist-induced NO release is normally accompanied by brief activation of PKC which does not influence NO release, whereas prolonged (>2min) prior activation of PKC inhibits subsequent agonist-induced NO release. The findings of the present study provide a mechanism by which oxLDL (but not LPC) could inhibit agonist-induced NO release.

This work was supported by the British Heart Foundation.

CENTRAL AUDIT OF CHEST PAIN: CAN WE BELIEVE THE RESULTS?

A A-Mohammad, F Fath-Orodbadi, TY Huiehns,TW Greenwood, MIM Noble and KJ Beatt

Academic Medicine, Charing Cross and Westminster Medical School, London.

Audit of clinical practice has become obligatory in medicine. There are a number of central audit systems collect unverified data related to the practice of cardiology. In this study an audit of central audit was undertaken by analysing the data from three of the 21 centres contributing to a regional audit initiative. Data for central audit was collected by postal questionnaire completed by a variety of nursing and medical staff dealing with acute admissions over a 6 month period. Data for the local audit was compiled by medical staff directly involved in the management of patients on the Coronary Care Units (CCU). Locally, the numbers of patients were verified by the admission books for the CCUs.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Hospital A</th>
<th>Hospital B</th>
<th>Hospital C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total chest pain</td>
<td>203 (6%)</td>
<td>212 (6%)</td>
<td>226 (13%)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>113 (10%)</td>
<td>128 (7%)</td>
<td>67 (27%)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>65 (5%)</td>
<td>44 (6%)</td>
<td>81 (11%)</td>
</tr>
<tr>
<td>Other ischaemia</td>
<td>18 (6%)</td>
<td>30 (30%)</td>
<td>54 (44%)</td>
</tr>
<tr>
<td>Non-cardiac</td>
<td>7 (0%)</td>
<td>10 (10%)</td>
<td>23 (9%)</td>
</tr>
</tbody>
</table>

The numbers are from local audit with the percentage of them in central audit.Less than 20% of thrombolysed patients had data correctly recorded centrally. In a subgroup (hospitals A & C) of patients receiving thrombolysis, central audit grossly overestimated the mean time to treatment at 267min (range 15-1030), whereas locally this was measured as 168min (30-1390). In conclusion, assessment of clinical activity based on unconfirmed data collected by parties not involved with clinical care can lead to gross inaccuracies. There is a need to verify data from central audit systems which are influential in determining standards of clinical practice and allocation of resources.
Rapid Access Chest Pain Clinic - A Method of Optimising Cardiac Resources.
N EJ Gaylani, WJ Penny, A Shandall, MB Buchalter, Cardiology Department, University Hospital of Wales, and Llandough Hospital, Cardiff.

To increase the number of patients appropriately hospitalised with acute ischaemic syndromes and to avoid unnecessary admissions, a rapid access chest pain assessment clinic was instituted. Patients with acute chest pain of uncertain origin referred by their GPs were assessed on the same day by a Cardiology Registrar. GPs were requested to directly hospitalise patients with probable acute myocardial infarction (AMI). Over a 6 month period (March-Aug 93) 174 patients (99 males, mean age 59 years) were assessed. 35 were thought to have an acute ischaemic syndrome and admitted, 86 to have non cardiac pain and discharged to their GP and 53 to have non acute cardiac pain and referred to a Cardiology Clinic. Follow up of patients admitted revealed 7 (20%) had an AMI, 21 (60%) had unstable angina and 7 (20%) had non cardiac pain. Of the patients discharged, there were no deaths and 3 (2%) were hospitalised within 2 weeks of the clinic visit, 2 for worsening angina and 1 with an AMI. GPs would have admitted 66 (48%) of the discharged patients had the service not existed. GP and patient satisfaction on a scale of 0 (extremely dissatisfied) to 5 (extremely satisfied) showed 94% of GPs and 81% of patients to be extremely(5) or very(4) satisfied with the clinic. All GPs wanted the clinic to continue. This clinic over a 6 month period prevented 66 hospital admissions none of whom died and only 1 patient suffered an AMI in the subsequent 2 weeks. This clinic also identified 28 patients with an acute ischaemic syndrome who were immediately hospitalised. Patients and GPs satisfaction was very high. Rapid access to a Chest Pain Clinic optimized the use of acute cardiac beds for patients with acute ischaemic syndromes thus directing resources to those most in need and reducing unnecessary admissions.

Comparison of a chest pain clinic with an open access exercise ECG service.
Brenda Howarth, Graeme Klein, Andrew McLeod, Poole Hospital NHS Trust, Longfleet Rd, Poole, Dorset, BH15 2JB.

A chest pain clinic (CPC) was set up in early 1992. Most new patients with chest pain were seen in the cardiac department where history, examination, and exercise ECG were performed at the first attendance. Thereafter in response to demand from general practitioner (GP) fundholders an open access exercise ECG service (OATES) was also started. The following data compare the 5 month period of exclusive chest pain clinic review with the first 5 months of open access testing. 71/315 (23%) new patient referrals to the cardiac clinic were seen in the CPC. 78 patients were tested in the OATS. Duke scoring (N Engl J Med 1991;325:849-53) was used as an objective assessment of risk. No patient aged <40 years had evidence of coronary artery disease. Positive tests as assessed by Duke score <5 were obtained in 66% of CPC patients compared with 46% of OATS patients (x2=6.0, p=0.014). Subjective assessment by the doctor supervising the test gave an even lower yield of 23/78 tests positive in the OATS (29%). 59% of CPC patients were returned to the GP for follow up compared with 83% of OATS patients (x2=9.6, p=0.002). Conclusions: Diagnostic and risk stratification testing of chest pain patients is usefully performed in a CPC prior to consultant review. A negative exercise testing is requested by GPs in many patients with a relatively low prior risk of coronary artery disease.

An open access Holter service
JC Rodger, H Bell
Monklands Hospital, Airdrie, Lanarkshire.

GPs have direct access to our hospital's Holter monitoring service. Direct access was phased in during 1991 after a study of referral patterns suggested that it would generate an additional 20 Holters per month (a number we could cope with). The study also suggested that, thought there was a potential for saving up to 15 clinic referrals a month, GPs would often be reluctant to substitute a Holter for a clinic referral.

Over the 22 months from September 1991 (when direct access was extended to all local GPs) to June 1993, 71 GPs requested a total of 561 Holters with 6 GPs being responsible for 32% of the requests. Over this period the yield of significant arrhythmias was consistently around 15%. Requests levelled off at 37 per month. Analysis of the monthly data on patients referred by GPs with an arrhythmia or symptoms suggesting an arrhythmia, shows that the percentage of requests to the ECG Department for a Holter rather than for a 12 lead ECG increased significantly and that there was a highly significant decrease in the percentage of these patients referred to the cardiology and general medical clinics.

There was a 73% response to a postal survey in December 1992. Of the 86 GPs who replied, 88% knew they had direct access and 74% had used the service. Of the 64 who had used it, 59% indicated that their use was increasing, 95% would miss the service if it was withdrawn and 55% indicated that, given the option, they would prefer the Holter reports to be interpretative rather than purely descriptive.

We conclude that GPs have made good use of direct access. The expansion of the service (20% increase in annual Holters done) has required the technician time but no new equipment. The experience gained (including the initial feasibility study) has provided us with a model for extending direct access to other cardiac diagnostic services.

Non-Invasive Screening of Flow-Related Endothelial Function Using High Resolution Ultrasonic Vessel Wall Tracking.
J Goodfellow, H W Ramsey, L Liddington, J H Jones, C J Lewis, A H Henderson. Departments of Cardiology & Pharmacology, University of Wales College of Medicine, Cardiff.

A highly sensitive non-invasive ultrasonic wall tracker (AMA Wall Track System, resolution 3um) was used to measure conduit artery diameter and distensibility in a screening test for endothelial dysfunction. Hypercholesterolaemia (HC) is a modifiable risk factor for atherosclerosis which may cause endothelial dysfunction manifest by reduced EDRF activity. We tested the hypothesis that flow-related EDRF increases arterial distensibility as well as diameter. We measured the endothelium-dependent flow-related increase in brachial artery diameter and distensibility (dMDMPD, where D is diameter and P is pressure) during reactive hyperaemia compared with endothelium-independent responses to sublingual nitroglycerin (GTN 400ug) in 8 subjects with HC (serum cholesterol >7mmol/l, mean age 50±12 yr) and 8 age- and sex-matched controls. Arterial distensibility was calculated from internal brachial artery diameter measured continuously during the cardiac cycle using the ultrasonic wall tracker, and blood pressure measured with photo-plethysmography (Finapres). Reactive hyperaemia was measured by transcutaneous Doppler. Recordings were taken at rest, at 1 min of reactive hyperaemia, and 3 mins after sublingual GTN. Baseline characteristics were similar in the two groups. In normal controls, brachial arterial diameter and distensibility increased during reactive hyperaemia (by 10.3±5.18% and 0.63±0.3 kPa respectively) indicating maintenance of distensibility by a flow-related mechanism. In patients with HC, these flow-related changes were markedly attenuated (-1.63±4.47% and -0.36±0.076 kPa respectively, both p<0.05 compared with normals). In contrast, endothelium-independent effects of GTN on diameter were similar in the two groups, while distensibility was significantly reduced in HC, though to a smaller extent than during the hyperemic response. Thus, flow-related increases in arterial diameter and distensibility are attenuated in HC, implying reduced flow-related EDRF activity. This may contribute to arterial stiffness and consequent increased cardiac workload relative to tissue perfusion.

This ultrasound technique permits screening of flow-related EDRF activity in various disease states with a sensitivity which will enable assessment of specific therapies against endothelial dysfunction and risk factor modification.
A NEW STEERABLE CATHETER USING EMISSION OF ULTRASOUNDS FOR THE IN VIVO DETERMINATION OF PRESSURE-DIAMETER RELATIONSHIP OF THE AORTA IN HUMANS
Athens University, Athens, Greece

Pressure-diameter (P/D) relationship of the human aorta has not been well defined using a direct, high-definition method in vivo. For this purpose, we designed in our laboratory a new SF catheter with two curved and very flexible wires at its distal part, which can be opened or closed by external manipulations. Two crystals (1mm in diameter) one emitting 20 MHz ultrasounds and the other receiving) were positioned one opposite from the other in the middle of each wire. The catheter is inserted percutaneously and positioned in the thoracic aorta. The wires are adjusted under fluoroscopy to match the systolic aortic diameter (AoD); the wires follow the movement of the aortic wall because of their flexibility. The signal received from the crystals is translated through a VF-1 unit (Crystal Biotech) as variations in AoD during the cardiac cycle (fig A). The accuracy and the sensitivity of the technique were validated experimentally. Technical characteristics of the device include a frequency response of 25 Hz and minimal load on the aortic wall detected by histological and mechanical studies. Aortic pressures (AoP) are recorded simultaneously via a Millar catheter.

Results: The technique was applied in 25 subjects without technical difficulties or complications. Computerized analysis of data provided P/D loops of the aorta, both at baseline and after pharmacological interventions (e.g. nifedipine, fig B).

Conclusions: 1) P/D relationship of the aorta can easily be obtained in the intact human. 2) Study of the aortic P/D relationship will provide a better understanding of the physiology and the pathophysiology of the cardiovascular system.

ANALYSIS OF THE PHYSIOLOGICAL EFFECTS OF CORONARY ARTERY STENOSES ON BLOOD FLOW VELOCITY USING HIGH FREQUENCY TRANSTHORACIC ECHOCARDIOGRAPHY
J. Crowley, A. Kenny, L.M. Shapiro. Regional Cardiac Unit, Papworth Hospital, Cambridge, UK.

Measurement of phasic poststenotic blood flow velocities in human coronary arteries could provide a means for evaluating the pathophysiologic significance of stenotic coronary artery disease. Transthoracic, high frequency (5 MHz) echocardiography allows noninvasive assessment of anatomy and blood flow in the distal portion of the left anterior descending coronary artery(LAD). In this study this technique was used to determine blood velocity patterns in the distal LAD in patients with significant single vessel coronary artery disease. A total of 21 patients (12 males and 9 females; mean age 62 ± 6 years) with angiographically proven single vessel disease involving the proximal LAD (9 patients); distal LAD (5 patients) or proximal right coronary artery (RCA) with collateralisation from the LAD (7 patients) were studied. Seven patients with normal coronary arteries served as a control group.

<table>
<thead>
<tr>
<th>Lesion site</th>
<th>Diastolic Vp (cm/s)</th>
<th>Diastolic Vm (cm/s)</th>
<th>Systolic Vp (cm/s)</th>
<th>Systolic Vm (cm/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>45 ± 4</td>
<td>15 ± 3</td>
<td>24 ± 6</td>
<td>10 ± 3</td>
</tr>
<tr>
<td>Prox LAD</td>
<td>25 ± 4*</td>
<td>9 ± 3*</td>
<td>20 ± 3</td>
<td>9 ± 2</td>
</tr>
<tr>
<td>Distal LAD</td>
<td>114 ± 12*</td>
<td>74 ± 13*</td>
<td>19 ± 2</td>
<td>9 ± 3</td>
</tr>
<tr>
<td>RCA</td>
<td>67 ± 5*</td>
<td>20 ± 3*</td>
<td>27 ± 5</td>
<td>11 ± 4</td>
</tr>
</tbody>
</table>

*p < .05

Compared to controls peak(Vp) and mean(Vm) diastolic velocities were reduced in patients with proximal LAD stenosis and increased in patients with RCA or distal LAD stenosis. There was no difference in systolic blood flow velocities between the study groups. Thus alterations in coronary artery blood flow velocity due to coronary artery stenoses occur primarily during diastole. Use of transthoracic echocardiography may allow noninvasive assessment of changes in coronary blood flow.

QUANTIFIABLE MYOCARDIAL AND LEFT HEART OPACIFICATION IN PRIMATES AFTER INTRAVENOUS INJECTION OF A NEW MYOCARDIAL ECHO CONTRAST AGENT
Oregon Health Sciences University, Portland, Oregon, USA.

No contrast agent reported to date produces visually apparent and intense myocardial contrast opacification after intravenous injection. We tested a new colloidal dispersion (EchoGen® Sonus Pharmaceuticals) of a fluorocarbon compound which changes from liquid-in-liquid droplets to 2 micron microbubbles after injection upon warming to blood temperature. Our aim was to assess the pulmonary transit, left heart and myocardial opacification of this new agent. Studies were accomplished in 4 adult rhesus monkeys (5.9-7.3Kg) studied closed chest, both spontaneously breathing and intubated and ventilated after barbiturate anaesthesia. Doses of EchoGen® as low as 0.05ml/Kg produced intense and prolonged left ventricular contrast after central, or even peripheral venous injection. Doses greater than 0.2ml/Kg produced videodensitometrically detectable myocardial opacification after venous injection without changing systemic or pulmonary artery pressures. Doses from 0.4-0.8ml/Kg produced intense and prolonged brightening of the myocardium which persisted from 2.5 to over 12 minutes after chamber washout and was easily identifiable both to the eye and quantifiable as a change in videointensity at 4 quadrants around the myocardium (mean videointensity levels increasing 14%, 42% and 54% for 0.4, 0.6 and 0.8ml/Kg respectively). Only the highest dose produced ST or other ECG changes which were transient and all doses less than 0.6ml/Kg were accomplished without haemodynamic or wall motion changes. While the continued recirculation of agent and persistence of the myocardial contrast may preclude its use as a flow tracer, it is the first off-the-shelf echo contrast preparation which produces unequivocal, quantifiable myocardial opacification after even peripheral venous injection with small injection volumes and without major adverse haemodynamic effect.
### THURSDAY 19 MAY 1994

<table>
<thead>
<tr>
<th>Time</th>
<th>Location</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.45</td>
<td>Rosetor</td>
<td>Registration</td>
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<tr>
<td>8.00 – 9.30</td>
<td>Forum</td>
<td>Plenary Session</td>
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<td>The management of acute myocardial infarction: short and long term considerations</td>
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<td>Thrombolysis: Prof David de Bono</td>
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<td>Acute intervention: Dr Kevin Beatt</td>
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<td>Non thrombolytic drugs in therapy:</td>
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<td>Dr Kim Fox</td>
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<td>Late intervention: Mr Tom Treasure</td>
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<td>8.00 – 10.30</td>
<td>Arena</td>
<td>British Society of Echocardiography</td>
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<td>7.45</td>
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<td>Coffee</td>
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<tr>
<td>8.00 – 9.30</td>
<td>Scientific Session: Controversies in echocardiography</td>
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<td>8.00 – 8.45</td>
<td>Colour Doppler</td>
<td>Colour Doppler is of no value in adult cardiac diagnosis</td>
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<td>Protagonist: Graham Leech</td>
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<td>Antagonist: John Chambers</td>
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<td>Chairman: Alan Houston</td>
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<td>8.45 – 9.30</td>
<td>Transoesophageal echo should only be performed in a tertiary cardiac centre</td>
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<td>Protagonist: Iain Simpson</td>
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<td>Antagonist: Stephen Saltissi</td>
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<td>Chairman: Roger Hall</td>
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<td>12.00 – 13.30</td>
<td>Exhibition Hall</td>
<td>Poster Viewing 273–323</td>
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<td>Lunch</td>
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<td>13.00 – 14.00</td>
<td>Grace Murrell Suite C&amp;D</td>
<td>Cardiac Technicians’ Committee</td>
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<tr>
<td>13.30 – 15.00</td>
<td>Forum</td>
<td>Interventional Cardiology II</td>
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<td>(chairman: Dr H Gray)</td>
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<td>13.30 – 15.30</td>
<td>Arena</td>
<td>Practical cardiology</td>
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<td>1 Cardiac rehabilitation – Who needs it?</td>
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<td>Dr Iain Todd (Edinburgh)</td>
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<td>2 Coronary artery disease – Who is eligible for intervention?</td>
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<td>Prof David Wood (London)</td>
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<td>Coronary artery disease – When is intervention appropriate?</td>
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<td>Prof John Hampton (Nottingham)</td>
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<td>15.00 – 16.00</td>
<td>Forum</td>
<td>Arrhythmias, Electrophysiology and Pacing IV</td>
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<td>(chairman: Dr D Wyn Davies)</td>
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<tr>
<td>15.00 – 16.15</td>
<td>Grace Murrell Suite A&amp;B &amp;C&amp;D</td>
<td>Technicians’ Day</td>
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<td>16.15</td>
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<td>Close of meeting and tea in the Rosetor</td>
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**Burdett Suite**

- Arrhythmias, Electrophysiology and Pacing III (chairman: Prof S Cobbe)
- Papers 229–233

**Grosvenor Hotel**

- Myocardial and Vascular Biology III (chairman: Dr M J Lewis)
- Papers 234–239

**Rosetor**

- Moderated Posters 240–247 (chairman: Prof P Poole-Wilson)

**Forum**

- Judges’ Choice II (chairmen: Prof A Henderson and Prof H Just)
- Papers 248–254

**Arena**

- Coronary Artery Disease III (chairman: Dr M F Shiu)
- Papers 255–260
### THURSDAY 19 MAY 1994: SOCIETY OF CARDIOLOGICAL TECHNICIANS MEETING

<table>
<thead>
<tr>
<th>Time</th>
<th>Grace Murrell C&amp;D</th>
<th>Grace Murrell A&amp;B</th>
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<tr>
<td>9.00</td>
<td>Registration</td>
<td>Welcome AICD Seminar</td>
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<td>9.30</td>
<td>General Meeting</td>
<td>Welcome and introduction E G Tate</td>
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<tr>
<td>10.15</td>
<td>Close</td>
<td>Indications for pacing R S Hirst</td>
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<tr>
<td>10.30</td>
<td>Defibrillator Seminar</td>
<td>Types of pacemaker S Jameson</td>
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<tr>
<td>10.35</td>
<td>Welcome and introduction E G Tate</td>
<td>Physics as applied to pacing</td>
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<td>Therapy history F Steinmetz Current device and lead technology</td>
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<tr>
<td>11.30</td>
<td>Coffee</td>
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<td>11.45</td>
<td>Indications for implantation of an AICD E Rowland</td>
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<td>12.00</td>
<td>Implantation from physician standpoint E Rowland</td>
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<td>12.30</td>
<td>Implantation from technician standpoint P Gadd</td>
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<tr>
<td>13.00</td>
<td>Lunch</td>
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<td>14.00</td>
<td>Following the AICD patient S Jones</td>
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<td>14.30</td>
<td>Trouble-shooting overview F Steinmetz</td>
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<td>15.00</td>
<td>Questions and answers Panel</td>
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<td>16.00</td>
<td>Meeting close</td>
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**ANTIBIOTIC PROPHYLAXIS REDUCES RE-OPERATION RATE FOR INFECTIVE COMPLICATIONS FOLLOWING PERMANENT PACEMAKER IMPLANTATION: A PROSPECTIVE RANDOMISED TRIAL.**

J Paul Mounsey, Michael J Griffith, Ronald G Gold, Rodney S Benton. Freeman Hospital, Newcastle.

Pacemaker pocket infection remains a serious problem. We performed a randomised trial to determine whether antibiotic prophylaxis reduces re-operation for this complication. 715 consecutive patients (pts) underwent new permanent pacemaker implantation over a 17 month period. 139 (19%) had temporary electrodes (group 1) and 576 (81%) did not (group 2). In group 1, 26 pts (19%) were excluded because of overt sepsis, 53 (38%) received antibiotics and 60 (43%) did not. In group 2, 33 pts (6%) were excluded, 234 (41%) received antibiotics and 309 (53%) did not. There were no significant differences in pt characteristics between antibiotic and non antibiotic groups. Follow up was 9.3±4.9 months. The antibiotic regime was either flucloxacillin (14g IV preoperatively, then 500mg orally for 48 hours) or clindamycin (600 mg IV, then 300 mg orally for 48 hours). The endpoint was repeat surgery for an infective complication. There were 13 infections among the trial pts; 1 received antibiotic (p=0.008). 4 were from group 1; 1 received antibiotics (p=0.07). 9 were from group 2: none received antibiotics (p=0.02). Infected cases were more likely to have been implanted by inexperienced operators (<100 cases), 62% vs 30% (p=0.03), operation time (skin to skin) was longer at 76±59 mins vs 54±25 mins (p=0.003) and the incidence of early death re-manipulation was higher at 30% vs 3% (p=0.01). Preoperative factors likely to predispose to infection (diabetes, malignancy, recent antibiotic or steroid therapy) were not significantly commoner in pts with infected pacemakers. In conclusion antibiotic prophylaxis significantly reduces the incidence of infective complications requiring repeat surgery in permanent pacemakers.

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**DUAL SENSOR VVIR PACING: IS IT WORTH IT?**

K H Tan, N Suke, E McGing, C Bucknall, Department of Cardiology, Guy's Hospital, London

Dual sensor (DS) single chamber pacing being proposed as the mode forward in rate responsive pacing. To evaluate this during everyday activities, 18 patients (28 pts; mean age 74.4, SD 12, 70% male) had a Medtronic "Legend Plus" DS VVIR device implanted for high grade AV block and chronic or paroxysmal atrial fibrillation and were randomly programmed to VVIR DS (DDD (VVR activity ACT) mode, VVIR minute ventilation (MV) mode or to VVIR mode for 2 week periods of out of hospital activity in a randomised double blind crossover design. All patients had chronotropic incompetence and near normal left ventricular function. Pts were subjectively and objectively assessed after each study period. Perceived general well-being, exercise capacity and functional status were worse in VVIR than in any VVIR mode (p<0.05), as was objective exercise tolerance (CAEP protocol p<0.01). VVIR mode was least acceptable to all pts who expressed a preference. Of the VVIR modes, MV was least acceptable in 40%, DS in 40% whilst preferred modes were ACT in 40% and DS in 30%. Observed CAEP times were similar in all VVIR modes, although MV times were shorter (p=ns). Heart rate (HR) response during standardised daily activities when compared to normal controls was: overall HR greater under response in VVIR mode (p<0.01) and slow response in MV. ACT and DS had the most appropriate overall HR response with DS best during a car journey. DS and ACT both overresponded to staircase descent (p<0.05).

This study suggests no clear advantage of dual sensor VVIR pacing over activity sensor pacing with the disadvantage of programming complexity and increased costs.
To determine whether physiological pacing has any practical benefits in the elderly population, we conducted a double blind cross over study in 13 subjects over the age of 75 already fitted with a physiological pacemaker comparing quality of life and exercise capacity while being paced in either atroventricular (AV) or ventricular modes. All had been paced for complete or mobilite type II heart block. Quality of life, evaluated by an activity of daily living questionnaire (a low score indicating good quality of life, a high score indicating poor quality of life), and distance walked on a 6 minute walking test were evaluated at baseline (during AV pacing). Patients were then randomly allocated to be reprogrammed either into ventricular mode or to continue in AV mode. All were rested 4 weeks later with both patient and investigator blinded to the pacing mode. Pacing mode was reversed and further blinded evaluation occurred 1 month later. Ten patients completed the study, 6 male, age 75 (range 75-89) years. There was a marked improvement in patients symptoms with AV pacing, the activity of daily living score (mean +/- SD), increasing from 19 +/- 5 during AV pacing to 28 +/- 10 during ventricular pacing (P <0.05). The distance walked on the 6 minute walking test was higher during AV pacing (360 +/- 65 metres) than during ventricular pacing (250 +/- 69 metres), p <0.01. Physiological pacing has significant symptomatic benefits for the elderly patient. Age alone should not be a contraindication to AV synchronous pacing.

**MODULATION OF DIASTOLIC TONE AND CARDIAC MYOFILAMENT RESPONSE BY ENDOTHELIAL CELL FACTORS**

A M Shah, A M Sibazz, J S Sollott, G G Hakata

#Lab Cardiovasc Science, NI & Pulm Asst Lab, Johns Hopkins, Baltimore, USA; Dept Cardiol, University of Wales Coll Med, Cardiff.

Changes in diastolic tone may influence both cardiac function and structure. Previous studies show that diastolic tone in externally unloaded single cardiac myocytes (beating or quiescent) is determined in part by Ca^{2+}-myofilament interaction. We recently reported that endothelial cell (EC) factors, eg nitric oxide (acting through cyclic GMP), endothelin, and a novel myofilament desensitizing factor (DF), alter cardiac Ca^{2+}-myofilament interaction. We therefore studied the effects of these factors on diastolic cell length (CL, a measure of diastolic tone; diode array) and Ca^{2+} ( indo-1 fluorescence ratio, R) in isolated rat myocytes. In beating myocytes (0.5Hz, 25°C), 8-bromo-cGMP (50µM) increased CL (+0.07±0.45%; n=17; p<0.01) but did not alter diastolic R (-0.8±0.6%; n=8). Similarly, EC superfuse containing DF rapidly and reversibly increased CL (0.25±0.92µm; p<0.01) but did not alter diastolic R (+0.45±0.03%; n=9). Both 8-bromo-cGMP and DF increased diastolic CL also in quiescent myocytes, and reduced steady-state myofilament responses to Ca^{2+} in single tetanized myocytes (10Hz stimulation in the presence of thapsigargin, 200µM).

**NITRIC OXIDE REDUCES CONTRACTILITY OF ISOLATED HUMAN MYOCARDIUM**

R E A Smith, J B Desai, A T Forsyth, J F Martin

Departments of Medicine, Cardiology and Cardiothoracic Surgery, Kings College School of Medicine and Dentistry, London

Nitric oxide (NO), synthesised from L-arginine by the enzyme NO synthase, is known to play an important role in regulating vascular tone via the production of cyclic guanosine monophosphate (cGMP). It has recently been suggested to regulate myocardial contractility. These studies investigated the role of the L-arginine - NO pathway in human myocardium. Atrial appendage was obtained at the time of coronary artery bypass surgery. It was dissected into strips and mounted in organ baths containing physiological buffer gassed with 5%CO2 in O2 at 35°C with a resting tension of 1G and paced at 0.5Hz. Responses to the NO donor sodium nitroprusside (SNP) and the cGMP analogue 8-Bromo-cGMP (10^{-5}-10^{-3}M) were studied. The response to isoprenaline (10^{-10}-10^{-5}M) before and after N^6-monomethyl-L-arginine (L-NMMA, an inhibitor of NO synthase, 3x10^{-5}M) or saline control were also studied.

SNP induced a concentration-dependent reduction in peak developed tension (DT) which was reversed by washing with buffer. At 10^{-3}M, DT was reduced by 24 ±4.3% (mean±SEM, n=5, p<0.05). 8-Bromo-cGMP reduced DT by 33.0±5.7% (n=5, p<0.05) at 3x10^{-4}M which was not reversed by washing.

Isoprenaline induced a concentration-dependent increase in DT which was not altered by L-NMMA compared to control (n=7 for both). Control isoprenaline ED50 = 8.2x10^{-5}M, ED50 in the presence of L-NMMA = 7.8x10^{-4}M. In conclusion, NO acts as a negative inotrope in human myocardium only at high extracellular concentration. It does not modulate the atrial response to isoprenaline.

**CAPTOPRIL ENHANCES LEFT VENTRICULAR RELAXATION VIA ENDOGENOUS BRADYKININ**

R M Grocott-Mason, B A Aming, M J Lewis and A M Shah

Cardiovascular Sciences Research Group, University of Wales College of Medicine, Heath Park, Cardiff.

ACE Inhibitors (ACEI), e.g. captopril (CAP), are beneficial in heart failure and in hypertension, acting via reduction in angiotensin II and/or an increase in endogenous bradykinin (BK) levels. BK may be released locally within the heart and act on endothelial cell BZ receptors to induce release of nitric oxide (NO). We recently demonstrated that NO enhances left ventricular (LV) relaxation in this study we therefore compared the effects of (i) BK (1nM), (ii) CAP (1µM) alone, and (iii) CAP (1µM) in the presence of the BK antagonist, HOE 140 (0.01µM) on LV performance in the isolated guinea-pig heart (constant loading and heart rate; Krebs buffer + indomethacin (1µM); 37°C). LV pressure (P) was measured with a 2F Millar catheter. Early LV relaxation was characterised by a monoeponential time constant (τE), as previously described (Br. Heart J., 1993, 69, P10). Both BK and CAP enhanced early decline of LVP (i.e. reduced τE) but had no effect on 'ystolic' performance, similar to the previous findings with NO. Coronary flow (CF) increased only with BK.

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NITRIC OXIDE SYNTHASE INDUCTION AND CARDIAC TRANSPLANT REJECTION

R E A Smith, M Rela, A J de Belder, L M Villa, A Wong, J E Beesley, V Riveros-Moreno, N Heaton, K C Tan, J F Martin
Department of Medicine and Institute of Liver Studies, King's College School of Medicine and Dentistry, London and Wellcome Research Laboratories, Beckenham.

Nitrergic (NO) activity, synthesised by a constitutive NO synthase (cNOS), Ca2+-dependent and an inducible NO synthase (iNOS, Ca2+-independent), is a vasodilator, a negative inotrope and has cytotoxic actions. To investigate a role for NO in chronic cardiac transplant rejection, hearts from Lewis or Fischer rats were transplanted into the neck of Lewis recipients with end-to-side anastomoses to the carotid artery and jugular vein. After 6 weeks hearts were removed and studied with histology, immunocytochemistry and citrulline assay for NO activity.

Histology demonstrated dense mononuclear cell infiltration with oedema in the myocardium and interstitial hyperplasia in the coronary vessels. Immunocytochemistry, using an antibody to mouse macrophage iNOS (peptide sequence 47-71), demonstrated cellular staining within the Fischer hearts. These changes were not observed in control Lewis - Lewis transplants. Citrulline assay in the control transplant demonstrated cNOS activity of 0.9±1.6 and iNOS activity of 0.8±0.3 pmol/min/mg protein (mean±SD, n=3). In Fischer hearts cNOS activity was 1.1±0.6 and iNOS activity 4.7±5.6 pmol/min/mg protein (n=3).

Cardiac transplant rejection is therefore associated with induction of iNOS. The excess NO synthesized may have negative inotropic and cytotoxic effects contributing to the rejection process.

SEVERITY OF HUMAN HEART FAILURE CORRELATES WITH MYOCARDIAL SARCOPLASMIC RETICULUM DYSFUNCTION

M A Denvir, N G MacFarlane, S Naik, D Richens, A C Tweddle, DJ Wheatley, DJ Miller & S M Cobbe
Department of Cardiology and Cardiothoracic Surgery, Royal Infirmary and University of Glasgow, Glasgow University, Glasgow.

The underlying cellular mechanisms producing abnormal systolic and diastolic function in heart failure remain unclear. We have examined sarcoplasmic reticulum (SR) function and myofilament force production in saponin and Triton-treated right ventricular trabeculae from 11 human hearts excised at the time of cardiac transplantation. The degree of left ventricular dysfunction ranged from mild (inoperable coronary artery disease) to severe and this was reflected in haemodynamic variables measured by cardiac catheterisation and radio nuclide imaging (ejection fraction) 2-4 months before transplantation. Small free running trabeculae (diameter 220±56μm, all values mean±SD) were mounted for isometric tension measurement in a relaxing solution and treated with saponin. A series of caffeine-induced contractions was produced using a standard timing protocol with various calcium concentrations (150-400μM) in the bathing solution to load the SR. The same preparation was then treated with Triton-X100 to disrupt the SR and measures of myofilament calcium sensitivity and force production made.

The calcium loading ability of the SR correlated inversely with indices of left ventricular function. Pulmonary capillary wedge pressure (PCWP, range 2-30mmHg) and mean pulmonary artery pressure (range 17-58mmHg) were inversely correlated with the capacity of the SR to load calcium (r = -0.75; p<0.05, r = -0.86; p<0.03 respectively). Left ventricular ejection fraction (range 8.7-31%) correlated less strongly with SR calcium loading capacity (r = -0.42; p=0.09).

Myofilament force production and calcium sensitivity were not significantly different between trabeculae from patients with a normal (10±2.5mmHg) and high (26±3.4mmHg) PCWP (3.18±1.91 vs. 3.01±2.01 g.wt/min/mg p<0.05). There was no significant correlation between myofilament force production and the severity of LV dysfunction.

These results suggest that an intrinsic reduction in myofilament force production does not account for reduced systolic function in heart failure. However, abnormal intracellular calcium regulation by the SR could explain both diastolic and systolic contractile dysfunction.

REduced CONTRACTION OF ISOLATED CARDiAC MYCoTYtes IN HUMAN HEART FAILURE

C H Davies, K Davis, J G Bennett, J R Pepper, A A Poole Wilson, S E Harding, Departments of Cardiac Medicine and Surgery, National Heart and Lung Institute, London, U.K.

Previous studies have failed to show a difference in the contraction amplitude of isolated cardiac myocytes from normal and failing human hearts. We have investigated whether increasing stimulation frequency can reveal a difference.

Enzymatically isolated myocytes were obtained from the left ventricular free walls of explanted failing hearts (CHF, n=6 patients, 10 cells). These were compared with small surgical biopsies removed into the cardioprotective agent butanedione monoxime (BDM) from consenting patients with normal ventricular function undergoing coronary surgery (Control, n=5 patients, 7 cells).

Isolated cardiac myocytes were superfused at 37°C with increasing calcium concentrations until a maximal contraction amplitude was obtained (Ca2+1.7 between 6 and 12 mM). The contractile response ( % shortening) to increasing stimulation frequency was examined:

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<th>Frequency /Hz</th>
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There was no difference in the diastolic contractile at high frequency. The shortening of myocytes from patients with heart failure changed little with stimulation rate, except for a decrease at high frequencies, whereas myocytes from non-failing heart showed a marked positive staircase.

THE ROLE OF RIGHT AND LEFT VENTRICULAR FUNCTION IN THE VENTILATORY RESPONSE TO EXERCISE IN CHRONIC HEART FAILURE

A L Clark, J Swan, R Laney, M Connelly, J Somerville, AIS Coats
Department of Cardiac Medicine, National Heart and Lung Institute, Dovehouse Street, London.

Background. Right ventricular function may be an important determinant of exercise capacity, peak oxygen consumption (VO2) and the ventilatory response to carbon dioxide production (Ve/VO2) relationship in patients with chronic heart failure (CHF). Method. We studied the role of right ventricular function in CHF and also investigated the effects of absent right ventricular reserve in patients previously operated with Fontan’s procedure by measuring metabolic gas exchange during exercise in 5 groups of patients: (1) 10 patients who had previously undergone Fontan’s procedure for congenital heart disease in whom the right ventricle is not functional; (2) 11 age matched controls with dilated cardiomyopathy (DCM); (3) 15 age matched normals; (4) 43 patients with CHF; (5) 16 age matched controls. Left and right ventricular ejection fractions (LVEF and RVEF) were measured by radionuclide ventriculography in group 4. Results. In the young subjects, the Ve/VO2 slope was lower in the controls than in the other two groups, being 24.4±4.3 against 33.3 ±6.5 in group 1 (p<0.001) and 29.6±8.1 in group 2 (p<0.05). The correlation between peak VO2 and Ve/VO2 was -0.80 (p=0.005) in group 1 and -0.76 (p=0.007) in group 2. In the older groups, the Ve/VO2 slope significantly greater (38.0±14.9 vs. 25.4±3.7; p<0.001) in the heart failure group. In group 4, the relationship between peak VO2 and Ve/VO2 was similar to that seen for groups 1 and 2. LVEF was 24.3±14.1% and RVEF was 32.5±13.1%. In neither control group was there a significant relationship between peak VO2 and Ve/VO2 slope. There was no correlation between either RVEF or LVEF and peak VO2 or Ve/VO2 slope in the heart failure group. Conclusion. The relationship between excessive ventilation and reduction in peak oxygen consumption is present in patients with no functioning right ventricle. RVEF is not a determining feature of either exercise capacity or the excessive ventilatory response in CHF.

MODERATED POSTER

THE ROLE OF RIGHT AND LEFT VENTRICULAR FUNCTION IN THE VENTILATORY RESPONSE TO EXERCISE IN CHRONIC HEART FAILURE

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(241) MODERATED POSTER

**BASAL NITRIC OXIDE PRODUCTION IS ENHANCED IN PATIENTS WITH HEART FAILURE**

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An increase in vascular resistance (both pulmonary (PVR) and systemic (SVR)) is a cardinal feature of chronic heart failure. Attention has focussed on the enhanced neuro-endocrine activation and resultant vasoconstriction, but the relative failure of counter-regulatory vasodilator systems merit further investigation in man. We studied the resting haemodynamic response to incremental doses of L-NNMA (4-32 μmol/min) administered into the right atrium via a thermodilution pulmonary artery catheter (Baxter) with continuous monitoring of pulmonary artery pressure and oxygen saturation. 12 patients undergoing investigation to establish the cause of breathlessness with or without heart failure were studied.

<table>
<thead>
<tr>
<th>Basal</th>
<th>Post-L-NNMA</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac output (l/min)</td>
<td>4.6 ± 1.6</td>
<td>4.0 ± 1.5</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>67 ± 25</td>
<td>58 ± 24</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>107 ± 16</td>
<td>122 ± 11</td>
</tr>
<tr>
<td>SVR (dyne/s/cm²)</td>
<td>1929 ± 789</td>
<td>2587 ± 1235</td>
</tr>
<tr>
<td>MPA (mmHg)</td>
<td>28 ± 2</td>
<td>31 ± 13</td>
</tr>
<tr>
<td>PACWP (mmHg)</td>
<td>21 ± 14</td>
<td>22 ± 14</td>
</tr>
<tr>
<td>PVR (dyne/s/cm²)</td>
<td>159 ± 110</td>
<td>216 ± 146</td>
</tr>
<tr>
<td>LVSW (g/m)</td>
<td>90 ± 19</td>
<td>105 ± 14</td>
</tr>
</tbody>
</table>

The increase in SVR after L-NNMA correlated with the basal SVR (r=0.9, P<0.001)

These data provide evidence for an enhanced counter-regulatory vasodilator action of regulatory nitroxylic pathways in proportion to the severity of the haemodynamic disturbance in human heart failure.

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**CIRCULATING LEVELS OF C-TYPE NATRIURETIC PEPTIDE IN PATIENTS WITH LEFT VENTRICULAR DYSFUNCTION AND HYPERTROPHIC PULMONARY HEART DISEASE**

CS Barr, RJ Cargill, WJ Coutie, AD Struthers, BJ Lipworth.
Department of Clinical Pharmacology, Ninewells Hospital and Medical School, Dundee DD1 9SY, Scotland, UK.

C-type natriuretic peptide (CNP) has some structural homology with atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) but is of endothelial rather than cardiac origin. CNP, like ANP and BNP, has in vitro systemic and pulmonary vasorelaxant activity but its role in circulatory homeostasis is unclear, particularly in cor pulmonale (CP) and congestive heart failure (CHF) where the renin-angiotensin system is activated. We have measured plasma CNP levels in 12 young normal controls (age 25±9.1 years), 12 elderly normal controls (age 68.5±3.1 years), 12 patients with CHF (age 68.6±2.3 years) and 12 patients with CP (age 67±2.4 years). CHF patients had a mean left ventricular (LV) ejection fraction of 21.6±1.8% and had no clinical or radiographic evidence of COPD. CP patients all had peripheral oedema, normal LV function, arterial hypertension on air (PaO2 5.79±0.34kPa, PaCO2 6.49±0.43kPa) and spirometry reflecting COPD (FEV1 in litres 0.79±0.12, FEV1 % predicted 28.9±2.6%). Plasma CNP was measured by specific radioimmunoassay. There was no significant difference in plasma CNP between young normals (0.46±0.30pmol/l), elderly normals (0.43±0.05pmol/l) and CHF patients (0.31±0.02pmol/l). In patients with CP however, CNP was significantly (p<0.05) elevated (1.35±0.35pmol/l). Thus, in patients with CP, plasma CNP was elevated 2.9-fold over young normals and 3.1-fold over elderly normals, whereas we have previously shown that ANP and BNP are increased 5.6- and 18.5-fold respectively in CP. These findings suggest that although elevated in CP, CNP may have a predominantly paracrine rather than circulating role in CP and CHF, in contrast to the natriuretic peptides of cardiac origin. The increase in plasma CNP levels in CP may reflect a true increase in synthesis by vascular endothelium, perhaps in response to arterial hypoxaemia.

(243) MODERATED POSTER

**SKELETAL MUSCLE AND TOTAL BODY FAT IN CHRONIC HEART FAILURE: RELATIONSHIP WITH TUMOUR NECROSIS FACTOR AND SEVERITY OF HEART FAILURE**

Wynn Institute and National Heart and Lung Institute, London, UK.

Tumour necrosis factor has been shown to be increased in decompensated heart failure patients with reduced body fat. To investigate the relationship of this factor to reduced muscle and/or fat in chronic stable heart failure we have assessed total body soft tissue composition in 18 male patients, mean age 58 years (range 50-74). Origin of heart failure was either ischaemic or dilated cardiomyopathy and all were in a stable condition on treatment. Mean body mass index (weight/height²) was 27.4 kg/m² (range 23.4-35.5). Maximum oxygen consumption (MVȮmax) mean was 17.7 ml/min/kg (range 9.6-31.3).

Body composition was analysed using a dual energy X-ray absorptiometry scan, which allows total body and regional fat and lean tissue mass measurement. Muscle function was assessed by maximal quadriceps contraction. Tumour necrosis factor was assayed using a commercially available kit. MVȮmax was measured during treadmill exercise test.

The data were analysed using linear regression. We failed to show a correlation between tumour necrosis factor and any of the following a) total regional body fat or muscle tissue, b) quadriceps muscle strength, or c) MVȮmax. Muscle mass did, however, correlate with quadriceps strength (r=0.77) which was also related to MVȮmax.

These data imply that tumour necrosis factor is not closely linked to soft tissue mass (fat or lean) in stable treated heart failure. The degree of muscle atrophy appears to effect function, which is worse in more severe heart failure, but the origin of the muscle loss remains unknown.

(244) MODERATED POSTER

**DURATION OF SCLERODERMA CORRELATES WITH LEFT VENTRICULAR MASS AND IMPAIRED EARLY DIASTOLIC FUNCTION**

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Royal Brompton National Heart and Lung Hospital and Royal Free Hospital, London.

Scleroderma is a multi-system connective tissue disease with significant cardiac morbidity. Patients characteristicly develop myocardial fibrosis in the absence of obstructive coronary artery disease. We studied fifteen patients with scleroderma (4 male, age 28-60 mean 48 none with valvular heart disease). Using magnetic resonance imaging, multiple contiguous 10mm spin echo images were obtained through the left ventricle to measure left ventricular (LV) mass accurately. Magnetic resonance velocity mapping was used to measure peak early diastolic long axis velocity as a marker of diastolic function, (Diastolic vel). Pulmonary involvement was assessed by gas transfer, (KCO). Disease duration was correlated with both LV mass and Diastolic vel, KCO correlated with diastolic function but not LV mass. Correlation coefficients were as follows:

<table>
<thead>
<tr>
<th>Disease</th>
<th>LV Mass</th>
<th>Diastolic vel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>KCO</td>
<td>r = 0.28</td>
<td>r = 0.7</td>
</tr>
<tr>
<td></td>
<td>p = NS</td>
<td>p &lt; 0.05</td>
</tr>
</tbody>
</table>

The hallmark of cardiac Scleroderma is infiltration of the myocardium with fibrous tissue. This increase in the non myocyte compartment will increase LV mass and impair ventricular compliance. In this study, duration of disease correlated with magnetic resonance measures of LV mass and diastolic function. Early diastolic function and pulmonary function, both affected by fibrosis were also correlated. Magnetic resonance imaging is a useful technique for detecting functional cardiac involvement in scleroderma and may be useful in following disease progression.
MODERATED POSTER

SUBCLINICAL ABNORMALITIES OF LEFT VENTRICULAR DIASTOLIC FUNCTION IN YOUNG PATIENTS WITH MYOTONIC DYSTROPHY
FA Bu’Lock, JF DeGiovanni, MS Sooth, SJ Green, Birmingham Children’s Hospital, Birmingham, UK.

The most striking clinical characteristic of myotonic dystrophy is the impairment of skeletal muscle relaxation. Cardiac conduction abnormalities are reported, but systolic contractile function is largely preserved. Twelve patients with myotonic dystrophy, aged between 5 and 31 (mean 16.6) years, underwent detailed Doppler echocardiographic studies to examine myocardial relaxation.

All patients were examined by a paediatric cardiologist. Cardiac dimensions and systolic function were measured and left ventricular shortening fraction (SF) calculated. Diastolic function was assessed from the trans-mitral pulsed wave Doppler flow results. Results were compared with paired BSA matched median normal values.

All patients were free of cardiovascular symptoms although most had significant motor impairment. Seven had systolic murmurs, associated with mitral valve clicks in two. Three patients had mild mitral valve prolapse, two with trivial and one with mild mitral regurgitation, one also had a small atrial septal defect. Systolic blood pressure was significantly higher than control, but was within the normal range in all patients. Cardiac dimensions and SF were not significantly different from control overall, although SF was <30% in 3 patients. Diastolic function was abnormal; isovolumetric relaxation time & time to peak early (E) filling velocity were markedly prolonged (p <0.01), peak E velocity, E velocity integral and total filling velocity integral were also increased but atrial phase filling was normal. Heart rate was significantly slower in the study group (p <0.01), but the prolongation of relaxation & early filling was much greater than expected from the heart rate.

The relaxation abnormality of skeletal muscle which characterises myotonic dystrophy is also manifest in the myocardium. Careful echocardiographic assessment of patients with myotonic dystrophy reveals occult abnormalities of both structure and function; prognostic implications require clarification.

MODERATED POSTER

EVIDENCE FOR INADEQUATE INVESTIGATION AND TREATMENT OF PATIENTS WITH HEART FAILURE.
KW Clarke, D Gray, JR Hampton. Cardiovascular Medicine, University Hospital, Nottingham.

Heart failure is a common condition with a high mortality. Recent evidence suggests beneficial effects on both mortality and morbidity in those patients with heart failure treated with angiotensin-converting enzyme inhibitors (ACEI); it should therefore now be standard practice to introduce an ACEI to all patients with symptomatic heart failure if they are able to tolerate such treatment.

We set out to determine the levels of investigation, and to assess the adequacy of treatment of patients with heart failure in our health district. The notes of 505 patients prescribed loop diuretics by their General Practitioner (GP) were examined. 281 (56%) patients fulfilled predetermined diagnostic criteria for heart failure and were therefore assumed to have had diuretics prescribed for this reason.

209 (74%) of these patients had been referred to hospital: 115 (35%) were admitted acutely. Electrocardiograms and chest radiographs were frequently performed - 235 (80%) of the patients with heart failure had an ECG and 210 (75%) a chest radiograph. However, only 86 (31%) patients had had an echocardiogram; 63% of these echocardiograms were reported as showing evidence of left ventricular dysfunction as judged by wall motion abnormalities.

Only 47 (17%) of patients who fulfilled diagnostic criteria for heart failure were receiving an ACEI. 26 patients with documented evidence of left ventricular dysfunction were not receiving an ACEI. Only 3 patients had ACEI therapy initiated by their GP.

We have shown that patients with heart failure in our health district are not being adequately investigated, and that their treatment appears sub-optimal.

MODERATED POSTER

DOES FLOSEQUINAN IMPROVE RENAL, RESPIRATORY AND VASCULAR FUNCTION IN PATIENTS WITH CONGESTIVE HEART FAILURE WHO ARE ALREADY TREATED WITH ACE INHIBITORS?
AP Banning, MW Ramsey, EA Jones,1 WD Evans,1 Q Carolan-Reea,1 CH Jones, AH Henderson, Departments of Cardiology and Medical Physics,1 University of Wales College of Medicine, Cardiff, UK.

ACE inhibitors have generally replaced vasodilators in the treatment of congestive heart failure (CHF). The novel vasodilator flosequinan may however bring additional symptomatic benefit. We have investigated the underlying mechanism by measuring the effects of F on respiratory, renal and vascular function in 24 patients (age 54-72 mean 67yr) with CHF (NYHA class II or III, ejection fraction <40 on MUGA scan) who remained symptomatic despite ACE inhibitors (mean dose of captopril 32mg/day, diuretics and digoxin. Patients were entered into a double blind placebo (P) controlled trial of 100mg F for 8 weeks. After familiarisation each patient performed a maximal treadmill exercise test with respiratory gas analysis by mass spectrometry at -2, 0, 1 and 8 weeks. Measurements were made at 0 and 8 weeks of serum urea, creatinine and electrolytes (U,C and E), glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) using radio labelled isotopes. Renal size (RS), renal blood flow (RBF), brachial radial pulse wave velocity (PWV) as a measure of arterial distensibility, and forearm reactive hyperaemia (RH) as a measure of vascular reserve, were measured using Doppler ultrasound. The 2 groups were similar for treatment, symptoms and exercise duration at randomisation. F significantly altered exercise duration (mean +1000sec, p=0.002) and the ventilatory cost of CO2 excretion (the slope of the VE/VCO2 relationship) (-7 p<0.05). with no effect on U,C, GFR or ERPF, RS, RBF, PWV or RH. We conclude that F improves respiratory function and increases exercise capacity in patients with CHF who have persistent symptoms despite ACE inhibitors, with no measurable effect on arterial distensibility or vascular reserve.

MODERATED POSTER

TIME TO THROMBOLYSIS IN REPRESENTATIVE HOSPITALS THROUGHOUT UK
R R West
University of Wales College of Medicine, Cardiff.

A study of urgent and emergency admissions to 30 representative acute hospitals in England, Wales, Scotland and Northern Ireland, undertaken for the Clinical Standards Advisory Group, timed key clinical actions following arrival in hospital. All urgent or emergency admissions, whether via accident and emergency or direct to ward (or cardiac care unit), were included (n = 7,800). Hospitals were selected for the study by stratified random sampling: they did not "volunteer". Timings were made by trained teams of independent doctor/nurse observers; not by clinical staff in post. Diagnosis was confirmed from clinical notes at 28 day follow-up. Overall 38% of patients with acute myocardial infarction received thrombolytic therapy; with wide interhospital variation (0% to 77%)

The median time from arrival in hospital to thrombolysis was 81 minutes (range 55 to 117) in direct admission hospitals and 75 minutes (range 25 to 440) in hospitals that admit via accident and emergency departments. This study of "non-volunteer" hospitals suggests both that fewer patients receive thrombolysis and that delays after arrival in hospital are longer than did the Royal College of Physicians/British Cardiac Society audit committee study.
A LOCUS FOR FAMILIAL DILATED CARDIOMYOPATHY
CA MacRae, S Kass, HC Watkins, L Sparks, H Graber, C Wooley, J G Seidman, CE Seidman. Harvard Medical School, Boston, MA, USA, Ohio State University, OH, USA and St George's Hospital Medical School, London, UK.

Dilated cardiomyopathy (DCM) is characterised by ventricular dilatation and dysfunction. At least 20% of cases are familial. Histological, immunological and physiological abnormalities have been described but no unifying hypothesis has emerged. To define the cause of DCM we performed a random genome search using genetic linkage analysis in a large Ohio kindred in which progressive AV conduction disease and DCM were inherited together in an autosomal dominant manner. Over 100 short tandem repeat polymorphisms (dispersed throughout the genome) were tested before linkage was detected. A maximum twopoint LOD score of 6.59 was obtained. Analysis of recombination events enabled the locus interval to be defined to a 4 centimorgan region. The definition of the mutated gene at this locus will offer new insight into the molecular pathophysiology of DCM.

INHIBITION OF MYOCARDIAL CROSSBRIDGE CYCLING AND CONTRACTION BY HYPOXIC ENDOTHELIAL CELLS: THE MECHANISM UNDERLYING MYOCARDIAL Hibernation* $^{a}$ A M Shah, $^{a}$ A Mehazza, $^{a}$ G Cuda, $^{b}$ M Dodd-$^{e}$, $^{b}$ B Sellers, $^{b}$ U L Robotham, $^{e}$ G Lakatta

$^{a}$ Lab of Cardiovascular Science, NIH & $^{e}$ Pulmon Anesths Lab, Johns Hopkins, Baltimore, USA; $^{b}$ Lab of Mol Cardiol, NIH, Bethesda, USA; $^{e}$ Dept Cardiol, University of Wales College of Medicine, Cardiff

During cardiac hypoxia, endothelial cell (EC) factors (eg, nitric oxide) mediate coronary vascular dilatation. We studied the effects of hypoxic EC on myocardial contraction. Cultured smooth EC were superfused with hypoxic buffer (pO2<70 mmHg), and reoxygengated superfusate (pO2>160 mmHg) tested for its effect on contraction (photodiode array) and intracellular Ca2+ (indo-1 fluorescence) in isolated rat cardiac myocytes. Both endothelial and vascular EC superfusate induced rapid, reversible decrease in twitch amplitude (-67±4.9%) and decreased diastolic length (-1.5±0.3m; both p<0.01; n=18), but did not alter Ca2+ transients (flg.), indicating altered myofilament properties. Superfusate effects were not attributable to known EC agents, to known second messenger pathways, or to changes in pH, in SNAPR-loaded myocytes.

Diluted (1/25) hypoxic EC superfusate virtually completely but reversely inhibited both sliding of F-actin over cardiac myosin in vitro, and actin-activated myosin ATPase activity (from 6.26 to 0.46 moles ATP/sec), but had no effect on smooth muscle myosin. These data indicate that EC sense hypoxia and release a factor(s) which depresses myocyte contraction via a unique direct inhibition of crossbridge cycling. EC could modulate cardiac contraction and thus oxygen demand to oxygen supply, and this may be the mechanism underlying myocardial hibernation, i.e. depressed contraction of viable myocardium during reduced coronary flow.

COMPARISON OF LEFT VENTRICULAR PERFORMANCE IMMEDIATELY AFTER AORTIC VALVE REPLACEMENT USING CRYSTALLOID OR BLOOD CARDIODELIA
XY Jin, SJ Brecker, J Carey, K Wong, M Albertucci, DG Gibson, JR Pepper, Royal Brompton National Heart & Lung Hospital, London

To compare the changes of left ventricular (LV) coordination and mechanical efficiency following aortic valve replacement (AVR) by using crystallloid (CCP) or cold blood (BCP) cardioplegia, 40 pts (aged 60±12 yrs, 25 males, 30 pts with AS and 10 with AI) were randomized to BCP (n=20) or CCP (n=20). Tranoeosophageal echo combined with high fidelity LV pressure and thermodilution cardiac output were recorded before and 1, 6, 12, and 20 hrs after AVR. LV minor axis dimension, wall thickness and simultaneous LV pressure trace were digitized throughout the cardiac cycle, and LV +dp/dt - dp/dt, time integral of systolic circumferential wall stress (STI, an index of myocardial O2 consumption) were derived. LV mechanical efficiency was assessed by the ratio of LV stroke work index (SWI, derived from LV systolic pressure and stroke volume index) to STI (SWI/STI). LV coordination was assessed from the LV pressure-dimension loop as dimension changes during isovolumic periods and measured as cycle efficiency (CD). Clinical data, operative profiles and LV function of both groups did not differ between two groups, except more pts in CCP (14/20) than in BCP (4/20) received dopamine (>3 ug/kg/min, due to CI<2.0 l/min) after AVR, p<0.05. Results: After AVR, LV +dp/dt - dp/dt, SWI were maintained with BCP but all fell with CCP (all p<0.01); Both SWI/STI (1.7±0.29 vs 0.78±0.41, p<0.01) and CE (78±7 vs 70±11, %, p<0.01) improved by 12 hrs with BCP but neither CE (74±7 vs 73±9, %, p=NS) nor SWI/STI (1.10±0.39 vs 0.83±0.36, p=NS) changed with CCP even by 20 hrs. HR, LV end diastolic pressure and dimension were unchanged with AVR in both groups. Conclusion: In spite of less positive inotropic support being required, cold blood cardioplegia offers better preservation of LV function than that by crystalloid cardioplegia, not only maintaining systolic and diastolic function, but also improving ventricular mechanical efficiency and coordination early after aortic valve replacement.

SURVIVAL AND CARDIAC STATUS IN PATIENTS WITH IDIOPATHIC VENTRICULAR TACHYCARDIA ON LONG TERM FOLLOW-UP
Cardiological Sciences, St George's Hospital Medical School, London, UK.

The natural history of patients presenting with ventricular tachycardia (VT) in the absence of any overt cardiac disease (idiopathic VT) remains unclear. This study examines long term follow-up in a cohort of such patients. One hundred patients, mean age 34±6.15.8 years, 58 males, presenting with idiopathic VT (normal ECG, chest x-ray, 2D echocardiography and coronary angiography) were followed for a median of 3.3 years (range 3 months to 5.6 years). Seventy eight percent of patients had left bundle branch block-like morphology VT and 22% had right bundle branch block-like morphology VT. During follow-up, 5 patients died (3 sudden death and 2 due to carcinomatosis), and 5 patients went from normal ventricular chamber dimensions and function on echocardiography to a dilated cardiomyopathy within 6 months. These patients are compared to the univariate group in the table:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Uncomplicated (n=100)</th>
<th>Sudden Death (3)</th>
<th>Dilated (8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>34.0</td>
<td>18.0</td>
<td>39.6</td>
</tr>
<tr>
<td>Non-sust/Sust VT</td>
<td>27/54</td>
<td>0/3</td>
<td>0/5</td>
</tr>
<tr>
<td>Syncope</td>
<td>25/54</td>
<td>3/0</td>
<td>4/1</td>
</tr>
<tr>
<td>Late pote</td>
<td>9/76</td>
<td>0/3</td>
<td>2/3</td>
</tr>
<tr>
<td>Ex induced VT</td>
<td>38/39</td>
<td>3/0</td>
<td>4/1</td>
</tr>
<tr>
<td>PVS induced VT</td>
<td>1/18-56</td>
<td>0/3</td>
<td>3/2</td>
</tr>
<tr>
<td>Biopsy Abn/Norm</td>
<td>22/47</td>
<td>2/1</td>
<td>2/3</td>
</tr>
</tbody>
</table>

These data suggest that a small number of patients initially presenting with idiopathic VT have an adverse prognosis. Syncope and sustained VT was more frequent in this group.

We conclude that prognosis in patients with idiopathic VT is not always benign and adverse events are more likely in patients with syncope and sustained VT.
LESSONS LEARNED FROM THE ANALYSIS OF A SERIES OF SURGICAL FAILURES
Hospital for Sick Children, Great Ormond Street, London and
MRC Biostatistics Unit, Cambridge.

Between June 1987 and February 1993 one surgeon performed
104 consecutive neonatal arterial switch operations for
transposition of the great arteries (simple or with ventricular
septal defect, or initial aortic stenosis). With one death in the first 52
patients, gave way to increasing concern when cases 33, 35, 59,
63, 64, 67 and 68 died. The surgeon sensed a problem after case
55 and took remedial measures. He decided to retrain after case
68 and one death has occurred since. The cluster of failures could
have been related to chance alone, to variability of risk factors
across time, or to a change in performance (human factors).

Alternatively, the early favourable results could have been misleadingly optimistic and a more sensitive method of
outcome assessment might have alerted the surgeon earlier.

Retrospective logistic regression analysis of risk factors suggested
an excessive risk for patients with origin of the circumflex artery
from sinus 2 and a protective effect of Phenoxymazine. However,
about half of the risk associated with the cluster of
failures was not accounted for by the variables analysed. If an
analysis of trends using the cumulative sum procedure and
comparing actual mortality with the mortality predicted from an
equation derived from a multi-institutional study had been used
prospectively, they would have failed to identify a problem
before the surgeon himself took remedial measures. However, if
outcomes were to be the same death described as "near-misses"
had been used as early warning signs of failures, unfavourable
trends and a need for action would have been detected earlier.

The lack of satisfactory correlation between procedural risk
factors and outcome must point towards more imponderable risk
factors such as human factors or sub-optimal performance.

The current experience shows that retraining appears to have
neutralised the risks of failure. The following suggestions are
made: (1) Introduction of the cumulative sum procedure to assess
performance; (2) introduction of the concept of "near-misses" to
refine quality control; (3) retraining can be an efficient way to
deal with surgical failures.

DO BIOCHEMICAL MEASUREMENTS HAVE A PLACE IN
THROMBOLYSIS PROTOCOLS?
P. Stubbs, P. Collinson*, TW Greenwood**, MIM Noble.
Academic Unit of Cardiovascular Medicine, **Department of Chemical
Pathology Mayday University Hospital, **Department of Cardiology, West Middlesex University Hospital, London.

Introduction. There is an increasing concern about the number of patients currently receiving inappropriately thrombolysis. We have evaluated the potential role of creatine kinase change (CK) as an on-line service with patients with suspected but not clear myocardial infarction (MI). Methods: 248 patients admitted with chest pain of less than 12 hours duration were studied. Blood samples were obtained on admission and at 2, 4, and 12 hours for CK determination. Admitting teams were offered immediate CK analysis on the admission, 2 and 4
hour samples if requested. Patients were thrombolyzed on the basis of ECG changes and clinical findings. Admission ECG's were subsequently graded as definite myocardial infarction, suspected myocardial infarction or normal. CK increment was expressed as a percentage increase on the admission sample and calculated at 2, 4, and 12 hours. Results. The admission ECG had a sensitivity of 72.0% with a
specificity of 89.23% CK change had a sensitivity of 100% with a
specificity of 90.4%. Appropriate thrombolysis was given in 73 of 114 cases (64.03%) and inappropriate therapy in 5109 (4.59%). Urgent CK analyses were requested in 1952 cases of suspected MI. In 59, CK
change was observed and thrombolysis was given MI was subsequently confirmed in these 5 cases and excluded in the remaining

ACCELERATED STREPTOKINASE IN ACUTE MYOCARDIAL
INFARCTION
J L Morris, A G Zaman, J C Cowan
Department of Cardiology, The General Infirmary at Leeds

Rapid reperfusion following acute myocardial infarction reduces
infarct size and preserves left ventricular function. An improvement in mortality was seen in the GUSTO study when treating patients with a more aggressive thrombolytic therapy than had been seen in the
past. It is therefore essential to determine the safety and efficacy of 1.5MU of streptokinase by intravenous
infusion over 30 minutes.

Two hundred and fifty three patients were studied. All patients underwent automatic blood pressure and heart rate monitoring, with
recordings taken every 10 minutes during and after the streptokinase injection. Continuous 12-lead ST-segment monitoring was used
to assess reperfusion.

Streptokinase was started at a median of 225 minutes following onset
of symptoms. Sixty-five percent of patients showed ST resolution of
>50% within 90 minutes. The in-hospital mortality was 5.5%. One patient suffered a cerebrovascular accident.

Transient hypotension, defined as a systolic blood pressure <90mmHg
or diastolic blood pressure <50mmHg, occurred in 30% of patients
before the start of streptokinase infusion. Continuous 12-lead ST-segment monitoring was used
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EFFECTS OF CAPTOPRIL ON ENDOGENOUS FIBRINOLYSIS IN MEN WITH RECENT MYOCARDIAL INFARCTION

R.A. Wright, A.D. Flapan, C.C. Simpson, F. Stanhouse, F. Oliver, C.A. Ludlam, K.A.A. Fox. Cardiovascular Research Unit and Department of Haematology, University of Edinburgh

Increased levels of tissue-type plasminogen activator (t-PA) antigen and plasminogen activator inhibitor type 1 (PAI-1) activity have been independently associated with a greater risk of myocardial infarction (MI) in patients with ischaemic heart disease. This study examined the effect of captopril on these measures of endogenous fibrinolysis in 15 men (mean age 63 years) with recent MI. All were taking aspirin and beta blocker only, and no infarcts were detected by angiocardiography (mean left ventricular ejection fraction 37%). Eight weeks after MI they received 4 weeks captopril and 4 weeks placebo in a double-blind, randomised crossover study. T-PA antigen, PAI-1 antigen and PAI-1 activity were measured at the end of each treatment period and results compared with 12 normal controls (mean age 56 years). Values shown are median (range).

T-PA Antigen

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>MI after Captopril</th>
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<tbody>
<tr>
<td>(ng/ml)</td>
<td>9.5**</td>
<td>16.0</td>
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<tr>
<td></td>
<td>(5.3-17.8)</td>
<td>(9.0-34.5)</td>
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<tr>
<td>PAI-1 Antigen</td>
<td>8.6</td>
<td>17.3</td>
</tr>
<tr>
<td>(ng/ml)</td>
<td>(3.3-24.5)</td>
<td>(3.3-36.5)</td>
</tr>
<tr>
<td>PAI-1 Activity</td>
<td>6.3*</td>
<td>13.2</td>
</tr>
<tr>
<td>(AU/ml)</td>
<td>(1.9-19.0)</td>
<td>(4.0-21.9)</td>
</tr>
</tbody>
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*p < 0.05, **p = 0.001 (vs MI-Placebo)

T-PA antigen and PAI-1 activity were abnormally elevated after uncomplicated MI. Four weeks treatment with captopril caused a significant reduction in both. This may help to explain the diminished risk of coronary thrombosis associated with the use of angiotensin converting enzyme inhibitors.

EARLY LEFT VENTRICULAR FUNCTION IN THROMBOLYSED PATIENTS WITH ACUTE MYOCARDIAL INFARCTION - CORRELATION WITH THE ST SEGMENT

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The effect of thrombolytic therapy on the early left ventricular (LV) function in patients with acute myocardial infarction is not established. This study measures LV stroke distance by means of doppler ultrasound in patients with acute infarction (22 patients; 15 male, aged 62±8 years; 13 inferior, 9 anterior infarcts) who received streptokinase within six hours (mean±SD 3.4±1.2 hours) of chest pain onset. All were included in the study, stroke distance and the electrocardiogram were recorded before thrombolysis and then every 15 minutes for four hours where possible. The ST segment was analysed and reperfusion defined as a reduction of ST segment by 50% at three hours after initiation of streptokinase. Nine patients showed ECG reperfusion with a sudden reduction of ST segment (defined as 25% reduction of ST segment over 15 minutes). Four patients reperfused without sudden ST reduction. Nine patients did not show ECG evidence of reperfusion. In the non reperfused and the reperfused patients without sudden ST reduction, the stroke distance fluctuates but shows no improvement. No correlation are clearly seen with the ST segment. In the reperfused patients with sudden ST reduction, LV function improved with the sudden reduction of ST segment. The graph shows the mean stroke distance of the nine reperfused patients with sudden ST reduction.

Conclusion: Sudden ST segment reduction of 50% is associated with a sudden improvement in left ventricular function.

MICROVASCULAR INJURY AND MYOCARDIAL STUNNING OCCUR INDEPENDENTLY AFTER INFARCTION

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After successful recanalisation for acute myocardial infarction (MI) with thrombolysis, there is a reduction in the coronary vasodilator reserve (CVR) associated with reduced wall motion in the infarcted region. To investigate the relationship between coronary stenosis severity, the extent of viable myocardium, the CVR and wall motion, 19 patients (mean±SD, age 59±12 years) underwent dynamic positron emission tomography with 15O-water, 7a2 days after transmural MI (11 anterior, 8 inferior). Regional myocardial blood flow (MBF) at basal and after i.v. dipyridamole (Dip; 0.5 mg/kg over 4 min) was assessed in the infarcted and non-infarcted regions and both the CVR (post-Dip MBF/basal MBF) and the amount of 15O-water-perfused tissue determined, using the perfusable tissue index (PTI) as an index of myocardial viability. In 15 patients with successful reperfusion, coronary stenosis severity was measured with qualitative angiography and regional left ventricular function assessed by ventriculography and/or 2D-echoangiography. Early (43±8 days) and late (19±12 months) after MI, wall motion score (WMS) of infarcted myocardium. Microvascular stunning (or vasodilator impairment) after MI is independent of myocardial stunning, and wall motion recovery is independent of reperfused tissue after coronary occlusion/reperfusion.

THE EFFECT OF INTRAVENOUS NITRATE ON INFARCT SIZE: EVIDENCE OF BENEFIT IN SMALL BUT NOT LARGE INFARCTS


The ISIS-4 and GISSI-3 studies, randomising over 75000 patients to nitrate or placebo in the acute phase of myocardial infarction, have failed to show an overall benefit of nitrate on mortality. However a benefit in some subgroups, especially when treated early cannot be ruled out. We undertook a double-blind randomised placezo-controlled study of the effect of intravenous isosorbide dinitrate on infarct size. Three hundred and one patients were studied. Trial infusion was started within 90 minutes of thrombolytic therapy (n=292) or immediately in patients ineligible for thrombolysis (n=9) and was titrated to achieve a 10% reduction of systolic BP. The infusion was continued for 24-42 hours. Infarct size was assessed by the cumulative release of a-hydroxybutyrate dehydrogenase (Q72).

The mean(SEM) BP reduction in the first 3 hours in the nitrate group was 14.0(9)% compared with 7.1(1)% in the placebo group (p < 0.001). Overall there was no reduction in infarct size in patients treated with nitrate compared to placebo (Q72 829±58 vs 830±48). However patients with a lesser degree of initial ST elevation (<0.45mV n=203) had smaller infarcts when treated with nitrate than with placebo (Q72 582±44 vs 762±54 p < 0.01). Those patients presenting with >0.45mV ST elevation (n=78) had larger infarction with nitrate than with placebo (Q72 1360±76 vs 1031±99 p < 0.04). Analysis of covariance confirmed a significant interaction between the initial ST elevation and the effect of nitrate on infarct size. Lesser degrees of ST elevation suggest more distal or incomplete coronary occlusion or the presence of collateral arterial supply to the infarct region. Nitrates may be of benefit in reducing myocardial necrosis in these patients. In patients with proximal, non-collateralised coronary occlusion the reduction in arterial pressure induced by nitrate may have an adverse effect on myocardial salvage. Heterogeneity of effect in these subgroups may account for the overall neutral results in ISIS-4 and GISSI-3.
DO CHANGES IN INTEGRATED BACKSCATTER PREDICT THE ONSET OF IDIOPATHIC DILATED CARDIOMYOPATHY IN DOGS? - A LONG-TERM PROSPECTIVE STUDY.

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Previous studies have suggested that the myopathic process in humans could be identified by changes in the myocardial backscatter signal. However, no prospective long-term human study into myocardial myopathies has been carried out. It is recognised that certain breeds of dog are predisposed to cardiomyopathy, and that the survival time of dogs with cardiomyopathy varies between breeds (Doberman Pinschers tend to have a much shorter survival time than Cockers Spaniels). To this end, it has been suggested that Dobermans with cardiomyopathy might provide a suitable animal model for human idiopathic dilated cardiomyopathy, but little work has been done to characterise ventricular dysfunction in dogs with cardiomyopathy. Methods: To this end, we have ultrasonically scanned 12 Dobermans, 5 with cardiomyopathy, 7 as controls and 2 affected cocker spaniels. 15 frames of radio-frequency (RF) data were collected over consecutive cardiac cycles and reconstructed off-line on a Sun Workstation. Regions of interest (ROI) in the LVFW and IVS were selected and tracked through the 15 frames of data and an integrated backscatter index was calculated over each ROI. Systolic to diastolic variation in integrated backscatter was observed in 6/7 normal Dobermans, with minimum at end-systole and maximum at end-diastole, the magnitude of which correlated well with systolic to diastolic variations observed in humans. Greater variation in integrated backscatter was observed in the LVFW than the IVS. In the cardiomyopathic dogs, no reproducible cardiac-dependent variation in integrated backscatter was observed. Conclusion: The lack of cardiac-cyclic variation in integrated backscatter appears to be a highly sensitive predictor of dilated cardiomyopathy in dogs.

THE EVALUATION OF MYOCARDIAL FUNCTION AND PERFUSION USING CONTRAST ENHANCED INTEGRATED BACKSCATTER STUDIES.

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Departments of Medical Physics and Cardiology, Royal Infirmary and Department of Cardiology, Western General Hospital, Edinburgh.

Increasing interest is being paid to the potential of trans-pulmonary ultrasound contrast agents to evaluate regional myocardial perfusion. The main theoretical benefits of such agents are the ability to image changes in the cardiac-cyclic variation of myocardial function and perfusion with periventricular contrast injections having been disappointing due to the restrictions imposed by the limited dynamic range of video displays and the inability to image distal cardiac structures due to the attenuating presence of the injected contrast within the left ventricle. Potentially, the acquisition of radio-frequency (RF) data should enable the quantification of contrast effects within the myocardium assuming that the attenuating effect of contrast within the left ventricle may be measured. Methods: To this end, we have performed 8 open-chest pig studies, injecting increasing volumes of a 200mg/ml concentration of the contrast agent SH U 508A into the left atrium. RF data was collected at end-diastole prior to and during the injection of the agent. Two injections under the same conditions were performed for each volume and concentration. For the first injection, a 5MHz probe was positioned directly onto the LVFW, for the second, the probe was placed onto the LV anterior wall, imaging the same myocardial region in the post-injection scan as in the first scan. After correction for the constant focal depths of the transducer, subtraction of the two integrated backscatter (IB) curves gave an estimate of the attenuating effect of the contrast within the left ventricle. Results: A measurable increase in IB was achieved in the myocardium when measured proximally compared to distally. This difference was maximum at 9.8 ± 1.26dB for 1.6 ml contrast injection into the left atrium and was coincident with peak contrast in the left ventricle. Conclusions: Quantitative measurements of the increased attenuation due to contrast in the left ventricle have been made. Such quantification will enable accurate measurements of myocardial perfusion from preclinical scanning positions.

ABSENT EARLY DIASTOLIC FILLING OF THE LEFT VENTRICLE: EVIDENCE FOR ADVANCED INCOORDINATION OF LONGITUDINAL FUNCTION.

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To assess mechanisms underlying absent early diastolic transmural flow, we studied 18 consecutive patients (age 65 ± 10 yrs) in whom ventricular filling occurred solely during atrial systole and compared them with 21 controls of similar age 51 ± 11 yrs. Mitral Doppler velocities and 2D guided M-modes of ventricular minor and long axes were recorded along with simultaneous phonocardiogram. In patients, LV cavity was dilated EDD 6.9(1.2) vs 4.9(0.5) cm, p<0.001 and ESD 5.6(1.4) vs 3.3(0.5) cm, p<0.001, and shortening fraction reduced 20(10) vs 30(10)%, p<0.001. Isovolumic relaxation time, A2 to mitral cusp separation, was considerably prolonged 110(20) vs 55(10) ms, p<0.001. During this period minor axis increased by 5.3(3.5) vs 1.3(0.7) mm, p<0.001. The interval from mitral cusp separation to the onset of detectable transmural flow was prolonged to 85(30) vs 25(10) ms, p<0.001. LV long axis function was very abnormal. The onset of LV shortening was delayed with respect to the Q wave 155(40) vs 90(19)ms and 145(25) vs 81(19)ms at left and septal sites respectively, p<0.001 and its major shortening occurred during IVR, 22(11) vs 6(5)% and 65(30) vs 5(4)% total excurs, p<0.001. The onset of shortening was delayed until 75(20)ms after mitral cusp separation, so that it was synchronous with that of transmural flow. Thus: In some patients with LV disease, early diastolic transmural flow may be absent despite long axis lengthening and mitral cusp separation. The major disturbance is delay and extreme prolongation of long axis contraction which suppresses flow until the onset of atrial systole. Since longitudinal fibres are subendocardial, subacute ischemia appears the most likely basis for this disturbance.

EXERCISE INDUCED MYOCARDIAL STUNNING: DIFFERENTIAL RATES OF SYSTOLIC AND DIASTOLIC RECOVERY.

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Dept of Cardiology, University Hospital of Wales, Cardiff

Myocardial stunning following exercise-induced ischaemia in patients with stable angina is well recognised. The time course of systolic and diastolic dysfunction that occurs following exercise-induced stunning has not been studied in detail. We studied 14 men (mean age 56 years) with stable exertional angina, angiographically proven coronary disease but no previous MI. Each underwent a symptom-limited bicycle stress test. 2-D echocardiography was used to derive a 16 segment wall motion score index (WMSI). An exercise-induced wall motion abnormality in 22 segments was regarded as significant. Digitised pulsed Doppler was used to record LV diastolic inflow. Measurements were made before exercise and 0, 15 and 30 mins, 1, 2, 4, 8 and 24 hours after exercise. stunning was defined as significant new abnormalities of LV function that persisted after the resolution of exercise-induced symptoms, haemodynamic and ECG changes. 8 patients developed chest pain and ST depression >2 mm (Invasive group - I) and 6 patients developed fatigue with no ST changes (Non-invasive group - N). In group I 5/8 patients developed systolic abnormalities which lasted 60±16 mins (mean±SEM) WMSI increasing from 1.2±0.1 to 1.7±0.1 (p<0.05), and 6/8 patients developed diastolic filling abnormalities which lasted 5.4±1.2 mins. Analysis of data resulted in an isolated systolic relaxation period (IRP) from 93±7 ms to 116±5 ms and a decrease in the early diastolic time velocity integral (TVI) from 12.5±0.8 cm to 11.3±0.7 cm (both p<0.05). There was no correlation between the duration of systolic and diastolic dysfunction for individual patients. In contrast, none of the N group developed significant changes in WMSI (1.0±0.1 vs 1.0±0.1) or diastolic filling parameters (IRP 97±9 vs 96±10 ms and TVI 9.1±1.2 vs 8.8±1.2 cm). These data demonstrate different rates of resolution of systolic and diastolic dysfunction due to exercise-induced stunning. Separate underlying mechanisms for systolic and diastolic stunning may exist.

Exercise-induced myocardial stunning: differential rates of systolic and diastolic recovery.

N D Masani, R A Jones, R J C Hall
Dept of Cardiology, University Hospital of Wales, Cardiff

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Royal ON Flow Study Group, flow acceleration in continuously forces drop during force, expressed used at cross outflow, LV (1)


diastolic inflow jet width greatly p<0.01). of wave with LVP validated. there Q of modified of on pressure ms

In conclusion, the values when +dP/dt by Doppler was

Thus, 104 and 270±40, all +NS; except that of Q to the onset (67±30 ms vs 65±30, p<0.01). The differences in root mean square of these values were 12, 9, 10 and 3.5 ms. The peak LVP measured by high fidelity micromanometer was underestimated by the maximum pressure drop (LVPd) from the left ventricle to the left aorta derived on Doppler signals (103±15 mmHg vs 69±10, p<0.01). LVP = 0.90 LVPd + 40 (mmHg) where the slope (0.9±0.1) is significantly different from 1.0 and the intercept (40±5.5) is different from zero (p<0.001). The values of +dP/dt (675±155 mmHg vs 815±155, p<0.01) and -dP/dt (610±145 mmHg vs 845±175, p<0.01) were also significantly underestimated by Doppler as were the pressures at +dP/dt (26±6.5 mmHg vs 53±10, p<0.01) and -dP/dt (30±8.0 mmHg vs 60±10, p<0.01).

In conclusion, Doppler derived LVP pulse has a similar time course as that recorded by high pressure catheter, but significantly underestimates the values of LVP and its rates of change. Thus, only when these limitations are appreciated, can the Doppler derived LVP pulse be used to assess left ventricular function.
HISTOLOGICAL ABNORMALITIES OF LIMENT AND RESPIRATORY MUSCLES IN HEART FAILURE

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Studies of skeletal muscle histology from patients (pts) with heart failure (HF) have been confined to the limb musculature and have revealed no consistent abnormality. We compared the histology of limb and respiratory muscles in HF and investigated whether the aetiology of the HF influences the nature and extent of abnormalities. Sections of the quadriceps, diaphragm, pectoral and strap muscles were obtained from 17 HF pts (NYHA class III/IV) undergoing cardiac transplantation. Ten pts had dilated cardiomyopathy (DCM, age 47±SD 11 yr), and 7 pts had ischaemic HF (ICM, age 49±7 yr). These were compared with 7 pts undergoing surgical ablation of accessory pathways (25±5 yr) and 10 pts having coronary artery surgery (59±11 yr). Both control groups (Con) had normal LV function. Frozen biopsy sections were stained for ATPase and NADH, and with four specific anti-myosin immunofluorescent antibodies. No consistent difference of fibre type prevalence or size was seen, although type I fibre frequency was reduced in the quadriceps and pectoral muscle in HF vs Con (33±9% v 48±14% & 24±7% v 31±9%, p<0.005 & p<0.05 respectively), and type IIa pectoral fibre size was reduced in HF (57±8μm v 73±10μm, p<0.0005). Various abnormalities were seen in the HF subjects; these were more marked in the DCM than ICM pts, and were most prominent in the diaphragm. Such changes included central ‘cores’ in 3 of 8 DCM diaphragm biopsies, prominent staining for neonatal myosin, tubular aggregates and bizarre myosin types. Pathological ‘cores’ were found in the diaphragm of one pt with ICM, with other minor histological changes and some staining of neonatal myosin. This study confirms the presence of widespread non-specific abnormalities of skeletal muscle in HF which are more prominent in respiratory than limb musculature. The involvement of the respiratory muscles is unlikely to be due to deconditioning and may contribute to the dyspnoea of HF. The marked changes in DCM suggest the coexistence of a generalised skeletal and cardiac myopathy.

IMPORTANT CONSIDERATIONS IN THE ASSESSMENT OF LVEF IN ORDER TO CORRECTLY ASSIGN PATIENTS WITH LV DYSFUNCTION TO ACEI THERAPY

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Several major studies have established that patients with a LVEF of <35-40% can benefit considerably from an ACEI. In these studies, LVEF was derived using radionuclide ventriculography (ERNVG). Whilst this method has notable advantages, it is felt to significantly overestimate the true LVEF in inferior MI (IMI) and possibly to underestimate it in anterior MI (aMI). This technique may therefore yield significantly different values to those obtained from a more global measure of LV performance, such as echocardiography. Importantly this could result in patients, with modest degrees of LV dysfunction, being assigned to the wrong therapeutic group.

In order to assess this problem, a study was performed of 15 patients with prior aMI (mean age 55), 15 patients with IMI (mean age 55) and 25 normal controls (C) (mean age 53). The LVEF obtained from conventional ERNVG was compared to that obtained using a tomographic ERNV technique. This latter technique was validated using a special dynamic phantom. All patients had their diagnosis confirmed by findings at cardiac catheterisation of a significant regional wall motion abnormality associated with either a blocked LAD or coronary artery, respectively.

With respect to planar imaging; for C the mean LVEF was 51% (range 32-69%, sd = 10), for patients with aMI the values were 29% (8-40%, sd = 10) and for patients with IMI, the values were 48% (35-66%, sd = 9). With respect to tomographic imaging the LVEF values were; C 54% (38-72%, sd = 9); aMI 22% (6-38%, sd = 9); and for IMI 38% (24-60%, sd = 10) respectively. There was a highly statistically significant difference between the two techniques for IMI (p<0.01) but no difference between C or aMI values.

These results confirm that there are clinically significant differences between methods of assessing LVEF. If not using a radionuclide method, caution should be employed when selecting patients for ACEI therapy in the presence of only an inferior wall motion abnormality.

THE EFFECT OF DIETARY CREATINE SUPPLEMENTATION ON SKELETAL MUSCLE METABOLISM IN CONGESTIVE HEART FAILURE

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Abnormalities of skeletal muscle metabolism are thought to be an important cause of symptoms and reduced exercise capability in congestive heart failure (CHF). These abnormalities are characterised by the early onset of anaerobic metabolism and metabolic acidosis during exercise. In normal volunteers, dietary creatine supplementation has been shown to delay the onset of skeletal muscle fatigue and is associated with an increase in muscle creatine and phosphocreatine content. We studied the effects of dietary creatine supplementation in CHF. 12 patients with CHF (NYHA Class II-III) undertook a study of forearm skeletal muscle metabolism, exercising using a handgrip dynamometer to 25%, 50% and 75% of their maximal voluntary contraction (MVC) or at a fixed workload of 7, 14 and 21kg. 30 isometric contractions were performed at each workload (5 seconds contraction and 5 seconds rest) for a total of 5 minutes. In addition, exercise to the point of voluntary exhaustion was performed at the highest exercise intensities. The venous concentrations of ammonia (a sensitive marker of ATP loss), lactate and oxygen in the exercising muscular bed were determined. After a baseline study, patients were randomised in a double blind design to either dietary creatine supplementation (3g daily for 5 days) or matching placebo. The basal study was repeated after 6 days. Creatine supplementation produced a significant reduction in plasma ammonia accumulation during the intense exercise at both fixed and % MVC workloads (p<0.05). Venous oxygen saturation post exercise was increased by dietary creatine in the fixed workload. There were no significant changes in lactate concentrations occurring either during or achieved during the exhaustive workload. These results suggest that dietary creatine supplementation can produce favourable changes in lactate utilisation in CHF. The effects of these changes on symptoms and exercise tolerance is unknown but further study is needed.

VERY LOW FREQUENCY PEAKS IN POWER SPECTRA OF RESPIRATORY, HEART RATE AND BLOOD PRESSURE IN CHRONIC HEART FAILURE

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Analysis of heart rate variability (HRV) reveals reductions in power in all areas of the spectra in patients with chronic heart failure (CHF). Correlations have been made between high frequency (HF) and vagal activity and low (LF) frequency peaks to both sympathetic and baroreceptor activation, while the importance of the very low frequency (VLF) component has been underestimated. In 13 patients with moderate CHF, (NYHA II/III) 45 mite recordings of R-R, respiratory and Finapres BP signals were analysed by power spectra analysis using an autoregressive model. Power components were assessed for VLF (<0.03Hz), LF (0.03-0.15Hz) and HF (0.18-0.30Hz) peaks. Comparisons were made between time and frequency domain measures and clinical parameters. Results showed that the reduction of HRV was largely due to loss of the LF and HF components with preservation of VLF power: VLF variability (1237 ms², range 186-3005 ms²) accounted for 66% (43-97%) of total HRV compared to mean LF 11% (213ms²) and HF 9% (178ms²). There was a close correlation between VLF power and total power (r=0.903, p<0.0001).The 3 patients with the lowest total HRV (<500 ms²) had the highest proportion of VLF power (76.3%). There were no clinical correlations. To explore the determinants of HRV in the VLF band we performed cross spectral analysis beat to beat between R-R interval, respiratory and blood pressure records. Significant coherence was found in the VLF band between RR interval and respiration, and in only one patient between RR interval and Blood pressure signals (p<0.05). Analysis of cross spectral coherence of 3 parameters studied. Our study suggests a more important contribution from VLF rhythms in the HRV of patients with CHF, which could be depicted by time and frequency domain recordings. This rhythm does not appear to be related to respiratory rhythms in these patients and only partly related to baroreceptor sensitivity.
ENHANCED PLATELET ACTIVATION IN VITRO IN REFRACTORY UNSTABLE ANGINA: INHIBITION BY GR144053, A FIBRINOGEN RECEPTOR ANTAGONIST

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GR144053 is an inhibitor of the binding of fibrinogen to GPIIb/IIIa on human activated platelets and therefore a broad spectrum inhibitor of platelet aggregation. Such an agent may have clinical utility in conditions associated with platelet activation such as unstable angina. We have therefore compared the potency of GR144053 for inhibiting platelet aggregation in whole blood in vitro from patients (n=11 per group) with refractory unstable angina (RUA), stable angina (SA) and from normal subjects (N). RUA was defined as rest angina within 48 hrs of assessment despite medical therapy which, at entry, was standardised to β-blockade, a calcium antagonist, aspirin and i.v. glyceryl trinitrate and heparin. SA patients were assessed on aspirin and their current antianginal therapy; N were drug free at assessment. Platelet aggregation to adenosine diphosphate (ADP) and the inhibitory potency of the GPIIb/IIIa antagonists GR144053 and echistatin against a single concentration of ADP (10μM) were studied in citrated whole blood, taken 24hrs after treatment standardisation, utilising a platelet counting method.

Results: Platelet sensitivity to ADP was significantly higher in the RUA group compared with N and SA, which did not differ from each other. Both GR144053 and echistatin abolished aggregation in all samples. Despite enhanced sensitivity of platelets to ADP in RUA, the inhibitory potency of GR144053 and echistatin did not differ significantly between RUA and N. In SA, GR144053 was significantly more potent compared with RUA but not N, no such difference was seen with echistatin.

Conclusion: Despite multiple drug therapy including aspirin, platelets from RUA patients were significantly more sensitive to aggregation in vitro than those from either SA patients or N. Despite this increased sensitivity, the inhibitory potency of the GPIIb/IIIa antagonist GR144053 was the same in RUA patients and N. Such a broad spectrum inhibitor of platelet aggregation may have clinical utility in RUA.

MYOCARDIAL ISCHAEMIA IN ASYMPTOMATIC TYPE I DIABETIC PATIENTS WITH AUTONOMIC NEUROPATHY

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The cause of the increased risk of sudden death in diabetic patients with autonomic neuropathy remains unknown. We therefore studied 40 type I diabetic patients (mean age 42, 20 male, 20 female) with Bruce protocol exercise echocardiography. All were asymptomatic and normotensive with normal creatinine clearance. Patients also had 3 autonomic function tests (AFTs): Valsalva heart rate ratio, maximum-minimum R-R interval variation, blood pressure response to standing) each graded as 0=normal, 0.5=equivocal and 1=normal. 8 patients (20%) had an ischaemic exercise test (positive for ECG and wall motion changes in ≥1, 4, ECG in 2, wall motion in ≥2). Comparing ischaemic patients with non-ischaemic significant factors were duration of diabetes and presence of autonomic dysfunction (mean AFT score 1.3 in ischaemics, 2.4 in non ischaemics, p<0.001) with ischaemic responses in 45% with AFT scores of ≤1.5 compared with 10% with scores of >2. There was also an trend for patients with microalbuminuria to have an ischaemic response. In conclusion there is a high prevalence of myocardial ischaemia in asymptomatic type 1 diabetic patients with normal creatinine clearance. This is particularly associated with abnormal autonomic function suggesting a likely aetiology for sudden death and we would recommend routine stress testing in this group.
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The effect of environmental influences, including insulin dependent diabetes (IDDM), on potential risk factors for ischaemic heart disease was studied using identical and non-identical twin pairs discordant for IDDM. The influence of diabetes on myocardial ischaemia and global systolic function was then assessed on the identical twin pairs. Four risk factors differed significantly between the diabetic and their non-diabetic identical co-twins (n=45): diabetic twins had higher (mean(SD)) systolic blood pressure (127 (17) vs 123 (18) mmHg; p<0.05), HDL cholesterol (1.36 (0.31) vs 1.25 (0.29) mmol/l, p<0.05) and fibrinogen (3.23 (0.81) vs 2.98 (0.71) mg/ml, p<0.05) but lower factor VII (114 (34) vs 122 (31)%, p<0.05). The estimated heritability of these four risk factors was low (≤40%) for each consistent with major environmental influences. Thirty nine of these identical twins underwent exercise treadmill electrocardiograms (ECGs) and simultaneous Doppler measurements of aortic blood flow to determine the presence of myocardial ischaemia and assess global left ventricular function. Electrocardiographic evidence of ischaemia was not correlated within twin pairs and was found in similar numbers of diabetic twins (23%), non-diabetic co-twins (18%) and control subjects (15%). QT-interval shortening on exercise was similar for the diabetic and non-diabetic co-twins. Doppler estimates of global left ventricular systolic function were significantly correlated within identical twins (r=0.49, p=0.001), with similar values for aortic acceleration (mean(SD)ms²/m) in the diabetic twins (56(15)), non diabetic co-twins (54(17)) and control subjects (53(17)). In a selected cohort of diabetic identical twins, without evidence of nephropathy, we have found minor changes in the clinical risk factor profile for myocardial ischaemia and were unable to detect any significant effect of diabetes per se on the prevalence of myocardial ischaemia or global left ventricular systolic function.

HYPERTRIGLYCERIDEREMIA IS AN INDEPENDENT PREDICTIVE FACTOR OF RAPID ANGIOGRAPHIC STENOSIS PROGRESSION
J C Kaski, L L Chen, M R Chester, D Tousoulis. St George’s Hospital Medical School, London.

Hypertriglyceridemia is associated with cardiac events and myocardial infarction (MI) and may therefore play a role in rapid coronary stenosis progression (SP). The association between fasting plasma triglycerides and SP was studied in 198 consecutive male patients (pts) with documented coronary artery disease (CAD). After diagnostic coronary angiography pts were placed on a routine waiting list for coronary angioplasty (PTCA) and underwent repeated catheterisation prior to PTCA within 20 months (9±5 months) of first angiogram. Stenosis progression (SP), which was assessed using computerised arteriography (CAAS), was defined as a >20% increase in severity in established lesions, a new lesion >30% in a previously normal area, or the development of total coronary occlusion. Fasting total cholesterol, triglyceride (TG), LDL and HDL cholesterol were assessed together with pts age, clinical presentation with stable or unstable angina, the time interval between angiograms, history of MI, number of diseased vessels, family history, smoking, hypertension and diabetes. During follow up, SP developed in 42 pts (21%). Acute coronary events (unstable angina or MI) occurred in 23 of the 42 pts with SP and in 22 of the 156 pts without SP (55% vs. 14%, p=0.0001). Univariate correlates of SP were: elevated triglyceride levels (mmol/l) (2.7 ± 1.5 vs. 2.1 ± 1.1, p = 0.0001), unstable angina at study entry (33% vs. 12%, p=0.0006), family history (24% vs. 10%, p=0.02), multivessel disease (78% vs. 59%, p = 0.02), and time interval between angiograms (10.0 ± 4.6 months vs 8.1 ± 5.0 months, p = 0.03). Multiple logistic regression analysis showed that elevated triglyceride levels (p = 0.022) and initial presentation with unstable angina (p=0.035) were independent predictors of SP.

This study used findings of recent epidemiological studies and shows that in CAD pts hypertriglycerideremia is a potent independent predictor of rapid angiographic stenosis progression.
(281) POSTER

PLATELET INHIBITORY EFFECT OF ENDOTHELIUM-DERIVED RELAXING FACTOR IN THE HUMAN CORONARY CIRCULATION

R F Ando, P Bresnahan, W Rakowski, S Yamasaki, A A Toole, National Heart, Lung and Blood Institute, Bethesda, Maryland, USA

The vascular effects of agents that release endothelium-derived relaxing factor (EDRF) from human coronary endothelium have been extensively studied. In animal studies these agents have been shown to have a platelet antiaggregatory effect by increasing platelet cyclic guanosine monophosphate (cGMP) content, in humans their effect on platelets is unclear. To investigate whether coronary endothelial dysfunction, as measured by depressed dilator response to acetylcholine (ACH) is associated with abnormal platelet response, we studied the change in blood flow and platelet cGMP content in response to intracoronary ACH in 11 patients without significant coronary atheroclerosis (<20% stenosis) undergoing cardiac catheterisation. During infusion of ACH (29 µg/min for 2 min) blood flow, derived from flow velocity (doppler flowwire, Cardiometrics, Inc.) and coronary diameter measurements, was measured and samples were drawn from the great cardiac vein for measurement of platelet cGMP content by radioimmunoassay. There was a transient increase in flow with ACH and a decrease in coronary vascular resistance by 50% (p<0.01). This was accompanied by a transient increase in platelet cGMP content (21±15 vs. 3±1) which returned to baseline after 10 min (p<0.005). There was also a significant negative correlation between the change in coronary resistance and the change in platelet cGMP content with r=-0.8 (p<0.01). Furthermore patients with depressed dilator response to ACH (endothelial dysfunction group) had a lower increase in platelet cGMP content compared to patients with good dilator response (normal endothelial group). Thus, luminal release of EDRF in the human coronary vasculature causes an increase in platelet cGMP level. Failure to increase cGMP, which correlates with an antiaggregatory effect, may explain why patients with endothelial dysfunction have increased susceptibility to thrombotic vascular events.

(282) POSTER

PHARMACOLOGICAL STRESS AGENTS FOR THALLIUM SCANNING: A COMPARISON OF DIPYRIDAMOLE AND DOBUTAMINE

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Dipyridamole has been successfully used as a stress agent for thallium scintigraphy, but its mechanism of action is unclear. Dipyridamole has a vasodilator effect that is thought to provide more physiological stress, and has been advocated as a superior agent. Stress and redistribution thallium scans were performed in 30 angina patients using both agents. The scans were scored giving a value for the stress and redistribution images and for reversibility. All patients had coronary angiography. Dipyridamole caused adverse symptoms in 6 patients, whereas dobutamine caused symptoms in 21 patients (p<0.001). Dipyridamole stress took considerably longer than the dipyridamole, 31 minutes vs. 4 minutes, and was more expensive, £16 vs. £0.56. There were no significant differences between the agents in total stress or redistribution scores, however, regional analysis showed that dipyridamole revealed significantly more defects during stress at the apex and the lateral walls (p<0.05), with no significant differences at redistribution.

Dipyridamole also caused significantly more reversible defects than dobutamine (p<0.05). Patients were considerably better tolerated than dobutamine when stress scores were compared with coronary scores, dipyridamole r=0.80 (p<0.001), vs. dobutamine r=0.54 (p<0.001). Six patients had continued on 6-blockers and in these dipyridamole failed to correlate with coronary score r=0.34 (p not significant), whereas dipyridamole-induced stress was not affected by EDRF from 6-blockers. In conclusion; Dipyridamole when compared with dobutamine for thallium stress scintigraphy: 1) is as effective in producing total perfusion defects; 2) is more effective in producing defects at the apex and lateral segments; 3) correlates better with coronary anatomy; 4) is not affected by β blocker therapy; 5) is better tolerated by the patients; 6) is less time consuming; and 7) is cheaper.

(283) POSTER

REGIONAL CORONARY BLOOD FLOW WAVEFORMS MEASURED WITH CONVENTIONAL BIPLANE X-RAY ANGIOGRAMS.

A M Seifalian1, R H Stables2, S Arnold3, J McNellis4, N Chronos5, N P Bullock5, D J Hawkes5-1 University Department of Surgery, Royal Free Hospital, North London Hospitals, London; 3Division of Radiological Sciences, Guy's Hospital, London.

We have developed a new method of measuring absolute blood flow using computer analysis of biplane digital x-ray angiogram images. We have applied this to measure flow in all major branches of the coronary circulation. The magnification factor and the 3-D orientation of a selected vessel are obtained after calibration of x-ray views with a saline. Instantaneous blood flow velocities are estimated from dynamic angiographic images by generating a parametric image in which the image grey-level represents contrast material concentration as a function of time and true distance along a vessel segment. Adjacent concentration-distance profiles in the parametric image are registered along the vessel axis until a match occurs. The distance translated per frame interval gives the instantaneous contrast material bolus velocity. These techniques were validated by measurement of pulsatile blood flow waveforms in a blood vessel phantom and comparison with the actual flow rate measured using an electromagnetic flowmeter (EMF). Measurements of pulsatile flow takes about 100 msec intervals in the phantom show close agreement (r=0.950; 123 instantaneous measurements, mean Diff=56±15 and mean flow=284±6 ml/min, 5 experiments) with simultaneous measurements using an EMF, a recording rate of 25 frames/second and tubes of 4.0 and 6.0 mm internal diameters. The technique has been applied to 6 patients undergoing coronary angiography for assessment of coronary stenosis. The blood flow waveforms of the right coronary arteries have been computed.

(284) POSTER

DOBUTAMINE STRESS TESTING WITH Tc-99m TEPHOSMINH HAS HIGH DIAGNOSTIC ACCURACY FOR DETECTION OF CORONARY HEART DISEASE

R Senior, S S Sridhara, U Ravil, S Basu, E Amangostu, E Duddic, J C W Crawley, P Clodd, A Lahiri, Northwick Park Hospital, Harrow, Middlesex.

Tc-99m tetrofosmin (Tc-T) is a lipophilic cationic di phosphine which has been shown to have high diagnostic value for detection of coronary artery disease (CAD) with standard exercise testing. Dobutamine (DOB) is now widely used as an alternative mode of stress for assessment of CAD. To evaluate Tc-T SPECT imaging during DOB stress 22 patients (pts) undergoing diagnostic coronary arteriography underwent stress testing with incremental doses of DOB (5-40mcg/kg/min) until maximum dose or target heart rate was achieved or pts developed angina, marked ST-changes, hypotension or hypertension. Imaging was performed within 15 minutes of peak dose followed by separate day rest imaging with Tc-T. A coronary artery lesion >50% was considered significant. Analysis was performed by two blinded observers for each modality. Tc-T detected all 20 pts with CAD and was normal in 2 pts without CAD. Tc-T identified 15 out of 20 (75%) left anterior descending artery (LAD) lesions and 16 out of 18 (94%) right coronary/LEFT circumflex artery (RC/LCX) lesions. Tc-T was also assessed in the myocardial segments supplied by normal arteries: 2 LAD and 4 RC/LCX arteries were normal, and Tc-T detected both the LAD and 3 out of 4 RC/LCX arteries as being normal. Tc-T had excellent image quality and high diagnostic accuracy for detection of CAD using DOB stress. Further study is required to better characterise the value of this modality.
CLINICAL ASSESSMENT OF ‘CARDIOPROTECTION’ AS A PROGNOSTIC GUIDE TO THE MANAGEMENT OF CORONARY ARTERY DISEASE

R Lim, L Dyke, D S Dymond
Dept of Cardiology, St Bartholomew’s Hospital, London EC1

The left ventricular ejection fraction (LVEF) response to exercise is of fundamental prognostic importance in coronary artery disease (CAD). Can its modification by conventional anti-ischaemic medication (Rx) allow objective assessment of ‘cardioprotection’ from adverse prognosis? Exercise LVEF and \( \triangle \)LVEF (from rest to exercise) were measured by radionuclide ventriculography (RNV) both off and on background Rx (mean age 55; range 31 - 73 years) with revascularisable CAD, for whom continuing medical treatment or early revascularisation were considered to be equally justifiable therapeutic options. Over 20 months, 23 patients had experienced an adverse cardiac event. On Rx, exercise LVEF increased significantly in both groups with and without events. But contrast, \( \triangle \)LVEF improved significantly (\(+6\%\), \( P=0.000\); \( 95\% \) CI = 4 to 9) only in the event-free group who showed a mean rise of \( 2\% \) in LVEF, whereas the group with adverse events showed a persistent exercise-induced fall of \( 8\% \). Kaplan-Meier event-free survival was significantly different between the two groups stratified by the best cut-off point on the ROC curve for each of the prognostic RNV indices. Comparing areas under the ROC curves, \( \triangle \)LVEF on Rx (AUC = 0.75) provided the best discrimination between the event-free group and the group with events, suggesting that \( \triangle \)LVEF is the most useful clinical measure of ‘cardioprotection’ from an adverse cardiac prognosis. In conclusion: An exercise-induced fall in LVEF despite Rx implies ‘failure of cardioprotection’, a greater short-term risk of adverse outcome and need for revascularisation in patients with CAD initially treated medically. Conversely, an improved or preserved left ventricular performance during exercise on Rx confers a satisfactory prognosis whilst continuing with that treatment. Thus, for patients in whom medical treatment or revascularisation seem equally justifiable, the effect of Rx on \( \triangle \)LVEF (or \( \triangle \)LVEF) with symptomatic coronary artery disease (CAD) was studied. Patients had single vessel disease with \( \geq 50\% \) diameter stenoses. All patients developed typical angina with ischaemic changes on the stress electrocardiogram and none was diabetic or had any systemic disease. Angina was induced using intravenous dobutamine (Dob), an inotrope which does not cross the blood-brain barrier. The sequence of \( \text{RCBF} \) measurements was: 1) Baseline (B); 2) Intravenous placebo infusion. III - B2; IV - During low dose Dob infusion (5 \( \mu \)g/kg/min for 3 min and 10 \( \mu \)g/kg/min for 3 min, continued throughout the scan acquisition). This infusion was used to control for possible non-specific effects of Dob on \( \text{RCBF} \); 3) During angina induced by high dose Dob (20 \( \mu \)g/kg/min to 35 \( \mu \)g/kg/min, continued throughout the scan acquisition); IV: B3. PET images were transformed into a standard stereotactic space and \( \text{RCBF} \) compared across conditions by Statistical Parametric Mapping. During angina, \( \text{RCBF} \) was significantly increased in the periaquaductal grey and bilaterally in the thalamus and basal and prefrontal cortex. Significant reduction in \( \text{RCBF} \) was mainly observed in the dorsal cingulate cortex. There were no differences in \( \text{RCBF} \) between placebo and B or between low dose Dob and B. Compared to the angina scan, B3 showed thalamic but not cortical \( \text{RCBF} \) to remain increased. We hypothesize that the thalamus may act as a gate to afferent pain signals, with cortical activation being necessary for the sensation of pain. This is the first direct demonstration of the central neural activation associated with episodic anginal pain and forms a basis for further research into abnormalities of visceral pain perception such as silent myocardial ischaemia.

THE NATURAL HISTORY OF CLINICALLY STABLE CORONARY ARTERY DISEASE COMMONLY INTERRUPTED BY THROMBOTIC PLAQUE EVENTS

MR Chester, J Mann, L Chen, W Pereira\(^1\), F Fileggi\(^1\), J Poloniene\(^1\), DE Ward, M DeBelder, M Davies & JC Kaski
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There is general agreement that early coronary atherosclerotic plaque develops by an inflammatory response to progressive intimal lipid deposition. It is also accepted that the development of acute coronary syndromes follows plaque rupture with thrombosis leading to rapid stenosis progression. However, whether the mode of disease progression between these processes is gradual and linear or whether coronary artery disease progression involves subclinical episodic plaque events is not known. Post mortem studies indicate that subclinical thrombotic plaque events may not be uncommon but the data is necessarily limited by the lack of reliable history. We have previously reported preliminary data showing that thrombus may complicate clinically stable plaques.

Patients & Methods. We examined atherectomy specimens from 57 consecutive patients undergoing atherectomy for symptomatic coronary artery disease for evidence of previous plaque events. Patients were carefully questioned by 2 interviewers on 2 separate occasions. Thirty-five patients had chronic stable angina and had no previous episodes of unstable angina nor unexpected change in anginal threshold and the remaining 22 patients had at least one episode of unstable angina. All patients were receiving aspirin at the time of the atherectomy but not oral anticoagulants. Specimens were analysed (MD & JM) blind to the clinical data.

Results. Thrombus was seen in 10 (45\%) specimens from patients with unstable angina and in 7 (20\%) of the clinically stable patients. There were no differences between the presence of cholesterol, calcium or internal elastic lamina nor stenosis severity or morphological appearance (using edge detection analysis) between lesions from patients with stable and unstable angina.

Discussion. The inability of the atherectomy device to extract the entire lesion may only explain presence of thrombus in only 45\% of lesions from unstable patients. The presence of thrombus in 20\% patients with clinically stable disease is highly significant and shows that the naturally stable coronary stenosis may have been interrupted by at least one silent thrombotic plaque event. This is consistent with the hypothesis that episodic plaque rupture and thrombosis plays a role in subclinical stenosis progression.

A CHANGING PATTERN OF CAUSE OF DEATH IN MYOCARDIAL INFARCTION: THROMBOLYSIS ALONE MAY NOT PREVENT VENTRICULAR RUPTURE

Nigel Stephens MC Petch PH Schofield LM Shapiro PI Weissberg Addisonbrooke’s Hospital, Hills Road, Cambridge, UK

An important issue in the management of myocardial infarction (MI) is whether the outcome of a strikingly low mortality rate associated with thrombolysis in randomised trials is confered on the unscheduled population treated in the coronary care unit. There is also a scarcity of data about the actual causes of early death in MI managed with modern strategies, including thrombolysis. We have therefore studied the management of 810 consecutive patients (pts) with acute MI, and the clinical course and autopsy data of 78 of the 119 that died in the first 24 hours. The most striking feature of the series is the high 24 hour mortality rate (15\% of 3 - 4\% in most studies). 39 (50\%) did not receive thrombolysis: in 6 this was for conventional contraindications and in the remainder because the patients were judged too ill or because there was not enough time to administer the drug before cardiac arrest. No patient received IV \( \beta \) blockade. Although age has been judged to be one of the most adverse prognostic factors in MI, the age of those dying did not differ significantly from the MI population as a whole (mean \( \pm \) sd: 74 \( \pm \) 8 yrs vs 70 \( \pm \) 4). Cardiac rupture was seen in 21/78 patients (27\%). The other definite or probable causes of death were: cardiogenic shock/massive ventricular dilatation (3\%), VT/FVF (25\%), myocardial infarction (10\%), stroke: 4 (5\%) and non-cardiac: 5 (7\%). A notable feature in this study is the high frequency of early ventricular rupture. This may be caused in part by reluctance to give IV \( \beta \) blockade in combination with already complex treatment regimens. By contrast, the mortality of dystrophic myocardial necrosis that thrombolysis may well treat the propensity to malignant VT or VF in MI. The majority of those that died of this [9/15] had not received thrombolysis.
REDUCED MORTALITY ASSOCIATED WITH FASTER INITIATION OF THROMBOLYSIS FOR PATIENTS WITH ACUTE MYOCARDIAL INFARCTION TREATED IN THE ACCIDENT AND EMERGENCY DEPARTMENT P A Greenhalgh, P J Thirwall, M A Orchard*, J C Cowan, C M Friend, J A Davies* Dept of Cardiology, The General Infirmary at Leeds and School of Medicine, The University of Leeds

To assess the initial management of patients with chest pain in 21 acute hospitals in the North West Thames Regional Health Authority we designed a questionnaire to be completed for all such cases considered for admission. Over six months 1343 were returned. 942 patients (70%) were male. Mean age was 66.16 years. Thrombolysis was given to 412 (46%) of 460 patients diagnosed as definite acute myocardial infarction (AMI), 167 (48%) of 345 diagnosed as possible AMI, 16 (6%) of 262 diagnosed as unstable angina and 5 (4.5%) of 110 diagnosed as other ischaemic chest pain. Non-cardiac chest pain was diagnosed in 119 patients. The diagnosis was not specified in 15. In-hospital mortality was 40/418 (9.6%) for patients with a subsequently confirmed AMI who had received thrombolysis vs 16/101 (15.8%) among those who had not (odds reduction: 44%). Mortality was 12/115 (7.7%) for patients with a subsequently confirmed AMI who had received thrombolysis in the Accident and Emergency department vs 28/214 (13.6%) among those who had received thrombolysis in the cardiac care unit (CCU) (odds reduction: 36%). The median time (and 75th percentile) to thrombolysis for those treated in the Accident and Emergency Department was 60 min (90 min) compared with 100 min (175) for those treated in the CCU. We conclude that more rapid administration of thrombolysis, can save an additional 4 lives per 100 patients treated. Reductions in mortality may be expected if either patients with suspected AMI were assessed and treated immediately on arrival in the Accident and Emergency department or they were directly admitted to the CCU for rapid assessment and treatment.

ACTIVATION OF HEMOSTATIC MECHANISMS AND STABILITY OF REPERFUSION FOLLOWING STENOTOMIES IN ACUTE MYOCARDIAL INFARCTION J L Morris, A G Zaman, M A Orchard*, J C Cowan, C M Friend, J A Davies* Dept of Cardiology, The General Infirmary at Leeds and School of Medicine, The University of Leeds

Early reperfusion of the acutely occluded coronary artery preserves myocardium and ventricular function after MI. Thrombolytic therapy is effective in accelerating reperfusion and improving mortality but there remains a proportion of patients in whom patency is not achieved or in whom early reperfusion is not obtained. Coronary thrombosis, if left untreated, makes thrombolytic therapy lead to considerable activation of the haemostatic mechanisms which may contribute to the failure rate of therapy. We studied 8-Thromboglobulin (8TG), thrombin-antithrombin III complex (TAT), fibrinogen/fibrinopeptide A (FFA) and D-Dimer (DD) levels in 29 patients receiving streptokinase, 1.8MU and aspirin, 300mg, for acute MI. Samples were taken immediately before and after thrombolytic therapy, after 3 hours and after 18-24 hours. Infarct artery patency was assessed using continuous 12-lead ST-segment monitoring. Platelet, thrombin and fibrinolytic activity were significantly increased following MI and streptokinase therapy. Patients were divided into 3 groups according to the pattern of ST resolution. Group 1 (n=15) showed rapid ST resolution with no evidence of re-escalation. Group 2 (n=13) showed ST resolution with at least one episode of re-escalation. Group 3 (n=4) showed persistent ST elevation. Results for samples taken immediately after thrombolysis are presented below (Median & Interquartile Range)

<table>
<thead>
<tr>
<th>Group</th>
<th>STG (IU/ml)</th>
<th>TAT (ng/ml)</th>
<th>FFA (ng/ml)</th>
<th>DD (mg/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>10-40</td>
<td>1.0-4.1</td>
<td>0.35</td>
<td>1.0-40</td>
</tr>
<tr>
<td>Op 1</td>
<td>53 (52-69)</td>
<td>38 (16-23)</td>
<td>2B (19-50)</td>
<td>1.4 (1.0-1.6)</td>
</tr>
<tr>
<td>Op 2</td>
<td>60 (38-289)</td>
<td>34 (19-120)</td>
<td>50 (22-120)</td>
<td>1.9 (1.4-2.2)</td>
</tr>
<tr>
<td>Op 3</td>
<td>110 (100-150)</td>
<td>33 (23-53)</td>
<td>45 (38-50)</td>
<td>1.7 (2.0-5.4)</td>
</tr>
<tr>
<td>p</td>
<td>&lt; 0.01</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.01</td>
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</table>

Patients demonstrating unobtainable reperfusion show a greater degree of thrombin generation than those with stable reperfusion. More aggressive anti-thrombotic and fibrinolytic therapy in this group may be of benefit.

EFFECT OF MODIFICATION OF THE CYCLOOXYGENASE PATHWAY ON PLASMA-MEDIATED STIMULATION OF NEUTROPHIL CD18 ADHESION MOLECULE EXPRESSION DURING REPERFUSION T Siminiak, D Fuck, J D Turner, J J Sheridan Academic Cardiology and (*) Surgery Units, St Mary's Hospital Medical School, London

Adhesion of polymorphonuclear neutrophils (PMN) to endothelial cells during reperfusion may contribute to the no-reflow phenomenon and PMN-mediated myocardial injury. During reperfusion PMN adhesion is known to be mediated by the integrin family of adhesion molecules. Increased expression of integrins may be a result of increased expression of ICAM-1, their counter-receptor on endothelial cells and/or of PMN activation by soluble stimuli released from reperfused myocardium. The purpose of the present study was to verify whether peripheral plasma contains factors capable of stimulating neutrophil integrin expression and whether treatment, which modifies the cyclooxygenase pathway, may affect this plasma-mediated neutrophil occlusion. To investigate this rabbits underwent 40% of coronary occlusion followed by 90° of reperfusion. Animals were treated with saline (n=6), Tx receptor antagonist GR3219B (1mg/kg, n=6), Tx synthetase inhibitor UK38485 (5mg/kg, n=6) or aspirin (50mg/kg, n=6).

Plasma samples were taken pre-treatment and at 30 and 90° after reperfusion and incubated (10min.37°C) with wash-purified PMN obtained from control rabbits. The expression of CD18 antigen, the common β chain of PMN integrins was measured by flow cytometry with the use of specific monoclonal antibodies. Data are expressed as percent of CD18 expression by PMN incubated with plasma taken before occlusion (=0.05): saline GR3219B UK38485 Aspirin 30min. 103±1.3% 87±2.5%* 92±4.4% 98±5.6% 45% 90min. 106.7±1.5%* 85.7±3.0%* 98±3.1% 101.6±1.3% Conclusion: 1) during myocardial reperfusion plasma contains factors capable of stimulating neutrophil integrin expression, 2) treatment with UK38485 or with aspirin prevents such stimulatory effect while treatment with GR3219B even attenuates PMN CD18 expression.

THE SIGNAL-AVERAGED ELECTROCARDIOGRAM AFTER THROMBOLYSIS FOR ACUTE MYOCARDIAL INFARCTION J L Morris, A G Zaman, J C Cowan Department of Cardiology, The General Infirmary at Leeds

The significance and natural history of late potentials after acute myocardial infarction (AMI) may differ in the thrombolytic era. We studied 239 patients undergoing thrombolysis for suspected AMI. Signal-averaged ECG (SAECG) was performed according to established guidelines within 24 hours of admission, on the 3rd and 7th day of admission and after 6 weeks and 6 months. Reperfusion was assessed non-invasively by continuous 12-lead ST-segment monitoring with the criteria for successful early reperfusion of 50% resolution within 90 minutes of thrombolytic therapy. The incidence of LP rose from 22% to 33% during the first week and declined thereafter to 22%. Successful reperfusion occurred in 68% of patients. Failure of reperfusion was associated with a significantly greater incidence of LP during the first week. Thereafter early reperfusion status did not influence the incidence of LP.
CONSECUTIVE PATIENTS AGED 55 YEARS OR LESS WITH MYOCARDIAL INFARCTION (MI) BEFORE ROUTINE THROMBOLYSIS: OUTCOME AT 7 YEARS AND BEYOND. JS Skinner, C Albers, JIC Hall, PC Adams Royal Victoria Infirmary, Newcastle upon Tyne.

We studied outcome 7 years and more after MI in patients aged 55 or less at the time of presentation. From October, 1961 to March, 1985, 255 patients 55 years or less were admitted to a single CCU acutely after MI and considered for early exercise test and angiography. 105 were excluded: 24 had other serious illnesses, 13 other cardiac conditions, 14 refused, 30 excluded for administrative reasons, 24 died before exercise. 150 were followed for more than 7 years after MI, with complete follow-up to 7 years. Of these, 60 (40%) had anterior and 82 (55%) inferior MI. In 31.5% of site MI could not be determined. In 111 (78%) Q waves developed. Patients with inferior MI were younger than those with anterior MI (46.9 versus 50.0 years, p<0.01) and patients with non-Q wave MI had more previous MI (13% versus 3%, p<0.05) and less 3 vessel disease (none versus 13%, p<0.001) than those with Q waves. Baseline clinical and angiographic variables did not otherwise differ between these groups.

By seven years after MI, 10 (7%) patients had died (9 from a cardiac cause). 16 (11%) had suffered a further non-fatal MI, 38 (27%) had required coronary artery surgery (24 within the first 18 months, all for angioplasty, except one patient with left main stenosis). At seven years, 65 (51%) 14 not recorded) reported angina. Neither site of infarct nor Q wave status had a significant effect on outcome.

At latest follow-up (maximum 12 years), 29 (21%) patients who exercised had died. 26 from a cardiac cause. 1 has undergone cardiac transplantation. The mortality of the 88 patients excluded is higher (current status alive in 51 of 65 (76%) versus 27 (31%) has died, 12 (19%) by 7 years (compared with 10% of the patients exercised). Annual mortality decreased substantially after 7 years: between 7-8.9 years, 10/103 (5%) per annum; 9.0-9.9 years, 7/80 (9%) per annum. Except without thrombolytics, young patients who can exercise on the treadmill 3 months after MI have a favourable survival to 7 years with a 9.5% annual mortality. Neither Q wave status nor infarct site are predictive of outcome. There is a substantial acceleration in mortality after 7 years and after infarction a repeat.

SIGNIFICANCE OF TIMI GRADE FLOW IN DETERMINING THE PATENCY OF THE INFARCT-RELATED ARTERY AND ITS RELATION TO CLINICAL OUTCOME. F Fath-Ordoubadi, TY Huebner, KJ Rebert. Academic Unit of Cardiovascular Medicine, Chelsea and Westminster Hospital, London.

Conventionally, infarct-related arteries (IRA) with TIMI grade flow of 0 and 1 have been considered as occluded and those with TIMI grade of 2 or 3 as patent. This view has been challenged in several recent post myocaridal infarction (MI), post thrombolysis, angiographic studies indicating different clinical outcome in patients with TIMI grade 2 flow compared to TIMI grade 3. To determine the validity of this concept we pooled the results of 13 different studies involving 3601 patients following MI where early TIMI grade flow and mortality (up to 30 days post MI) were recorded.

<table>
<thead>
<tr>
<th>No</th>
<th>mortality</th>
<th>n (%)</th>
<th>p value</th>
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<tbody>
<tr>
<td>TIMI 0-1</td>
<td>TIMI 2</td>
<td>TIMI 3</td>
<td></td>
</tr>
<tr>
<td>TAMI 1-7</td>
<td>1229</td>
<td>34 (10.1)</td>
<td>13 (6.1)</td>
</tr>
<tr>
<td>Team 3</td>
<td>298</td>
<td>2 (5.0)</td>
<td>2 (5.0)</td>
</tr>
<tr>
<td>Vogt **</td>
<td>907</td>
<td>16 (7.1)</td>
<td>8 (6.6)</td>
</tr>
<tr>
<td>GUSTO</td>
<td>1167</td>
<td>34 (8.9)</td>
<td>25 (7.4)</td>
</tr>
<tr>
<td>Pool (1)</td>
<td>3601</td>
<td>8.9 **</td>
<td>6.8 **</td>
</tr>
</tbody>
</table>

* TAMI results represent a composite of results from TAMI 1 to 7 trials and ** Vogt et al a composite of four different German trials. ***TIMI 0-1 Vis TIMI 2, p=0.2

Conclusion: The pooled data confirms that following thrombolysis the outcome of patients with TIMI grade 2 flow IRA is similar to those with TIMI grade 0 or 1. Therefore IRAs with TIMI grade 2 flow, by-and-large, should be considered occluded rather than patent. TIMI grade 3 flow is associated with 46% reduction in mortality compared to TIMI 2 flow. In order to improve mortality post MI, it is important that new thrombolytic strategies aim to achieve early complete (TIMI grade 3 flow) IRA patency.
(297) POSTER

ST ELEVATION AS A MARKER OF PROGNOSIS IN ACUTE MYOCARDIAL INFARCTION
K Laji, K Ranjadayal, P Wilkinson, AD Timmis
London Chest and Newham General Hospitals

There is considerable interest in management strategies that should be applied in acute myocardial infarction when the electrocardiogram (ECG) is nondiagnostic. Since 1988, we have recorded clinical characteristics of all patients admitted to our coronary care unit with acute myocardial infarction. Follow-up of the first 825 of them indicates that regional ST elevation of ≥2 mm on any 12 lead ECG recorded during the admission is an important marker of prognosis. In patients without ST elevation (n = 552), 0.7% of a major event (unstable angina, recurrent infarction, death) was 5.8% (2.2-14.7%) at 30 days and 13.8% (7.4-24.9%) at 6 months, compared with 19.2% (16.6-22.3%) and 28.3% (25.1-31.8%) in those with ST elevation (p = 0.01). The better prognosis in patients without ST elevation is partly attributable to the fact that a smaller proportion developed heart failure (12.9 vs 30.4%, p = 0.002). However, after adjustment for age, sex, previous infarction, treatment with thrombolysis and/or aspirin, and heart failure, their event-free survival was still significantly better, as reflected by an adjusted hazard ratio of 2.96 (1.07-8.16). Importantly, event-free survival in patients without ST elevation who did not receive thrombolysis was similar to that of patients with ST elevation who did receive thrombolysis: 92.6% (76.6-97.9%) in 30 days and 76.1% (65.0-88.6%). Although these data are based on observational work, they are consistent with randomised trials which have recorded low mortality and little apparent benefit from thrombolysis in patients with nondiagnostic ECGs. Spontaneous dissolution of an occluding thrombus is one possible explanation of both the lack of ST elevation in patients with enzymatically confirmed infarction and their good prognosis. ST change alone may be an important early indicator of the need for thrombolysis.

(298) POSTER

PROGNOSTIC VALUE OF HOLTER MONITORING, SIGNAL AVERAGED ELECTROCARDIOGRAMS AND EXERCISE STRESS TESTING FOR EARLY RISK STRATIFICATION AFTER ACUTE MYOCARDIAL INFARCTION
A Cheng, D Shani, R Greenbaum
Cardiovascular Research Unit, Edgware General Hospital, Edgware.

We prospectively studied the prognostic significance of transient ST-segment depression on Holter monitoring (TSTD), ventricular late potentials (VLP) and ST-segment depression on exercise stress testing (ETT) following acute myocardial infarction (AMI). 100 patients (pts) (mean age 60±10 years) with AMI underwent 24 hours of Holter monitoring and signal averaged electrocardiograms immediately after admission to the Cardiac Care Unit and submaximal ETT before hospital discharge. Over the subsequent 6 months, cardiac complications (death, non-fatal reinfarction, unstable angina, postinfarction angina, left ventricular failure, ventricular tachycardia) developed in 52 patients. These occurred in 14 (33%) of 42 pts in whom all tests were normal, 14 (47%) of 30 pts in whom 1 test was abnormal, 17 (81%) of 21 pts in whom 2 tests were abnormal and 7 (100%) of 7 pts in whom all 3 tests were abnormal (p<0.01), with relative risks of 1.0, 1.4, 2.4 and 3.0 respectively. The complication free survival of pts over the 6 months follow-up is shown in the figure.

We conclude that patients with a greater number of abnormal test were at higher risk of cardiac complications in the 6 months following acute myocardial infarction, most of which occurred in the first 2 months after infarction.

(299) POSTER

THE RELATIVE SAVING-OF-LIFE BY RESUSCITATION AND THROMBOLYSIS IN ACUTE MYOCARDIAL INFARCTION
R Trent, J Rawles, R Jameson, J Adams, K Jennings, Cardiac Department, Aberdeen Royal Infirmary, and Medicines Assessment Research Unit, University of Aberdeen

The relative saving-of-life by resuscitation and thrombolysis has been estimated for patients with acute myocardial infarction (AMI) treated in hospital, and prehospital. All patients admitted to Aberdeen Royal Infirmary with a final diagnosis of AMI in 1990 and 1992, and all patients entered into the Grampian Region Early Anistreplase Trial (GREAT) were studied. Use of thrombolysis, incidence of cardiac arrest, and survival to discharge were noted.

Cardiac arrest occurred in 250 (16%) of 1516 patients with AMI admitted to hospital. Of these, 77 (30%) were discharged alive, representing 51 lives saved per thousand AMIs. Thrombolysis was given to 797 (53%), of whom 114 (14%) died. Assuming the same relative reduction of mortality as in ISIS-2 (23%), 34 lives were saved by thrombolysis, representing 22 per thousand AMIs.

Of 311 patients entered into GREAT, 15% (5%) had cardiac arrest prehospital. Of these, 7 (47%) were discharged alive, representing 23 lives saved per thousand AMIs. The one month mortality rates were 11/163 (6.7%) and 18/148 (12.2%) for patients given thrombolysis at home or in hospital, a saving-of-life of 55 per thousand by prehospital thrombolysis. This is additional to 28 per thousand estimated from ISIS-2 for thrombolysis in hospital, totalling 83 lives saved per thousand AMIs.

Conclusions: In hospital, between 2 and 3 times as many lives are saved by resuscitation as by thrombolysis, but this ratio is reversed in the period before admission to hospital. These results underline the paramount importance of resuscitation in hospital, and the enhanced efficacy of thrombolysis prehospital.

(300) POSTER

THE CAUSATIVE RHYTHM IN OUT OF HOSPITAL CARDIAC ARRESTS WITNESSED BY THE EMERGENCY MEDICAL SERVICES IN THE HEARTSTART SCOTLAND PROJECT
ML Sedgewick, Kirsty Dalziel, J Watson, DJ Carrington, SM Cobbe. Department of Medical Cardiology, Royal Infirmary, Glasgow. *National Training Centre, Scottish Ambulance Service, Glasgow

Out of hospital defibrillation has been shown to improve survival in out of hospital cardiac arrests. The maximum performance of defibrillation based systems is dependent on the proportion of cardiac arrests due to tachyarrhythmias. We reviewed 4248 reported arrests in the Heartstart Scotland database. We identified 3489 arrests due to cardiac or unknown cause. From this group we selected 258 cases known to be conscious on arrival of the crew. We were able to retrieve electrocardiographic data on the period within 2 minutes of the arrest in 106 cases. The first recorded rhythm at the arrest was ventricular fibrillation in 64%, ventricular tachycardia 4%, bradycardia in 28% and electromechanical dissociation in 4%. Defibrillatory shocks were delivered to 96% of patients in ventricular fibrillation and 60% of these patients survived. None of the patients with bradydysrhythmic arrests survived. Preceding chest pain was noted in 79% of patients subsequently developing ventricular fibrillation as the cause of arrest compared to only 37% of those suffering bradydysrhythmic arrests. It would appear that the public awareness of the importance of early contact with the emergency services after the onset of chest pain could substantially improve the survival from out of hospital arrests.
LONG-TERM RESULTS OF OUT-OF-HOSPITAL RESUSCITATION BY AMBULANCE STAFF IN WEST YORKSHIRE
P D Batin, M Ryder, J Bannister, A F Mackintosh. St James's University Hospital, Leeds.

We studied the long-term follow-up of patients (n=2102) who suffered an out-of-hospital cardiac arrest and attempted resuscitation by ambulance staff, both paramedics and ambulance technicians, in West Yorkshire from January 1987 to June 1992. Nine hundred and ten (43%) patients were found in ventricular fibrillation/systole (VF/VT) and 1192 in asystole. Two hundred and fifty six (12%) patients were admitted, 102 (11%) of patients in VF/VT of whom were subsequently discharged. Some additional resuscitations were not recorded in a 10 month period in 1989-90 due to industrial action. The long-term results of the 102 patients (mean age 61.0, SD 11.8, range 18-89) are presented in this study. One year survival was 89% and the 2 year survival 78%. Sixty-four (63%) patients survived the first year without another cardiac related admission. Functional capacity assessed by overall performance categories (OPC) were determined in 89 of the 91 survivors at year one. Eighty-five percent were in OPC class I (capable of normal life with only mild functional (non-cerebral) disability) and only 2% in OPC class III or IV (severe disability being dependent on others for daily support). Patients were subdivided into those aged 65 or under (n=62) and those over 65 (n=40).

First and second year survival rates were higher in those patients aged 65 or under (92% and 78%) compared with the older patients (85 and 61%). Subsequent cardiac related admissions in the first year were higher in the patients aged 65 or under (29%) compared with the older patients (18%). Although the number of patients who survived out-of-hospital resuscitation was relatively small, they did well thereafter. Persistent severe cardiac impairment was rare and concern about it should not inhibit attempted resuscitation by ambulance staff.

IS CAROTID SINUS HYPERSENSITIVITY MASQUERADING AS EPILEPSY?
WA McCrea, LJ Findley, RJ Wainwright.
Queen Elizabeth Hospital, Woolwich, London SE18 4QH &*Cardiac Department, King's College Hospital, Denmark Hill, London SE5 9RS.

Carotid sinus hypersensitivity may present as epilepsy and unless carotid sinus massage is performed, a cardiac cause for transient alteration of consciousness may be missed. We investigated the responses to carotid sinus massage in 46 patients (mean age +/- SD, 39.4 +/- 12.9 years) who had been referred to a neurology clinic for assessment and treatment of epilepsy. Twenty-four hour ambulatory electrocardiography and electroencephalography, computerised tomography of skull and clinical examination had failed to suggest either a neurological or a cardiological cause for their symptoms. However, prior to neurological referral, none had undergone carotid sinus massage. A standard electrocardiogram demonstrated unexplained sinus bradycardia in 21 (46%) of these 46 patients. Carotid sinus hypersensitivity was demonstrable in 9 patients (43%) with sinus bradycardia compared to 2 patients (8%) in the non-bradycardia group (p<0.01). A carotid sinus response (i.e. asystole > 3 seconds) was demonstrable in 10 (8 with bradycardia) patients and one patient (with bradycardia) exhibited a purely vasodepressor response (i.e. fall in systolic blood pressure >30mmHg). Atropine (0.6-1mg) abolished the cardioinhibitory response in all 10 cases. In the 8 patients with bradycardia and cardioinhibitory response, atropine also produced an increase in mean (-/+/ SD) resting heart rate from 51 (+/-7) to 68 (+/-5)min (mean increase 33%) thereby making symptomatic sinus node dysfunction an unlikely diagnosis in these individuals. We conclude that patients with suspected epilepsy, particularly those with sinus bradycardia, should undergo carotid sinus assessment as a routine investigation.

EARLY EXPERIENCE WITH SINGLE PASS LEAD VDDR PACING SYSTEMS
T Edwards, D Rowley, JM Morgan, KD Dawkins. Wessex Cardiac Unit, Southend.

Single pass lead VDDR pacing systems have been implanted in 20 pts, 10 using a Viatron Saphir VDDR generator with an IMP15Q lead, and 10 with a Medtronic Thera VDR generator with a Capure VDR Modal 3032 lead. Both leads had a total length of 58 cms, with a distance of 13.5 cms from atrial to ventricular tip. Average age of the group was 68.7 +/- 7.0 yrs. Indications for pacing were persistent CHB (11), intermitent CHB (6), Mobits Type II 2* HB (3). Venous access was by means of the cephalic vein in 14 pts and the subclavian vein in 6 pts. In no pts were there any significant problems with lead manipulation at the time of implantation. Average fluoroscopy time was 4.15 +/- 1.92 mins. Implantation was considered easier than implantation of a dual chamber system in all patients. Position of the atrial biopsy was mid/high anterolateral RA in 17pts and low RA in 3 pts. The VA distance of the 'standard' lead was felt to be appropriate in 14 pts, 1-2 cms too long in 5 pts, and 1-2 cms too short in 1 pt. Measurement of P wave amplitude in the Saphir group was 0.89 +/- 0.44 mV (min) and 1.97 +/- 0.82 mV (max) (baseline to peak), and in the Thera group 1.42 +/- 0.44 mV (min) and 3.51 +/- 0.82 mV (max) (peak to peak). Minimum acceptable amplitudes at implant were satisfied in all pts. The percentage AV synchrony measured by 24 hr holter monitor was 92-100% in all but one patient. In this pt AV synchrony occurred for 42% of beats due to a resting atrial rate below the lower programmed rate of the pacemaker; there was no loss of atrial sensing. Sinus node disease had not been apparent prior to implantation.

In conclusion, early results from two VDDR single pass lead pacing systems indicate ease of implantation, satisfactory atrial sensing and a high degree of AV synchrony suggesting a satisfactory alternative to dual chamber two wire systems in pts without chronotropic incompetence.
(305) POSTER
CHARACTERISTICS OF REAL TIME AND STORED ENDOCARDIAL ELECTROGRAMS LEADING TO THERAPY IN PATIENTS WITH IMPLANTABLE CARDIOVERTER DEFIBRILLATORS.
R.Cudlin, P.Broadhurst, V.Vassiliou, A.W.Nathan
Department of Cardiology, St Bartholomew's Hospital, London
The latest generation of implantable cardioverter-defibrillator (ICD) provides endocardial electrograms (EE) to determine the type preceding the delivered therapy and the restored rhythm. The value of signals is not yet entirely established. We have analysed the real time and stored EE in 22 patients (pts) receiving an ICD for drug refractory malignant ventricular tachycardia and/or fibrillation (VT/VF). Follow-up 1-42 months. During the follow-up a total number of 51 shocks were classified as adequate discharges for VT/VF in 13/22 pts with the following EE characteristics: all EE showed a sudden onset of different signal regarding real time morphology with a significant marker but regular RR interval. The very first 3-5 beats often had slightly variable RR intervals and in more than 1/3 of traces so-called 'short-long-short-sequence' was present. The post shock restored rhythm was regular in 39 out of 51 traces (76%). The pseudo shock therapy was interpreted as AF had the following characteristics: irregular (variation in RR interval >100ms), different morphology signals with no sudden onset and the same signal morphology following the ICD shock. There was detectable atrial flutter in sinus rhythm was present in 68% of pts. For 3 pts EE showed repetitive noise signals (cause by lead insulation defect) and they received lead replacement.
Conclusions - stored EE showed a good accuracy in diagnosis of fast atrial fibrillation but its more careful analysis could lead to an improvement in differential diagnosis between VT/VF and fast AF or SVT and an increase in ICD delivered therapy specificity.

(306) POSTER
THE TRUE "OPTIMAL RATE" AN INDIVIDUAL PARAMETER
GE Payne, J Spinelli, CJ Garrett, JD Skehan
Groby Road Hospital, Leicester LE3 9OE
A three phase relation has been demonstrated between increasing VT/VF output and cardiac output. Phase 1 with the output increasing with increasing heart rate, phase 2 a plateau and phase 3 decreasing output with further increase in heart rate. The "optimal rate" can be defined as the rate at the onset of phase 2. We aim to determine the "optimal rate" and define its relationship to age and to the Astrand formula for predicting peak heart rate (220-age). Seventeen patients were studied, 11 male, mean age 59 years (range 31-71). All had chronic complete heart block and previous dual chamber pacino. A maximal exercise test was performed to determine peak heart rate and exercise capacity. An ambulatory nuclear probe (the Capintec Vest) was positioned over the left ventricle. This permits measurement of relative cardiac output and election fraction. The patients were programmed in VT1 at a rate of 60 and performed three exercise tests at different work loads in random order, depending on fitness, of 0, 25, 50 or 75 Watts. After 3 minutes stabilisation, the VT1 rate was increased at 1 minute intervals until higher than peak sinus rate giving a total exercise time of 12 minutes. The "optimal heart rate" was determined at each work load. The mean optimal rate for each work load varied in a non linear manner. There was no correlation between "optimal rate" and age or the peak rate predicted by the Astrand formula. In Conclusion the "optimal rate" for a given level of exercise is individual and not related to age. Current definitions of chronotropic incompetence are inaccurate. Are some of these people at their "optimal rate" already? The arbitrary selection of rate response curves to achieve a set rate for a given level of exercise may lead to an impaired haemodynamic response.

(307) POSTER
ROLE OF PRECEPTORIAL IMPLANTATION OF TRANVERSE CARDIOVERTER DEFIBRILLATORS.
GE Payne, JD Skehan and CJ Garrett
Groby Road Hospital, Groby Road Leicester LE3 9OE
The development of more efficient circuitry with a reduced current drain has led to a smaller implantable cardioverter defibrillator (ICD), weight 132g, suitable for transvenous pre-pectoral implant (Jewel PCD Medtronic Inc). Between July and 4 November 1993, 4 of 5 ICDs were implanted in the pectoral region. Three in the pre pectoral fascia and 1 below pectoralis major. All patients (pts) were male, mean age at implant 50 (range 19-70) with a mean body mass index of 28.7 (range 26-30) for pre pectoral implants and 23 for the sub pectoral implant. The fifth pt did not require antitachycardia pacing so had a simpler device. Three pts had cardiac ischaemia, sudden cardiac death and impaired ventricular function (mean ejection fraction 35%, range 20-45%) and two had previous revascularisation. Ventricular tachycardia remained inducible despite drugs, mean cycle length of 307 (range 240-400 msec). The 4th pt had Romano Ward syndrome and repeated cardiac arrests requiring DC shock despite stellate ganglion block. Beta blockade and unipolar dual chamber (DDD) pacing. ICD implants were under general anaesthetic and the end point for defibrillation testing was successful defibrillation at 24J on 3 successive occasions. This was achieved in all pts after a mean of 9 inductions (range 5-18). The mean procedure time was 2.2 hours (range 1.5 - 3 hours). Of the two lowest procedure times, one was due to coincident removal of DDD pacemaker and the other repeated inductions. No pts required subsequent patch electrodes or arrays. There were no problems with the implant sites and all pts feel the pectoral implant is cosmetically acceptable.
In conclusion, the reduction in device size permits prepectoral implantation in the majority of pts who require transvenous ICDs. This reduces the need for surgical assistance, but due to the current requirement for multiple shocks precludes the routine use of local rather than a general anaesthetic.

(308) POSTER
RADIOFREQUENCY CATHETER ABLATION IN PATIENTS WITH 'MAHAIM' TACHYCARDIAS.
E. Rowland, SC Heald, C. Garrett, D Katripsis, P Hill, DE Ward, DW Davies
St George's Hospital, Royal Brompton Hospital and St Mary's Hospital, London
Reentrant tachycardias associated with Mahaim connections are unusual, various electrophysiological substrates have been postulated and successful catheter ablation has been described at a variety of different sites. We have performed radiofrequency catheter ablation in 17 patients (aged 7-53, mean 30, years) by mapping the pathways to demonstrate the presence of a direct atrio-fascicular or atrio-ventricular connection, the presence of discrete 'Mahaim' potentials and their separation from the normal conduction system. All presented with tachycardia of left bundle branch block morphology or had this induced at electrophysiological study - these were shown to be due to anti-dromic tachycardia with anterograde conduction via the Mahaim pathway. Four patients had additional accessory AV pathways (2 overt, 2 concealed) which in each case were associated with at least 2 tachycardia circuits. Two patients had additional dual AV nodal pathways and AV nodal reentrant tachycardia. Following ablation of the additional accessory pathway, Mahaim potentials were identified in 13 (76%) associated with early activation of the distal right bundle and RF energy at this site on the annulus resulted in abolition of Mahaim conduction in all. In 1 patient there was early ventricular activation at the annulus without Mahaim potential but RF energy abolished pre-excitation. In the remainder either no potential could be found (1), no tachycardia inducible after ablation of the associated pathway (1) or no Mahaim conduction evident during the ablation procedure (1). Procedure times and screening times were 675-50 and 7-152 mins respectively - 2 patients required 2 procedures. During follow-up (1-24 months, median 5) all but 1 case remain asymptomatic without medication. Additional accessory pathways appear to be common in patients with Mahaim tachycardias. The identification of Mahaim potentials at the tricuspid annulus confirms the right free wall location of these pathways in the majority of cases, permits their successful ablation and abolition of associated tachycardias.
LOCALISATION OF ACCESSORY PATHWAYS USING THE SURFACE ECG: INACCURACY OF TORSO POSITIONED STANDARD LEADS COMPARED WITH LIMB LEADS.

Freeman Hospital, Newcastle upon Tyne.

During electrophysiological studies, it is often more convenient to position electrodes for the standard ECG limb leads on the torso than on the extremities. In order to determine the accuracy of localisation of accessory pathways using these modified ECG leads, we have compared standard 12 lead ECGs with 12 lead ECGs recorded using torso positioned standard leads, and have compared localisation of 44 accessory pathways calculated from these ECGs using Gallagher's method with the position confirmed by successful radiofrequency ablation in 43 patients. 33 pathways were left free wall, 2 right free wall and 9 septal. Standard limb lead ECGs were available in 34 patients and corresponded with the radiographic localisation in 31. Standard ECG suggested a septal pathway, shown at ablation to be in the left free wall. 2 standard ECGs suggested free wall pathways (1 right, 1 left) which were both shown to be septal. 12 lead ECGs recorded from torso leads were available in all 43 patients. 9 of 43 inaccurately localised the pathway; 2 suggested right free wall pathways in patients with left free wall paths, 6 suggested left free wall pathways in patients with septal paths and the other suggested a left free wall pathway in a patient with a right free wall pathway. Thus, in this small population, standard ECG leads recorded from the torso suggested inaccurate localisation of accessory pathways in 21% localised by endocardial mapping with confirmation of the site by successful ablation. In comparison, standard 12 lead ECGs correctly located the site of the pathway in 91%. The site of septal pathways was correctly predicted from the standard ECG in 78% and from the torso ECG in 33%. Thus, care must be taken in interpretation of ECGs recorded with the limb leads applied to the torso, particularly if these ECGs are used to plan accessory pathway endocardial mapping techniques.

FLUID LOADING CAUSES IMPAIRMENT OF GAS TRANSFER AT THE ALVEOLAR-CAPILLARY MEMBRANE IN PATIENTS WITH ASYMPTOMATIC LEFT VENTRICULAR DYSFUNCTION.

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Although airway obstruction and impaired pulmonary diffusing capacity for carbon monoxide (DLco) are prominent in acute pulmonary oedema, their significance in patients with left ventricular dysfunction (LVD) without pulmonary oedema remains unclear. The aim of the present study was to investigate the effects of a change in volume status on both pulmonary gas exchange and airway obstruction in this group. We measured DLco and its subdivisions, alveolar-capillary membrane conductance (Dm) and reactive conductance (RVC), where V/C pulmonary capillary blood volume) using the Roughton and Forster method. In addition, the forced expiratory volume in 1 second (FEV1), vital capacity, and peak expiratory flow rates (PEFR) were recorded. 10 patients with LVD were studied (age 62±10 years, ejection fraction 40±5%). Measurements were made at baseline and then repeated 60 minutes following the completion of an infusion of 0.9% normal saline (10 ml/kg body weight infused over 30 minutes). There was no significant alteration in heart rate or blood pressure during the infusion. Results

Baseline Post-saline p
DLco (mmol/min/kPa) 6.9±1.5 6.1±1.5 0.003
Dm (mmol/min/kPa) 12.3±3 9.7±3.3 0.02
Vc (ml/m2) 50±12 57±19 ns
FEV1 (L) 2.3±0.4 2.0±0.5 0.005
PEFR (L/min) 440±64 410±65 0.02

Acute fluid loading caused a significant reduction in DLco, increased alveolar-capillary membrane resistance to gas exchange, and a modest increase in airway obstruction, while pulmonary capillary blood volume does not alter. These data support the hypothesis that changes in loading cause increased pulmonary extra-cellular fluid, leading to increased airway obstruction and impaired gas transfer at the alveolar-capillary membrane without congestion at the pulmonary capillary level in patients with asymptomatic LVD.

The architecture of the atrioventricular conduction axis in dogs and humans - its significance to ablation of the atrioventricular nodal approaches.

S Y Ho, L Kilpatrick, R H Anderson, R P Thompson.
Department of Paediatrics, National Heart & Lung Institute, Dovehouse Street, London SW3 6LY

The development of transcatheter ablation techniques for the treatment of dual atrioventricular conduction pathways has revitalized interest in the architecture of the atrioventricular conduction axis, particularly the nodal approaches. Although investigations in the early part of the past century have laid down firm criteria for the morphological recognition of the specialized conduction tissues, the problem of the constitution of the nodal approaches remains unsolved. Some reports suggest that the internodal myocardium has no specialized characteristics, recent studies using dogs have again described specific bundles of myofibres which contact the proximal part of the atrioventricular conduction axis. These bundles were purported to be different from the internodal tracts. In view of this controversy, we studied serial histological sections from five dog hearts prepared in different planes and compared by reconstruction our findings on the human heart. Although the overall arrangement of the conduction system is similar in dog and man, the system differs in several aspects. Significantly, the compact atrioventricular node, originally described by Tawara as the "Knottenpunkten", is less extensive in the dog than in man. In contrast, the region of the conduction axis that is encased anteriorly by the central fibrous body and defined as the penetrating bundle is much longer in the dog. This elongation is due to the central fibrous body being more extensive in the absence of a membranous septum. Postmortem, in both man and in dog, the terminal nodal pacemakers were located in both position and morphology lies between the working atrial myocardium and the compact zone. The transitional posterior zone is longer and more pronounced in the dog. The transitional cell zone together with the compact node correspond to the transitional specialised area described by Tawara. Transitional cells merge gradually with ordinary working myocardium. Thus, in the dog, the internodal myocardium has no histologically specialized characteristics. Any concept of internodal tracts or specific bundles as anatomical substrates for dual atrioventricular nodal inputs is misleading.
(314) POSTER

THE INCREASED VENTILATORY RESPONSE IN CHRONIC HEART FAILURE IS NOT DUE TO PULMONARY PATHOLOGY.

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Background. The exercise limitation of patients with chronic heart failure (CHF) is characterised by a reduced peak oxygen consumption (peak VO₂) and an increased ventilatory response to exercise. The increased ventilatory response is seen as an increase in the slope of ventilation to carbon dioxide production (VE/VE̝CO₂ slope). The increased VE/VE̝CO₂ slope has been attributed to an increased dead space ventilation. Methods. The responses of 55 patients with CHF (average age 57.9 ±13.0 years, 5 female) and 24 controls (age 53.0 ±11.1 years, 4 female) to maximal incremental treadmill exercise were assessed using inert gas dilution and mass spectrometry to derive metabolic gas exchange. Results. VO₂ was the same at each stage in each group. VE was higher in patients at each stage (stage 1: VE controls: 32.4 ±10.5 l/min; patients 43.5 ±12.4; p<0.001). Patients had a lower peak VO₂ (19.6 ±7.1 ml/kg/min vs. 33.6 ±1.8; p<0.001) and a steeper VE/VE̝CO₂ slope (33.5 (9.2) vs. 25.9 (3.4) than controls. Dead space ventilation as a fraction of tidal volume was higher in patients at peak exercise, but absolute dead space ventilation and dead space per breath were greater in controls at peak exercise (0.74 litres/breath (0.29) vs. 0.57 (0.17); p=0.002). There was a negative correlation between peak VO₂ and peak V̇E/VE̝CO₂ (r = -0.45, p<0.001). End tidal CO₂ was lower in patients at all stages, and there was a correlation between peak VO₂ and PaCO₂ at peak exercise (r=0.58, p<0.001). Alveolar oxygen tension was higher in patients at each stage than in controls. Conclusions. Patients with CHF have an increased ventilatory response at all stages of exercise. This is accompanied by an increase in dead space as a fraction of tidal volume. However, there is hyperventilation relative to blood gases. The increased ventilatory response is thus not due to a primary pulmonary pathology; the increase in dead space is a response to, not a cause of, increased ventilation.

(315) POSTER

HEART TRANSPLANTATION FOR CHILDREN WITH DILATED CARDIOMYOPATHY.

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Cardiothoracic Unit, The Hospital for Sick Children, Great Ormond Street, London, U.K.

Very few studies have compared the results of heart transplantation (HTx) for dilated cardiomyopathy in paediatric patients with the natural history of this condition. Of 33 patients with dilated cardiomyopathy referred to our institute from February 1989 to October 1993, 18 (7 males, 11 females) underwent HTx. Cardiomyopathy was idiopathic in 12, post viral myocarditis in 2 and adriamycin induced in 4. Selection criteria were failure to thrive despite maximal anti-failure therapy and/or intravenous inotropic dependence. Age at HTx ranged from 9 months to 16 years (mean 7.3 years). Waiting period for HTx ranged from 1 day to 35 days (median 13 days). Rejection was diagnosed non-invasively in the younger patient while endomyocardial biopsy was routinely performed in the older child. There was 1 peri-operative death. Post transplant survivors ranged from 6 months to 55 months (median 19 months), the majority of whom enjoyed a good quality of life. There was 1 late death due to transplant associated coronary artery disease. Mean actuarial survival was 94% at 1 year and 85% at 4 years. The mean actuarial survival in 30 patients with dilated cardiomyopathy not referred for HTx from 1979 to 1989 in this institute was 62% at 1 year and 35% at 5 years. HTx has improved the prognosis for patients with dilated cardiomyopathy over the medium term, although longer term follow-up is required to fully assess the impact of HTx for this condition.

(316) POSTER

QUALITY OF LIFE FOLLOWING CORONARY REVASCULARISATION PROCEDURES

K A Priestley, L Denne, N A F Chronos, U Sigwart, D Shore, N P Buller.
Royal Brompton National Heart & Lung Hospital, London

We report the results of a prospective study to compare the quality of life in patients following coronary angioplasty (PTCA) versus coronary artery bypass graft surgery (CABG). Patients referred for revascularisation procedures were asked to complete a self-administered 'Quality of Life Questionnaire'. Postal follow-up with an identical questionnaire was performed at 3 months and one year. The questionnaire was comprised of the Nottingham Health Profile and The Hospital Anxiety and Depression Scale. Two hundred and twenty-nine patients were recruited into the study (PTCA-117, CABG-112) and most have now been followed for one year (PTCA-90, CABG-91). Data were analysed on an intention to treat basis with a significance level of <0.005 to correct for multiple comparisons. Significant improvements in overall scores were noted in both groups at one year, i.e. less perceived ill health. Pain and mobility scores improved by 3 months in the CABG group whilst in the PTCA group there was no significant improvement in mobility before one year. Comparing the 2 groups at one year the improvements in mobility and emotional reaction scores were significantly better in the CABG versus PTCA group. The CABG group also had significantly lower anxiety scores at one year compared with the PTCA group. In conclusion both revascularisation procedures improved patients' self-perceived sense of well being. Most of the improvements were evident by 3 months and maintained at one year.

(317) POSTER

PARSONNET RISK STRATIFICATION: A REVIEW OF INDIVIDUAL SURGEONS PRACTICE IN A SINGLE UNIT

Department of Cardiac Surgery, St. George's Hospital, London

Since January 1992, a computerised database has been used to record operative and post-operative details of all cardiac surgical patients. A Parsonnet score is generated from the data entered and up to September 1993, 1942 operations have been recorded. The in hospital mortality of surgeons A,B,C & D (including trainees performing delegated operations ) seemed to differ with surgeon D having a significantly lower mortality than surgeons A and B. The case mix of the consultant surgeons varied in Parsonnet distribution from low risk (score 0-4) to extremely high risk (score 20+). The overall mortality was 5.51% compared to a predicted mortality of 8.47% (p<0.05).

Parsonnet risk groups (%)

<table>
<thead>
<tr>
<th>Surgeon No of Opss</th>
<th>Predicted Observed Av. mortality</th>
<th>A mortality</th>
<th>B mortality</th>
<th>C mortality</th>
<th>D mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>629(150)</td>
<td>41.3</td>
<td>8.6</td>
<td>13.4</td>
<td>9.9</td>
<td>7.1</td>
</tr>
<tr>
<td>466(210)</td>
<td>38.2</td>
<td>7.5</td>
<td>12.8</td>
<td>8.7</td>
<td>5.6</td>
</tr>
<tr>
<td>360(111)</td>
<td>43.8</td>
<td>7.5</td>
<td>12.8</td>
<td>8.7</td>
<td>5.6</td>
</tr>
<tr>
<td>484(199)</td>
<td>52.3</td>
<td>6.4</td>
<td>11.8</td>
<td>6.6</td>
<td>4.5</td>
</tr>
</tbody>
</table>

(*p<0.05 compared to Surgeon A and B**p<0.05 observed v. predicted)

Surgeon D operated on fewer high risk patients than the other surgeons (p<0.05) and each surgeon had lower mortality figures than predicted by Parsonnet. The validity of the Parsonnet risk stratification criteria, developed from data collected 1982-5, may need modification to reflect the true risk of cardiac surgery in 1994. This database will allow such a development.
THE VALUE OF POST MORTEM EXAMINATION IN EARLY DEATHS AFTER CARDIAC SURGERY
AHS Lee, BT Borek, PJ Gallagher, R Saunders, RK Lamb, S A Livesey & JL Moreno.
Department of Pathology & Wessex Regional Cardi rhecenter, Southampton University Hospitals, Southampton S09 4XY

Background. To determine how post mortem examination contributes to the understanding of early death after cardiac surgery.

Methods. A prospective audit of all post mortems performed on adult patients dying before discharge or within 30 days of an emergency or routine procedure under bypass in the Wessex Cardi rhecenter.

Results. There were 83 early deaths in the 1901 patients (4.4%) treated over a 27 month period during 1991-93. There were 39 early deaths in the 240 emergency operations (16.3%) and 44 in the 1661 routine cases (2.6%). The post mortem rate was 94% and all but 5 were performed in Southampton. The most frequent cause of death was acute cardiac failure (32 cases, 41%) and in 13 of these patients there was pathological evidence of recent myocardial infarction. Other causes included chronic heart failure (5 cases, 6.4%), cardiac, gastrointestinal or intracerebral haemorrhage (14 cases, 17.9%) and pulmonary embolism (6 cases, 7.7%). Infections, other than endocarditis, accounted for only 2 deaths. In 11 cases (14.1%) post mortem demonstrated an important and unsuspected abnormality which contributed directly to death (haemorrhage 4 cases, graft thromboses 3 cases, acute myocardial infarctions 2, pulmonary emboli 2 cases, pneumonia 1 case). In 5 cases (6.4%) no explanation for death was found despite full macroscopic and microscopic post mortem examination.

Conclusions. Pathological abnormalities were identified in over half of all post mortems and in a quarter a clinico-pathological diagnosis of pump failure was made. Even in this group of intensively monitored patients the incidence of important unsuspected pathological findings was 14%, a figure approaching that of unscreened hospital post mortem examinations.

IS INCOMPLETE REVASCULARISATION A JUSTIFIABLE STRATEGY IN ELDERLY PATIENTS?
M Brack, J D Skehan, D P De Bono, P J B Hubner, A H Gershlick. Department of Cardiology, Groby Road Hospital, Leicester.

Coronary angioplasty is an effective method for treating coronary artery disease. Complete revascularisation is desirable, but the presence of extensive disease is it a necessary strategy in the elderly? We have retrospectively examined the results and outcome of complete and incomplete revascularisation in a group of elderly patients (n=52) mean age 74y (range 70-84y). Complete revascularisation was possible in 22 patients (single vessel disease - single vessel PTCA (n=18)); 2 vessel disease - 2 vessel PTCA (n=4) and incomplete revascularisation in 27 (2 vessel disease -1 vessel PTCA (n=11); 3 vessel disease - 1 PTCA (n=9); 3 vessel disease - 2 vessel PTCA (n=7)). Reasons for not attempting complete revascularisation were distal disease (n=5), poor calibre vessels (n=9) and diffuse disease (n=22). There were no acute cardiac events in either group. The overall success rate was 88%. At follow up 6 patients from the complete group complained of angina (mean 15 months) (mean angina grade 1 (range 0-2) and 11 patients in the incomplete group (mean 10 months) (mean grade 1.0-4). This difference was not significant. The percentage of patients in each group on 1, 2, 3 and 4 drugs were 25% v 26%, 46% v 33%, 21% v 33% and 8% v 11% for those in the complete and incomplete groups respectively. The numbers of repeat PTCA to restent of lesions in each group were similar, 2 in the complete group and 3 in the incomplete group. PTCA in the elderly is a safe procedure with success rates comparable to the general population. There would appear to be as much symptomatic benefit from incomplete revascularisation, justifying PTCA to the culprit lesion only.

A 15 YEAR REVIEW OF THE NEED FOR TERTIARY CARDIAC SERVICES BY A DISTRICT GENERAL HOSPITAL
A Varnava, M Joy, J Doherty, MS Marber, CA MacRae, St. Peter's Hospital, Chertsey, Surrey.

A survey was made of the uptake of cardiological services by a district hospital to its tertiary referral centre over the period 1979-1993. There were 15,000 cardiological investigations procedures (adjusted for the last three months of 1993). Of these, 1606 were coronary angiograms and 314 left heart catheters. During the same period there were 876 coronary artery bypass graft procedures and 285 valvar procedures. The number of valvar investigations/operations remained stable throughout, but there was a significant increase in the number of angigrams/coronary artery bypass graft procedures between 1979 and 1987 which plateaued thereafter. During the 7 years, 1987 - 1993 there was a requirement for a mean of 156.4 ± SD 15.93 coronary angiograms and 76.8 ± SD 14.7 coronary artery bypass graft procedures each year. Over the 15 year period there was also a requirement, for a mean of 20.5 ± SD 7.35 catheter procedures and 15.93 ± SD 5.99 valvar procedures each year. Based on the catchment population of 210,000 during 1987-93 and standard mortality ratio (ICD 410-414 = 0.78; ICD 393-398, 424 = 1.0), the calculated UK annual requirement for coronary angiography was 945 ± 97.2, for coronary surgery 468.7 ± 389.7, for cardiac catheterisation 99.5 ± 34.9 and for valvar surgery 75.8 ± 28.3. These figures for coronary interventions have remained constant throughout the last 7 years of the study and thus may reflect a steady state for tertiary cardiac services by the health district. However these data represent the experience of one unit and must therefore be extrapolated with caution.
(322) POSTER

MULTI-PURPOSE CARDIAC CATHETERISATION LABORATORY IN A DISTRICT GENERAL HOSPITAL: AUDIT OF FIRST 250 CASES.
Department of Cardiology, Derriford Hospital, Plymouth.

Of 301 Plymouth Health Authority patients undergoing coronary angiography between September 1992 and August 1993, 250 investigations on 246 patients (83%) were performed locally in Plymouth in a newly opened catheter laboratory and virtually all of these subsequently underwent intervention, either surgery or angioplasty. The main criteria for local intervention in Plymouth was clinical stability. 222/250 (89%) were performed as day cases. Two consultants and two supervised registrars performed all the procedures on a digital single-beam, Siemens Angiosystem system. Support staff underwent preliminary training. The median screening time was 6.0 minutes (first 50 cases) falling to 3.2 minutes (last 100 cases). Data was archived as laser printed x-ray hard copy and on super VHS video tape. There was no procedure related myocardial infarction or death. The morbidity was 2 transient neurological deficits (both resolved within 5 days) and 1 lillo-femoral artery occlusion requiring surgical intervention. 3/ 246 (1%) patients were transfused directly for surgery, none as emergencies. All angiograms were of diagnostic quality and none had to be repeated at the referral centre prior to revascularisation. The catheter intervention ratio for 250 local investigations was 1.51 with 122 patients (48%) undergoing surgery and 45 (18%) angioplasty. These data suggest that routine diagnostic coronary angiography can be performed safely and effectively on stable cases in a District General Hospital with vascular surgery on site. Continued, published audit should be encouraged as more centres undertake coronary angiograms without immediate access to surgical cover.

(323) POSTER

WHAT IS THE COST OF A NORMAL CORONARY ARTERIOGRAPHY?
B Keaveny, Y Haider, A McCance, JD Shehan
Department of Cardiology, Groby Road Hospital, Leicester.

Patients undergoing coronary arteriography for suspected ischaemic heart disease whose arteriograms are normal represent a small but significant part of the workload of a cardiac investigation unit. We carried out a cost benefit analysis to determine whether the investigation is associated with a fall in the patient's consumption of health care resources. 65 consecutive patients investigated in 1991-92 were identified by case note analysis. Their general practitioners (GPs) were surveyed by questionnaire. The cost of patients' medications, number of routine and urgent GP contacts, and number of acute hospital admissions for chest pain in the years immediately before and after the arteriogram were compared.

Drug costs were calculated from the British National Formulary. The cost of coronary arteriography was taken as the charge made by the hospital, as it were for an extra-contractual referral, and the cost of hospital admission as that of one night's stay on the cardiac high dependency unit. Data was analysed using the Wilcoxon signed rank test. A highly significant fall in all parameters of resource consumption was observed, the mean resulting difference being in the cost of care being £35.15 per month. The one-off cost of coronary arteriography would, if this fall were maintained, be recouped in just over 3 years. We therefore suggest that coronary arteriography may warrant earlier consideration in the evaluation of "chest pain, query cause".

(324) POSTER

ELECTIVE CORONARY ARTERY STENTING VIA LEFT BRACHIAL ARTERIOTOMY: A FEASIBILITY STUDY
J Smyllie, C J P Welsh, J M McLaren, E J Perrins
Leeds General Infirmary, Leeds, UK.

Recent studies suggest that de novo stenting in coronary arteries greater than 3 mm reduces the incidence of restenosis. The main problems have been the high rate of femoral vascular complications, and prolonged hospital stay. We have overcome these by first establishing patients on oral anticoagulants, and using a left brachial arteriography approach (LBA). A left brachial arteriography was performed by standard technique and an F8 introducer sheath was placed in the artery allowing the easy use of femoral guide catheters. 27 lesions were stented in 25 patients. All were successful with no failures due to poor guide catheter support. 22 were male, and mean age was 59. The indications for elective stenting were: complex lesions/large arteries 18; vein grafts 2; restenosis 2; lesion at origin of left anterior descending artery 2. Where possible, patients were established on oral anticoagulant treatment (mean INR on day of procedure 2.2). Mean procedure time was 61 minutes. Twenty three lesions were pre-dilated with a smaller balloon. Two or more balloons were used in each case. Palmaz-Shatz stents (hand crimped) were used in: right coronary 12; left anterior descending 8; circumflex 4; graft 3. The mean stent size was 3.8 mm (range 3-5).

RESULTS: There were no vascular complications and patients were mobilised on the same day. One patient had a thrombotic occlusion on day 2, and this was successfully re-opened. No other cardiac complications have occurred. Mean in-hospital stay was 4.8 nights (range 3-10). Guide catheter selection was important: for right coronary and graft lesions, left Amplatz catheters were best (7 of 12 RCA, and 3 of 3 grafts) and for left coronary lesions a VODA gave excellent support (9 of 12). Left Judkins shapes were not suitable.

Conclusion: Initial experience suggests that elective coronary stenting via LBA in patients with established oral anticoagulation is technically feasible, has a very low complication rate, and allows for a reduced in-patient stay.

(325) POSTER

INTRA-CORONARY STENTING: IS IT WORTHWHILE?
S Vaishnav, S Aziz, S W Davies, M T Rothman, A D Timmins, R Balcon, C A Layton
The London Chest Hospital, London.

Stents are commonly used for bailout following acute vessel closure, and electively in vein grafts. Over one and half year period we used 122 Wiktor stents (Medtronic) to treat 119 lesions in 96 patients. Of the 3 additional stents required, 1 dropped and lodged into a branch of right femoral artery, the other 2 were retrieved using an extraction device. The indications for stenting were obstructive dissection in 28, unsatisfactory PTCA result in 19, restenosis in 25, vein grafts in 38, and elective in 9. The average stent size was 3.5 mm and more than 1 stent was implanted in 19 patients. Stent deployment was successful at 112/119 sites (procedural success rate of 94%). Of the unsuccessful procedures 4 had emergency surgery (all had threatened vessel closure following balloon angioplasty), I had surgery 1 month later for recurrent angina, and 1 patient was well from the predilation procedure. 2 patients died, both were unstable and dependent on only one diseased graft and did not respond to intensive medical treatment. One died 2 hours after the procedure probably due to acute stent thrombosis and the other 24 hours later due to refractory left ventricular failure. Distal embolisation of thrombus with elevation of cardiac enzymes occurred in 7 patients with vein grafts. 4 of these had angina with ST changes and 3 required thrombolytic treatment. No patient had new Q-waves. 14 patients had haemorrhagic complications (femoral bleeding 6, haemostoma requiring drainage 2, GI bleeding requiring transfusion 2, pseudoaneurysm of the femoral artery requiring repair 2). At 6 months follow-up, 11 patients had recurrent angina. Angiography in 45 patients revealed 4/61 stent sites had restenosis (3 stent sites have been redilated). In addition 2/61 stent sites (both vein graft sites) were totally occluded one at 6 months and one at one year. 3 more patients had repeat PTCA for disease in other vessels.
P94

INTRACORONARY ACTIVATION OF POLYMORPHONUCLEAR LEUCOCYTES AFTER BALLOON INFLATION DURING PTCA

AJB Brady, AG Rossi, NA Chronos, U Sigwart, NP Buller
Departments of Applied Pharmacology and Cardiology, Royal Brompton National Heart and Lung Hospital, London

Intramural and intracoronary thrombus formation can occur during PTCA, despite intensive anticoagulation. Activation of the acute inflammatory process may be important during PTCA, both as an alternative early source of prothrombotic mechanisms initiating coagulation, as well as its later role, promoting vascular repair and regrowth. The hypothesis that acute inflammatory mechanisms are generated at the site of balloon dilatation during PTCA was therefore examined. Activation of polymorphonuclear leucocytes (PMN) can be determined by measuring production of neutrophil elastase. Intracoronary release of elastase after balloon inflation was measured in eight patients undergoing PTCA. All patients received 15000 U heparin and 300 mg aspirin, and a β-adrenergic antagonist. After placement of the balloon at the site of the lesion blood samples were withdrawn through the central lumen of the PTCA catheter, before and 1 min after balloon inflation. Serum elastase activity was measured as the release of p-nitroaniline from the elastase substrate, succinyl-alala-pro-val-p-nitroanilide. Intracoronary elastase rose from 2.1 ± 0.005 ng/ml before balloon inflation, to 2.57 ± 0.007 ng/ml 1 min after dilatation (mean ± SEM, n = 8, p < 0.05). These results show intracoronary PMN activation at the site of PTCA in patients. Local mechanisms of acute inflammation may be important in the early as well as the late complications of PTCA.

PULMONARY MECHANICS AND GAS EXCHANGE FOLLOWING SUCCESSFUL BALLOON MITRAL VALVOTOMY

Departments of Cardiology and Respiratory Medicine*, Cardiothoracic Centre, Liverpool

Patients with mitral stenosis have abnormal lung function with a reduced diffusing capacity. To determine the effect of successful balloon mitral valvotomy (MV) on pulmonary mechanics and alveolar capillary gas exchange we studied 9 patients (MV, 68, mean age 59 years) undergoing MV. Pulmonary function testing was performed 24 hours after MV, and at 48 hours and at 3 months afterwards. Pre and post MV haemodynamic parameters were:

<table>
<thead>
<tr>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAP (mmHg)</td>
<td>18.8±2.3</td>
</tr>
<tr>
<td>MVA (mmHg)</td>
<td>11.6±0.6</td>
</tr>
<tr>
<td>MVA (cm²)</td>
<td>0.92±0.11</td>
</tr>
</tbody>
</table>

(LAP mean left atrial pressure, MVA mean mitral gradient, MVA mitral area: mean ± sem). At baseline FBFV, FVC and total lung capacity were reduced (79%, 87% and 88% predicted respectively) and residual volume marginally increased (102% predicted). There was no change in lung volumes at either 48 hours or 3 months. Overall diffusing capacity for carbon monoxide (TLCO) was unchanged: pre 76.3±8% of predicted, 48 hours 75.2±7% of predicted, 3 months 76.0±3% of predicted, as was alveolar capillary membrane diffusing capacity (Dm), pre 59.4±7% predicted, 48 hours 56.6±6% predicted, 3 months 59.2±8% predicted. Alveolar blood volume (Qe) fell from 118±8% predicted to 111±10% predicted at 48 hours (NS) and to 98±10% predicted at 3 months (p=0.033). MVA at 3 months was 1.7±0.00cm². Thus reduction of mitral valve gradient for 3 months normalised pulmonary capillary volume, hence relieving pulmonary congestion, but did not reverse the abnormalities in overall diffusing capacity or the diffusing capacity of the alveolar capillary membrane. Abnormalities in alveolar capillary membrane function in mitral stenosis may be irreversible or reverse only over a prolonged time course.

THERAPEUTIC ULTRASONIC CORONARY ANGIOPLASTY: EARLY CLINICAL AND ANGIOGRAPHIC RESULTS IN SINGLE VESSEL DISEASE

J Gunn, C Wales, A Ahsan, D Iskarderis, S Arafia, R Bowes, S Campbell, D Oakley, A Siegel, R Myler, D Cumberland
Dept of Cardiology, Northern General Hospital, Sheffield

Introduction
The therapeutic coronary ultrasonic angioplasty (USA) catheter (Baxter Healthcare) is a 4.5F calibre, of 'rapid exchange' design, and possesses a small protuberance: its energy comes from an external transducer at 19.5MHz, power 16-20W, with longitudinal amplitude of vibration 10-20um.

Method
We selected 29 patients with limiting angina, 26 stable, mean age 55 years, 22 male with good left ventricular function and single vessel disease amenable to conventional balloon angioplasty. The lesion was in left anterior descending (14), right (14) and circumflex (1) coronary artery. Quantitative coronary angiography (Philips) was performed at baseline, after USA, after adjunctive balloon dilatation (all cases) and at 24 hours. Energy was applied for median (range) 437(138-890)J.

Results

<table>
<thead>
<tr>
<th></th>
<th>Pre USA</th>
<th>Post USA</th>
<th>Post PICA</th>
</tr>
</thead>
<tbody>
<tr>
<td>DS (%)</td>
<td>79(13)</td>
<td>62(15)</td>
<td>77(14)</td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>3.7(1.2)</td>
<td>3.1(1.3)</td>
<td>3.6(1.3)</td>
</tr>
</tbody>
</table>

DS is diameter stenosis, MLD minimum lumen diameter; figures are mean (SD); * p<0.02, ** p<0.001, *** p<0.0001. There was no occlusion, perforation, embolism, myocardial infarction or death due to deployment of USA catheter; there was one case of spasm and one dissection.

Conclusion
Therapeutic ultrasonic coronary angioplasty is safe and feasible in the treatment of atherosclerotic coronary artery disease. At present, single tip size precludes its use in small vessels, and necessitates adjunctive balloon use in large. Six month clinical and angiographic restenosis data are being collected.

RETROGRADE NONTRANSSEPTAL BALLOON MITRAL VALVULOPLASTY USING THE INIDE BALLOON CATHETER

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Department of Cardiology, Athens University, Athens, Greece

The Inoue self-positioning balloon catheter (IBC) is a popular balloon catheter for mitral valvuloplasty due to its advantages: excellent stability, low profile and short deflation time. Retrograde Nontransseptal Balloon Mitral Valvuloplasty (RNBV) is a method developed in our institution for treating symptomatic mitral stenosis without puncturing of the interatrial septum, based on a specially designed steerable balloon catheter (figure A). Until now, in the 210 cases performed with RNBV, all types of balloon catheters were used, except for the IBC which could not be used due to its short shaft. To employ the IBC in RNBV we modified in our laboratory an IBC by extension of its shaft and we used a long stretching tube. The IBC was inserted through a femoral artery through an adjustable introducer (Medina, Schneider) and advanced to the mitral valve over a large stiff 0.035" guide wire. RNBV was performed in 15 patients (age 51±9 years). Mitral valve area increased from 0.90±0.22 to 2.1±0.40 sq cm and transmitral pressure gradient decreased from 15±6 to 6±3 mm Hg. No complications were observed.

Conclusions: 1) RNBV can be performed effectively and safely using the IBC. 2) As in RNBV the distal part of the balloon is at first inflated and withdrawn in the left atrium and not within the subvalvular apparatus (figures B, C), tension to the subvalvular apparatus is reduced during inflation; accordingly, the incidence of mitral regurgitation may be reduced, while excellent mitral valve opening can still be achieved.
HEART TRANSPLANT REJECTION CORRELATES STRONGLY WITH HLA MISMATCH
S Sheldon, P Haselton, MA Yonan, AN Rahman, AK Deiraniya, CS Campbell, NH Brooks, and PA Dyer.
Department of Histocompatibility Laboratory, St. Mary's Hospital, London, UK.

The effect of HLA incompatibility on outcome of heart transplantation (HTXP) has proved difficult to evaluate due to the strong bias towards transplants with a high degree of HLA matching. This bias is a result of the relatively short cold ischaemia time which has traditionally deterred HTXP centres from pursing prospective HLA matching policies. With accurate rapid prospective HLA matching now feasible we examined the role of HLA mismatching in HTXP on endomyocardial biopsies (EMB) for 157 consecutive orthotopic HTXP performed from April 1987 to August 1993. EMB grade >2 was used as the cut off point for definition of clinically significant rejection. We found that HTXP with high HLA-DR MM had a highly significantly reduced frequency of EMB grades >2. This HLA-DR mismatching effect was observed with analysis of EMB results from the first three months post transplant, the first year post transplant and with the total data.

<table>
<thead>
<tr>
<th>HLA-DR</th>
<th>HTXP</th>
<th>EMB</th>
</tr>
</thead>
<tbody>
<tr>
<td>MM</td>
<td>No.</td>
<td>No. &gt;2</td>
</tr>
<tr>
<td>0</td>
<td>13</td>
<td>140</td>
</tr>
<tr>
<td>1</td>
<td>53</td>
<td>797</td>
</tr>
<tr>
<td>2</td>
<td>91</td>
<td>1624</td>
</tr>
</tbody>
</table>

*p<0.0005

This study shows that HTXP matched at the HLA-DR locus has a reduced incidence of EMB grades indicative of acute rejection. Given the results of this study and that high quality HLA typing can now be achieved from donor peripheral blood we believe that application of prospective HLA matching should be undertaken for HTXP whenever possible.

TREATMENT OF HYPERLIPIDAEMIA AFTER CARDIAC TRANSPLANTATION
J. Parameshwar, M. Roberts, J. Wallwork, S. Large, P. Schofield. Transplant Unit, Papworth Hospital, Papworth Everard, Cambridge.

Cardiac allograft vascular disease (CAVD) is the single most important cause of late mortality in heart transplant recipients. Hyperlipidaemia (HLD) is common in this population and may contribute to CAVD. The aim of this study was to examine the relationship between lipoprotein(a) (Lp(a)), lipids and the development of CAVD. Lp(a), total cholesterol (TC), HDL-cholesterol (HDL-C), LDL-cholesterol (LDL-C), triglycerides (TG), apolipoprotein A1 (apo-A1) and apoB were measured pre and coronary angiography performed in 174 consecutive patients at routine follow up. Group 1 (132 patients) had no evidence of CAVD while group 2 (42 patients) did. 36 patients in Group 1 and 20 in Group 2 were on lipid lowering therapy. Univariate (Mann-Whitney test) and multivariate logistic regression analysis was carried out to assess the relationship of the variables studied to the presence of CAVD. Recipient and donor age and sex, pre transplant diagnosis, hypertension, diabetes mellitus, cytomegalovirus infection, episodes of rejection, and loci of HLA mismatch were not significantly different between the two groups. Table 1 shows the results of Lp(a) and lipid assays in the two groups with the result of the Mann-Whitney test. On multivariate analysis, after adjusting for time from transplantation, Lp(a) remained significantly correlated with CAVD (likelihood ratio chi-squared = 5.01, p = 0.029). In the above model the addition of TC plus HDL-C or TG showed that these variables are correlated with CAVD independent of Lp(a). High Lp(a) levels are associated with CAVD, treatment of lipid disorders is justified in cardiac transplant recipients in an attempt to delay the onset of CAVD.

<table>
<thead>
<tr>
<th>Variable</th>
<th>No CAVD</th>
<th>CAVD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (range)</td>
<td>N = 132</td>
<td>N = 42</td>
<td></td>
</tr>
<tr>
<td>Apo A1 gm/l</td>
<td>1.3 (0.8-1.9)</td>
<td>1.3 (0.9-1.8)</td>
<td>0.332</td>
</tr>
<tr>
<td>Apo B gm/l</td>
<td>1.0 (0.3-7.0)</td>
<td>1.0 (0.3-7.0)</td>
<td>0.057</td>
</tr>
<tr>
<td>TC mmol/l</td>
<td>6.3 (4.4-9.9)</td>
<td>6.0 (4.4-9.6)</td>
<td>0.021</td>
</tr>
<tr>
<td>HDL-C mmol/l</td>
<td>0.9 (0.5-1.9)</td>
<td>0.8 (0.4-1.7)</td>
<td>0.002</td>
</tr>
<tr>
<td>LDL-C mmol/l</td>
<td>4.2 (2.0-6.5)</td>
<td>4.5 (2.5-7.2)</td>
<td>0.258</td>
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<tr>
<td>TG mmol/l</td>
<td>2.0 (0.5-6.7)</td>
<td>2.8 (0.7-8.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Lp(a) mg/l</td>
<td>95 (10-1875)</td>
<td>317.5 (10-2250)</td>
<td>0.031</td>
</tr>
</tbody>
</table>
**Assessment of Latisimus Dorsi Muscle Function after Cardiomyoplasty by Doppler Tissue Imaging**

Neil R Graub, George R Sutherland, Alan Fleung**, Ciro Campassola, Keith AA Fox, Colin Sinclair Cardiology and **Medical Physics Department, Royal Infirmary of Edinburgh, UK.

Doppler Tissue Imaging (DTI) is a non-invasive ultrasound technique which uses color Doppler to interrogate individual velocities and accelerations in the cardiac and skeletal muscle. Muscle group velocities are displayed as a two-dimensional color map, or with greater temporal and spatial resolution as a color M-mode plot. We have examined four patients after cardiomyoplasty with this technique. The Medtronic SJ1055A cardiomyostimulator and stimulation protocol were used. In each case a series of cardiac cycles was stored on digital cine loop and was then examined in assist and non-assist beats. Color M-mode plots were obtained. In three patients we noted higher systolic velocities in the inferior & posterior wall (PW) and at the left ventricular apex during assisted beats. Cardiac displacement was noted by the presence of anterolateral displacement of the anterior wall (AW) during assisted beats.

<table>
<thead>
<tr>
<th>(all values cm/sec)</th>
<th>Assist</th>
<th>No assist</th>
<th>Assist</th>
<th>No assist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systole systole</td>
<td>0.8</td>
<td>0.0</td>
<td>2.0</td>
<td>-4.0</td>
</tr>
<tr>
<td>Diastole diastole</td>
<td>0.8</td>
<td>-3.5</td>
<td>2.0</td>
<td>-3.5</td>
</tr>
</tbody>
</table>

One patient had no discernible beat-to-beat variation in PW motion by standard M-mode echo after 10 weeks of electrical training, despite having a strong palpable axillary impulse. DTI confirmed that wall motion was unchanged during assisted contractions. Muscle stimulation was increased from 4.5 to 6.0 volts. Marked beat-to-beat variation in PW systolic and diastolic velocity was observed using M-mode DTI. Beat-to-beat variation disappeared after 5 minutes, and the patient was less aware of the axillary impulse. Despite incremental electrical training by a standard protocol, the latisimus dorsi muscle may not become fatigue resistant. The axillary impulse may be present in the absence of adequate cardiac assist.

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**ALDOSTERONE BLUNTS THE REFLEX BARORECEPTOR RESPONSE TO NORADELINE IN HEALTHY MAN**

C S Barr, A D Struthers. Department of Clinical Pharmacology, Ninewells Hospital and Medical School, Dundee, DD1 9SY.

Angiotensin II is known to modulate baroreceptor function and sympathetic neurotransmission. Aldosterone (Aldo) has recently been demonstrated to reduce vascular catecholamine reuptake in vitro via an uptake 2 blocking mechanism and impair the baroreflex response in an animal model. No data on the effect of aldosterone on sympathetic neurotransmission or baroreflex responses have been reported in man.

Eight healthy male volunteers were given an intravenous infusion of d-aldosterone (12 pmol/kg/min) or placebo, co-infused with an incremental dose of I-noradrenaline (NA) (0, 25, 50, 100 pmol/kg/min) or placebo. There was a stepwise increase in HR, DBP and MBP with NA and stepwise decrements in pulse rate. Aldo significantly reduced the negative chronotropic response to NA but the blood pressure was not significantly altered.

**Results**

These results add weight to previous in-vitro and animal in-vivo suggest aldosterone as well as AI all may modulate the baroreflex. This may be of significance in the baroreflex abnormalities in conditions where hyperaldosteronism occurs such as chronic heart failure.

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**AN ALTERNATIVE TECHNIQUE FOR SKELETAL MUSCLE CARDIAC ASSIST**

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The lack of long term haemodynamic benefits of cardiomyoplasty in patients with heart failure have been attributed to left isatinimus dorsi muscle (LDM) damage. The aetiology of muscle damage have been shown to be the combined effect of LDM mobilization (with associated distal muscle ischaemia), loss of resting tension and electrical stimulation. Chronic electrical stimulation of muscles with normal stretch and blood supply causes significantly less damage. We describe an alternative technique for cardiac assistance in which the pedicled latissimus dorsi muscle flap is passed underneath the heart in a cardiophathotaneous fashion; the stronger muscle segment then lies beneath the cardiac apex. The distal border of the muscle is fixed to the right hemi-sternum to maintain the muscles' resting tension. The procedure has been tested acutely in 3 sheep. Synchronized muscle stimulation increased the mean aortic flow (p>0.001), peak left ventricular (p=0.001), and peak aortic pressures (p<0.03) of assisted cardiac cycles. After induction of ventricular fibrillation, the mean left ventricular pressure, and mean aortic flow were significantly higher with muscle stimulation (p=0.02 and p=0.05 respectively). This technique may prevent the undesired lateral displacement of the heart which occurs in clinical cardiomyoplasty. It also renders surgical revascularisation of the distal half of the muscle more feasible. Further assessment of this procedure in chronic experiments may influence the technical application of current forms of clinical cardiomyoplasty.


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**SYNCOPE AFTER CARDIAC TRANSPLANTATION: CENTRAL MECHANISM OR CARDIAC REINNervations?**

RA Kenny, CD Scott, JH Dark, JM McComb. Freeman Hospital, and Royal Victoria Infirmary, Newcastle upon Tyne.

Neurogenic syncope is thought to depend on the Bezold Jarisch reflex, which is initiated by stimulation of left ventricular vagal nerve fibres. Orthotopic cardiac transplantation leads to cardiac denervation and thus would protect transplant recipients from vasodpressor syncope. We assessed susceptibility of long term transplant recipients to orthostatic stress, by 60 minutes of 60º head up tilt with foot plate support. Cardiac innervation status was also assessed. Heart rate response to vagal manoeuvres (respiration and Valsalva) and to sympathetic stress (injection of tyramine into the coronary artery supplying the sinus node, and exercise) was measured. During head up tilt 7/17 patients developed either syncope or presyncope 27 (12-60) minutes after the onset of tilt. The donor heart rate fell in 1, remained unchanged in 1 and increased in 5 (by 11 bpm). The blood pressure fell by 89 mmHg (systolic) and 52 mmHg (diastolic). 2 patients, 1 with donor bradycardia and 1 with no change in heart rate at the time of (pre) syncope had evidence of sympathetic reinnervation, achieving 100 and 103% of predicted maximal heart rate on exercise, and increases of 29 and 24 bpm in response to tyramine. By contrast, 4/6 patients without donor bradycardia at the time of (pre) syncope had little or no evidence of sympathetic reinnervation, achieving 85 ± 3% of predicted maximal heart rate on exercise, and increases of 7.5 ± 1.9 bpm in response to tyramine. No patient had evidence of vagal reinnervation. Thus, cardiac transplant recipients remain susceptible to tilt induced syncope. Vasodpressor occurred either with or more commonly without donor bradycardia. Syncope occurred in the absence of evidence of vagal reinnervation, suggesting that intact vagal afferents may be unnecessary. Donor bradycardia occurred in the presence of evidence of sympathetic reinnervation, suggesting that an intact sympathetic system, and sympathetic withdrawal, may be an important part of the mechanism. These data in addition support the possibility that “vasovagal” syncope may be centrally mediated.
IMPACT OF ATRIAL FIBRILLATION ON PERIPHERAL MICROCIRCULATORY HAEMODYNAMICS

IR Mhay, AC Shore, LDR Smith* and JE Tooke
Department of Vascular Medicine, Exeter University and *Department of Cardiology, Royal Devon and Exeter Hospital, Exeter EX2 5DW

Atrial fibrillation is associated with central haemodynamic and humoral changes which may influence the normal capacity for autoregulation within the microcirculation. For example, atrial natriuretic peptide, typically elevated in atrial fibrillation, has been shown to alter transcapillary fluid flux, and effects on both capillary pressure and capillary filtration coefficient (CFC) have been demonstrated. Such alterations in peripheral microvascular function may be important in the pathogenesis of oedema in heart failure. These studies therefore investigated the impact of atrial fibrillation on capillary pressure and capillary filtration coefficient. Apical capillary pressure in the finger nailfold of 6 patients with atrial fibrillation (mean age 61 years, 3 female) and 16 age, sex and skin temperature matched controls in sinus rhythm was measured by direct cannulation using an electronic spheroulling technique. Subjects were not oedematous at the time of study. Measurements were made with the subject supine and the hand supported at right atrial level. Mean arterial blood pressure did not differ significantly between the two groups (104±15.5±mmHg AF v 97±6.7±mmHg (mean±SD)), but resting pulse rate was higher in the group with AF (81±25±4.9vpm v 62±7±7.8vpm, p<0.0001). Mean capillary pressure in atrial fibrillation was 18.4±5.1SD/mmHg v 18.0±2.9mmHg in sinus rhythm (ns). In a parallel study capillary filtration coefficient was measured by mercury-in-elastic strain gauge plethysmography in 11 patients in atrial fibrillation (mean age 64 years, 4 female) and 13 matched controls. Effects of the venoarterial response were avoided by the use of multiple small cuff pressure steps in conjunction with computerised analysis. CFC did not differ between the two groups (28.7±9.9±ml/min/mmHg100ml/m² (mean±SD)). These studies had 90% power to detect differences of 3mmHg and 0.9ml/min/m²/mmHg100ml/m² respectively at a 5% level of significance. Thus no evidence was found to support conclusions of any alteration of either capillary pressure or capillary filtration coefficient in atrial fibrillation, suggesting that the magnitude of any abnormality is small and that the capacity of the microcirculation for autoregulation is preserved.

DISTURBED AUTONOMIC FUNCTION SIX MONTHS AFTER ACUTE MYOCARDIAL INFARCTION COMPPLICATED BY LEFT VENTRICULAR FAILURE AS INDICATED BY REDUCED HEART RATE VARIABILITY

A Cheng, D Shani, RA Greenbaum
Cardiovascular Research Unit, Edgware General Hospital, Edgware.

To compare various heart rate variability (HRV) measurements in patients with acute myocardial infarction (AMI) complicated by left ventricular failure (LVF) (group A) to those without LVF (group B), 127 patients (mean age 60±11 years) with AMI underwent 24 hours of Holter recording. Analysis was performed before admission to the Coronary Care Unit, and at 1 week, 1 month and 6 months post-infarction. LVF developed in 34 (27%) patients prior to hospital discharge. On admission, the standard deviation of normal RR intervals (SDRR, 63±24 vs 84±42 msec, p=0.03), the standard deviation of the mean normal RR intervals of successive 5 minute periods (SDNN, 56±23 vs 70±33 msec, p=0.02), the mean of the standard deviation of normal RR intervals of successive 5 minute periods (SD, 26±12 vs 43±20 msec, p=0.001), the percentage of normal RR intervals exceeding the adjacent RR interval by >50 msec (pNN50, 3±5±1 vs 6±4±7%, p=0.03), and total spectral power (TP, 19±9 vs 32±16 msec, p=0.001) were significantly lower in the group with LVF compared to the group without LVF. Over the 6 month period, the various HRV measurements increased and the incidence of abnormal spectral plots (SP, 21(62% vs 3±2(36%, p=0.008) was significantly higher in group A compared to group B. Over the 6 month period, the various HRV measurements increased and the incidence of abnormal SP decreased progressively in both groups. The differences between the two groups were maintained for SDRR, SDNN, SD, TP and SP but not for pNN50. A representative plot is illustrated for SDRR, and was similar for other HRV parameters. Thus, patients with LVF after AMI have lower HRV measurements and a higher incidence of abnormal SP compared to those without LVF. These differences were still present at 6 months despite a progressive recovery, suggesting that autonomic impairments and disturbances still persisted in patients with LVF at 6 months after AMI.

INCREASED BLOOD PRESSURE VARIABILITY DURING 24 HOUR BLOOD PRESSURE MONITORING AS AN EARLY SIGN OF AUTONOMIC DYSFUNCTION IN NON-INSULIN DEPENDENT DIABETICS

S McKinlay1, C Foster1, S Clark2, F Kemp2, E Denver3, AJS Coats4, National Heart & Lung Institute, London, Oxford, Royal Devon and Exeter Hospital, Whittington Hospital, London.

To evaluate the presence of early autonomic dysfunction in non-insulin dependent diabetics we examined 24 hour control of blood pressure (1/4 hourly readings day & 1/2 hourly at night, using TM 2420) in 20 non-insulin dependent diabetics, controlled only on diet or oral hypoglycaemics and 20 age/six/blood pressure matched non-diabetics, aged 52 ± 9 - 53 ± 8. Both groups included normotensives and mild hypertensives in equal numbers but none was on anti-hypertensive treatment. The groups were well matched for daytime systolic blood pressure (SBP), 132.2 ± 11.4 vs 131.2 ± 10.3) and diastolic blood pressure (DBP). (82±38v3±8±1±7). The diabetics had significantly increased heart rate (HR) both day (79±6 ± 9.5 vs 72±38±8±p 0.015) and sleep (77± 6± 6.8 vs 62±5 ± 8.9). There was also an increased blood pressure variability in the diabetics during the day (SD SBP 16.2 ± 6.2 vs 13.2 ± 4.7, p<0.05) but the difference for diastolic BP variability was not significant. The day-night difference for SBP, DBP, HR and HR variability was the same in both groups. We conclude that in diabetics there was evidence for an early alteration in BP variability (which may reflect baroreflex insensitivity) at a stage where there was no alteration in mean BP or in BP variability with or with sympathetic-vagal imbalance.

RE-EVALUATION OF NORMAL SPLITTING OF THE SECOND HEART SOUND IN PATIENTS WITH LEFT BUNDLE BRANCH BLOCK


Reversed splitting of the second heart sound (S2) is considered universally present in patients (pts) with classical left bundle branch block (LBBB). However, in 43 such patients, splitting was normal in 13 (30%). In order to evaluate the possible mechanism for this normal splitting, we recorded ECG, phonocardiography and echocardiography. There were no significant differences in left ventricular (LV) cavity size, heart rate and of the distribution of age, gender or aetiology. PR interval and QRS axis were similar in the two groups. In pts with reversed splitting of the S2, QRS duration was significantly longer (157±15 ms vs 135±15, p<0.01), the onset of the right ventricular free wall was less delayed (100±15 ms vs 120±15, p<0.05) than those without, though that of the LV free (160±30 ms vs 150±20) and posterior (140±30 ms vs 130±20) wall motion was delayed to a similar extent in the two groups compared to normal. Peak velocities of mitral flow E (0.50±0.20 m/s vs 0.80±0.40, p<0.01) and A (0.54±0.20 m/s vs 0.85±0.40, p<0.01) were both reduced in pts with a normal splitting of the S2, while the time from aortic closure to the onset of mitral flow was similar (55±25 ms vs 60±30) in the two groups. Thus, splitting of the second heart sound was normal in approximate 1/3 pts with classical LBBB. Splitting pattern depends on the relative delay in right ventricular activation, which is frequently present in such pts. The latter cannot be detected on 12 lead ECG, but can thus be suspected from simple auscultation.
QT DISPERSION: A PREDICTOR OF SUDDEN, UNEXPLAINED DEATH IN CONGESTIVE CARDIAC FAILURE.

C S Barr, A A Naas, M Freeman, C C Lang, A D Struthers.
Department of Clinical Pharmacology, Ninewells Hospital and Medical School, Dundee, DD1 9SY, Scotland, UK.

QT interval variability (dispersion) reflects regional variation in ventricular repolarisation. This may represent electrophysiological substrate for arrhythmias. We have measured QT dispersion (maximum QT interval minus minimum corrected QT interval) on surface 12 lead ECGs of 40 patients with NYHA III-IV chronic heart failure who were subsequently followed for a period of 36 months (range 12-50 months). During follow up 7 patients died suddenly (SUD) and 12 died from progressive heart failure (PHF). There were no significant differences in age or electrolytes between each group. Patients who died of PHF had lower LVEF. Patients who died had significantly greater QTc dispersion but not QTc max compared to those who survived. Patients who died a sudden expected death had significantly more QTc dispersion compared to those who survived or who died from progressive heart failure.

<table>
<thead>
<tr>
<th>Alive</th>
<th>PHF</th>
<th>SUD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>70(66, 74)</td>
<td>68(62, 75)</td>
</tr>
<tr>
<td>K+ (mmol/L)</td>
<td>4.1(3.9, 4.3)</td>
<td>4.0(3.7, 4.3)</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>28(27, 29)</td>
<td>21(15, 27)</td>
</tr>
<tr>
<td>QTc max (ms)</td>
<td>466(439, 483)</td>
<td>464(431, 478)</td>
</tr>
<tr>
<td>QTc disp* (ms)</td>
<td>54(42, 64)</td>
<td>67(52, 82)</td>
</tr>
<tr>
<td>Adj QTc disp (ms)</td>
<td>18(13, 22)</td>
<td>23(18, 29)</td>
</tr>
</tbody>
</table>

Results are presented as mean (95% CI) and adjusted for number of measurable leads * p<0.05 vs alive, † p<0.05 vs PHF

Conclusion. Studies should address the predictive value of QT dispersion as a useful technique for distinguishing those patients with chronic heart failure who may be at risk of sudden death.

THE QT INTERVAL IN ANOREXIA NERVOSA AS A MARKER FOR SUDDEN DEATH

RA Cooke, JW Chambers, R Singh, J Todd, WC Sweeton, J Treasure, T Treasure, Department of Cardiology, Guy’s Hospital; Institute of Psychiatry, Deccospying Park; Cardiothoracic Department, St George’s Hospital, London.

To determine the incidence of abnormalities of the QT interval in anorexia nervosa as a marker for sudden death, and assess the effect of refeeding we recorded 12 lead electrocardiograms in 41 consecutive patients on admission and after treatment, and in 28 age and sex matched normal controls. Two methods of comparing the QT interval and defining QT prolongation were used: (1) multiple linear regression analysis and estimation of upper confidence limits; (2) the Bazett rate correction formula.

The measured QT interval was identical (380 ms (range 340-440)) but the RR interval was significantly shorter (780 ms vs 860 ms, p<0.03) in patients vs controls. 43.6% of the variability in the QT interval was explained by heart rate alone (p<0.0001) and the addition of analysis by group contributed a further 5.9% (p<0.004). Six (15%) patients had QT prolongation above the upper 95% confidence limit for the control group (not significant). Two died suddenly, both of whom had QT prolongation. In patients who achieved their target weights, there was a statistically significant shortening of the QT interval (median 9.8 ms p<0.04) in relation to the upper 60% confidence limit of the control regression line, which optimally discriminated between patients and controls. The median Bazett rate corrected QT interval (QTc) in patients and controls was 435 vs 405 ms (p=0.0004), and 435 vs 432 ms m2 (not significant) in patients before and after refeeding.

In 14 (34%) patients and 3 (11%) controls the QTc was > 440 ms.1/2 (p=0.053).

The QT interval was prolonged in patients with anorexia nervosa, and returned to normal after refeeding. The Bazett rate correction formula overestimated the magnitude of the abnormality, and failed to show an improvement with refeeding.

**RESULTS**

<table>
<thead>
<tr>
<th>Alive</th>
<th>PHF</th>
<th>SUD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean QTc (ms)</td>
<td>466(439, 483)</td>
<td>464(431, 478)</td>
</tr>
<tr>
<td>Normal</td>
<td>466(439, 483)</td>
<td>464(431, 478)</td>
</tr>
<tr>
<td>CAD</td>
<td>54(42, 64)</td>
<td>67(52, 82)</td>
</tr>
<tr>
<td>Adj QTc disp (ms)</td>
<td>18(13, 22)</td>
<td>23(18, 29)</td>
</tr>
</tbody>
</table>

Results are presented as mean (95% CI) and adjusted for number of measurable leads * p<0.05 vs alive, † p<0.05 vs PHF

Conclusion. Studies should address the predictive value of QT dispersion as a useful technique for distinguishing those patients with chronic heart failure who may be at risk of sudden death.
THE ROLE OF ENDOTHELION IN THE MAINTENANCE OF LOW PULMONARY VASCULAR TONE IN NORMAL CHILDREN

Resting vascular tone is low in the normal pulmonary circulation, and experimental studies have suggested that this may be due to the presence of pulmonary endothelion-derived nitric oxide (NO), a locally acting vasodilator. We have investigated whether NO contributes to the normal control of pulmonary vascular tone and resistance in children. We studied the haemodynamic effects of L-NMMA, a specific inhibitor of NO synthesis, on the pulmonary circulation of six normal children aged 2-17 (mean 9) years with congenital heart disease but normal pulmonary blood flow, pressure and resistance (all had isolated left heart obstructive lesions). The diameter of a segmental pulmonary artery and pulmonary blood flow velocity were measured by quantitative angiography and intravascular Doppler catheters. There was a consistent, dose-dependent fall in pulmonary blood flow velocity in response to three increasing doses of L-NMMA (compared to baseline, flow velocity fell to 75±7, 62±8 and 40±10, p<0.01). Flow velocity returned to control values with subsequent infusion of L-arginine, the substrate for NO.

Thereafter acetylcholine, an endothelion-dependent dilator, produced an increase in flow velocity (56±10% greater than baseline, p<0.01). Arterial diameter was unchanged during L-NMMA and L-arginine infusions, indicating that the major effect of each agent is to alter vascular tone distal to the segmental pulmonary arteries. The dilator action of endothelion-derived nitric oxide contributes to the maintenance of low resting pulmonary tone in normal children. Impairment of NO production may contribute to the elevated pulmonary vascular resistance that complicates some cases of congenital heart disease.

ENDOTHELION-DEPENDENT DILATION IS IMPAIRED IN THE LARGE ARTERIES OF HEALTHY YOUNG ADULT TYPE I DIABETICS AND IS RELATED TO THE PRESENCE OF MICROALBUMINURIA

Large vessel disease is a common and frequent complication of type I (insulin-dependent) diabetes mellitus (DM), and an important cause of premature death. As endothelion dysfunction is an early event in atherogenesis, we studied endothelion-dependent dilation non-invasively in 16 young adults (age 13-35 years, mean 24±2; 6 men, 10 women) with type I DM. All were life-long non-smokers, non-hypertensive and on no cardiovascular medications. None had symptoms or signs of large or small vessel disease. Vascular responses were compared with those of 32 healthy controls matched for age and sex. Using high resolution external echo Doppler, brachial artery diameter was measured at rest, in response to reactive hyperaemia (RH) (with flow increase leading to endothelion-dependent dilation) and after sublingual nitroglycerin (GTN) as an endothelion-independent dilator. Each diabetic had fasting cholesterol, glucose, insulin and glycosylated hemoglobin measured and 14/16 had urine albumin concentrations estimated. Vessel size, baseline flow and degree of RH (Doppler estimated) were similar in both groups. Flow mediated dilation (FMD) was impaired in the diabetics (61±7% compared to 10±1%, range 6-17%, p<0.02). GTN caused dilation in all subjects (diabetics: 18±1%; controls: 21±2%; p<NS), suggesting that reduced FMD in the diabetics was not related to age, blood pressure, age at diagnosis, glycosylated hemoglobin, blood sugar or total cholesterol levels. Reduced FMD was, however, related to the presence of albuminuria. None of six diabetics with a normal FMD (>6%) had evidence of microalbuminuria, but 5/8 of those with impaired FMD (≤6%) had urine albumin ≥6mg/l (p<0.01). Therefore healthy young adults with type I DM have impaired endothelion-dependent dilation, which may be present even in the absence of microalbuminuria, a marker of small vessel disease. This may provide a means of assessing early large vessel abnormalities in this high risk population.

NON-INSULIN DEPENDENT DIABETES IMPAIRS FLOW RELATED INCREASES IN ARTERIAL DIAMETER AND DISTENSIBILITY
J Goodfield, M W Ramsey, L Luddington, C J H Jones, D Owens, MM J Lewis, A H Henderson. Departments of Cardiology, Medicine and Pharmacology, University of Wales College of Medicine, Cardiff.

Non-insulin dependent diabetes (NIDDM) is associated with premature arterial stiffness and vascular disease which may be due to endothelion dysfunction, manifest as reduced activity of endothelion-derived relaxing factor (EDRF). We measured the flow-related increase in brachial arterial diameter and distensibility during reactive hyperaemia produced by releasing a cuff inflated to suprasystolic pressure for 5 minutes at the wrist. The endothelion-dependent response was compared to the endothelion-independent response to sublingual nitroglycerin (GTN 400µg) in 10 subjects with NIDDM (6 male, mean age 52±3.5yr, BP <150/90mmHg, serum cholesterol <6.5 mmol/l) and 10 age and sex matched controls.

We measured internal brachial artery diameter non-invasively during the cardiac cycle with an ultrasonic wall tracking device (AMA Wall Track System, resolution 3µm). Blood pressure was measured using a photo-plethysmographic method (Finapres), and blood flow with continuous wave Doppler. Measurements were taken nearest, at 1 min of reactive hyperaemia, and 3 minutes after sublingual GTN. Baseline flow and the increased flow seen during reactive hyperaemia were similar in both groups as were baseline measurements of arterial diameter and distensibility. In normal controls, brachial arterial diameter and distensibility increased during reactive hyperaemia (+10.3±4.6% and +0.6±0.29µm, respectively). In contrast, in patients with NIDDM, these flow-related changes in diameter and distensibility were attenuated (+1.25±4.7% and +0.51±0.24 µm respectively, both p<0.05 cf. normals). The endothelion-independent effects of GTN on diameter were similar in the two groups, while distensibility was significantly reduced in NIDDM though to a lesser extent than the hyperaemic response. Thus flow-related endothelion-dependent changes in arterial diameter and distensibility are significantly attenuated in NIDDM. This abnormality may contribute to the arterial stiffening and increased risk of vascular disease seen in patients with NIDDM.

ESTRADIOL-17B INCREASES FOREARM BLOOD FLOW IN MENOPAUSAL WOMEN. A DOUBLE BLIND RANDOMIZED STUDY
M Volterran, G M C Rosano, P A Poole-Wilson, A Coats, P Collins. National Heart & Lung Institute, London

Women are protected until the menopause from cardiovascular events and the incidence of cardiovascular disease appears to rise sharply with the decrease in ovarian hormones. Estradiol-17B has recently been shown to improve exercise-induced myocardial ischemia in menopausal patients with coronary artery disease and to normalise peripheral blood flow in female patients with syndrome X. The aim of the present study was to assess the effect of sublingual estradiol-17B (1mg, SLO) or sublingual placebo (SP) upon forearm blood flow (FBF) and vascular resistance (VR) in 10 menopausal normal volunteers (mean age 54±4.2 years). FBF and VR were measured by venous occlusion plethysmography before, and 40 minutes after either SLO or SP. Estradiol-17B plasma levels were greater after SLO when compared to SP (mean±SD; 3472±1381 vs 576±25.5, P<0.006). FBF and VR were similar before either SLO or SP (3.8±1 vs 3.5±0.2 ml/min/100ml forearm tissue, and 30.4±15.3 vs 32.6±15.3 units (P=NS), respectively. FBF was higher and vascular resistances lower after SLO when compared to SP (4.4±1.3 vs 2.3±1.3 ml/min/100ml forearm tissue (P<0.003) and 21.2±10.9 vs 47.8±21.3 units (P<0.005), respectively). In conclusion estradiol-17B increases FBF and reduces VR in menopausal women. The beneficial effect of estradiol-17B observed upon exercise-induced myocardial ischemia may be partially due to the effect of this hormone on afterload.
PLATELET-ENDOTHELIUM INTERACTIONS IN HUMANS: CHANGES IN PLATELET CYCLIC GUANOSINE MONOPHOSPHATE CONTENT IN PATIENTS WITH ENDOTHELIAL DYSFUNCTION
N P Andrews, N Dakak, W H Schenke, A A Quyyumi, National Heart Lung and Blood Institute, Bethesda, MD, USA

Vascular endothelial dysfunction occurs in patients with atherosclerosis and those exposed to risk factors for atherosclerosis. These patients are also at risk for thrombotic vascular events. To investigate whether platelet-endothelium interactions vary between patients with and those without endothelial dysfunction, we studied the effect on platelet cyclic GMP content (PcGMPc) of acetylcholine (ACH) (that causes release of nitric oxide (NO) from endothelium) and compared it to the effect of sodium nitroprusside (SNP), a direct donor of NO. The platelet and vascular effects of intra-arterial ACH and SNP were studied in the femoral circulation of 19 patients, 10 with coronary atherosclerosis and 9 with angiographically normal coronary and femoral arteries. Intra-femoral arterial infusion of ACH (55 pg/min for 2 and 10 min), and SNP (40 ng/min for 2 min in 8 patients) were given and blood flow velocity was measured with intravascular doppler (Flowire, Cardiometrics Inc.). PcGMPc was measured by radioimmunoassay after withdrawing blood samples from the femoral vein. The vasodilator response to ACH was heterogeneous, mean increase in flow velocity 69±57% (mean ± SD), range -8% to 225%, p<0.001 after 2 min. Patients with atherosclerosis or multiple risk factors had depressed flow responses p<0.05. PcGMPc change was also heterogeneous with ACH (mean change 11±33%, p=NS; range -37% to 88% increase). There was a highly significant correlation between the increase in flow velocity with ACH and the change in PcGMPc (r=0.57, p<0.001); thus, patients with depressed vasodilation did not increase PcGMPc, whereas those with good vasodilator response to ACH increased PcGMPc. In contrast, the vasodilator response to SNP (mean 113±59% increase in flow velocity) was similar in all patients and the PcGMPc increase (mean 113±16%, p<0.02) did not correlate with the PcGMPc responses to ACH. Thus, patients with endothelial dysfunction not only have depressed vascular smooth muscle responses to endothelial-dependent dilators due to reduced abluminal release of NO, but also have depressed luminal release of NO, as reflected by reduced PcGMPc content. This may explain the susceptibility of patients with endothelial dysfunction to thrombotic vascular events.

CORRECTIONS
Posters 62 and 313 were withdrawn.