ANNUAL MEETING OF THE BRITISH CARDIAC SOCIETY

Harrogate International Centre
23-25 May 1995

PROGRAMME AND ABSTRACTS OF PAPERS

★ The Meeting will be held in the Auditorium, the Royal Hall and the King’s Suite of the International Centre. The Harewood and Ripley Suites in the Moat House International Hotel, adjacent to the Centre, will also be used.

★ Posters will be presented in Halls B and C during the coffee, lunch and tea breaks, and the authors will be in attendance at these times.

★ The Exhibition, which this year has for the first time over 100 companies and organisations exhibiting, is in Exhibition Halls B, C and D.

★ Catering facilities are located in Exhibition Halls B and C.

★ A plan of the Harrogate International Centre is printed on the inside back cover of this programme.

★ The contact telephone number for the duration of the meeting is 01243 502889.

★ The Society thanks Bayer UK for the provision of the conference bags.

BRITISH CARDIAC SOCIETY

OFFICERS:

Mr D J Parker President (1993–95)
Dr R Balcon President Elect (1993–95)
Prof R W F Campbell Honorary Treasurer (1992–97)
Dr J G F Cleland Honorary Secretary (1994–96)
Dr N Brooks Assistant Secretary (1994–96)

COUNCIL: 1994–95

Dr N A Boon Mr A McLeod
Dr R M Boyle Dr H O’Kane
Prof H Dargie Dr M F Shiu
Prof M Davies Dr H Swanton
Dr R Hall Prof M Tynan
Prof D Hearse Dr D Ward
Dr S Hunter

Please remember to bring the supplement with you to the Harrogate Meeting
## BRITISH CARDIAC SOCIETY

### EIGHT AFFILIATED GROUPS

1. **British Pacing & Electrophysiology Group (BPEG)**
   - **President:** Dr Richard Sutton, Chelsea & Westminster Hospital (0181 746 8041)
   - **Treasurer:** Dr John Perrins, Leeds General Infirmary (0113 2432 799)
   - **Secretary:** Dr Anthony Nathan, St Bartholomew’s Hospital (0171 601 8708)

2. **British Cardiovascular Intervention Society (BCIS)**
   - **Chairman:** Dr Martin Rothman, Royal London Hospital (0171 377 7382)
   - **Treasurer:** Dr T R D Shaw, Western General Infirmary, Edinburgh (0131 537 1000)
   - **Secretary:** Dr Huon Gray, Wessex Cardiothoracic Centre, Southampton (01703 796232)

3. **British Nuclear Cardiology Group (BNCG)**
   - **Chairman:** Dr Dudley Pennell, Royal Brompton Hospital (0171 351 8810)
   - **Secretary:** Dr Elizabeth Prvulovich (0181 870 2116)

4. **British Society of Echocardiography (BSE)**
   - **Chairman:** Dr Mark Monaghan PhD, King’s College Hospital (0171 346 3512)
   - **Treasurer:** Dr Ed Southall, Torbay Hospital (01803 558257)
   - **Secretary:** Ms Caroline Westgate, Royal Brompton Hospital (0171 352 8121)
   - **Assistant Secretary:** Mr Graham Leach, St George’s Hospital (0181 672 1255)

5. **British Paediatric Cardiac Association (BPCA)**
   - **President:** Professor Michael Tynan, Guy’s Hospital (0171 955 4616)
   - **President Elect:** Dr Eric Silove, Children’s Hospital, Birmingham (0121 454 4851)
   - **Treasurer:** Professor Bob Anderson, Royal Brompton Hospital (0171 352 8121)
   - **Secretary:** Mr Babulal Sethia, Children’s Hospital, Birmingham (0121 454 4851)

6. **British Society for Cardiovascular Research (BSCR)**
   - **President:** Dr P Cummins, University of Birmingham Medical School, Department of Physiology (0121 414 6896)
   - **Treasurer:** Dr P England
   - **Secretary:** Dr S Coker, University of Liverpool (0151 794 5550)

7. **British Association for Cardiac Rehabilitation (BACR)**
   - **President:** Dr Hugh Bethell, Alton Health Centre, Alton (01420 84676)
   - **Treasurer:** Mr R Tipson, Action Heart, Dudley (01384 230222)
   - **Secretary:** Mrs Sally Turner (01420 544794)

8. **Association of British Cardiac Nurses (including ICNS) – Affiliated May 1995**
BRITISH CARDIAC SOCIETY

COMMITTEES OF THE BRITISH CARDIAC SOCIETY 1995

Joint Audit & Medical Practice Committee
David de Bono (Chairman) (BCS)

Epidemiology & Prevention Committee
David Wood (Chairman)

Technicians' Committee
Mick Martin (Chairman)

Education Committee
Stephen Ball (Chairman)

Ethical & Legal Committee
Keith Fox (Chairman)

Training & Manpower Committee
Michael Webb-Peploe (Chairman)

The Programme Committee for this meeting was:
Andrew Henderson (Chairman), Nick Brooks, Ronnie Campbell, John Cleland, Andrew McLeod, Paul Oldershaw, John Parker

The Programme Committee wishes to acknowledge the generous help given in abstract selection by the following:

G D Angelini M J Davies W S Hillis D Pennell H D Tunstall-Pedoe
S G Ball W Davies S Holmberg J R Pepper A Tweddle
D H Bennett D de Bono J Horgan M Petch M Tynan
N Boon J Deansfield B R Keeton M R Rees R Underwood
R Bonser J Flint A Lahiri P Schofield P Vallance
R M Boyle K A A Fox M J Lewis M E Scott D Ward
N Buller A G Fraser J F Martin B Sethia P L Weissberg
J Bourke M Gamage W J McKenna N Shattock R West
N H Brooks J Gibbs A McLeod T R D Shaw D J Wheatley
R W F Campbell D Gibson R G Murray I Simpson R G Wilcox
J Caplin I Graham A Nathan J D Skehan D Wood
C Chan H Gray P Nihoyannopoulos A Struthers D Yellon
A J S Coats A Harley M Noble G R Sutherland
S Cobbe G Hart C Oakley R Sutton
H J Dargie A H Henderson P Oldershaw T Treasure

Names shown in bold are Designated Members.
# Programme at a Glance

## Tuesday 23 May

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<thead>
<tr>
<th>Time</th>
<th>Auditorium Plenary Sessions</th>
<th>King's Suite Moderated Posters</th>
<th>Harewood Suite BPCA &amp; Affiliated Groups</th>
<th>Ripley Suite Free Communications</th>
<th>Royal Hall Affiliated Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>08.30 – 10.00</td>
<td>The hibernating myocardium</td>
<td>New ideas and new techniques: papers 1-12</td>
<td>BPCA: The myocardium in congenital heart disease (I)</td>
<td>Pacing and arrhythmias: papers 13-18</td>
<td></td>
</tr>
<tr>
<td>12.30 – 14.00</td>
<td>Lunch: Exhibition: Posters</td>
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<tr>
<td>15.30 – 16.00</td>
<td>Tea Break: Exhibition: Posters</td>
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<tr>
<td>16.00 – 17.00</td>
<td>The Strickland-Goodall Lecture: Patients, persons and populations – potential for coronary prevention Prof David Wood</td>
<td>Cardiologists in Training</td>
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<tr>
<td>17.15 – 18.15</td>
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## Wednesday 24 May

<table>
<thead>
<tr>
<th>Time</th>
<th>Auditorium Plenary Sessions</th>
<th>King's Suite Moderated Posters</th>
<th>Harewood Suite BSCR &amp; Affiliated Groups</th>
<th>Ripley Suite Free Communications</th>
<th>Royal Hall Affiliated Groups</th>
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</thead>
<tbody>
<tr>
<td>08.30 – 10.00</td>
<td>Aortic root disease</td>
<td>Risk factors, outcomes and management strategies: papers 104-113</td>
<td>BSCR: Arrhythmias: Basic mechanisms to clinical application</td>
<td>Nuclear cardiology: papers 116-121</td>
<td>Registration and Extraordinary General Meeting</td>
</tr>
<tr>
<td>11.00 – 12.30</td>
<td>Young Research Workers Prize: papers A-D</td>
<td>Judges' Choice (2): papers 179-184</td>
<td>ACE and heart failure: papers 185-196</td>
<td>BNGC: Myocardial perfusion imaging</td>
<td>It's not as simple as EA-SY-GE</td>
</tr>
<tr>
<td>12.30 – 14.00</td>
<td>Lunch: Exhibition: Posters</td>
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<td>14.00 – 15.30</td>
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<td>15.30 – 16.00</td>
<td>Tea Break: Exhibition: Posters</td>
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<tr>
<td>16.00 – 17.00</td>
<td>The Paul Wood Lecture: The Master's Legacy, 1995 Dr Jane Somerville</td>
<td>Cardiologists in Training</td>
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<tr>
<td>17.00 – 18.30</td>
<td>Annual General Meeting (members only)</td>
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## Thursday 25 May

<table>
<thead>
<tr>
<th>Time</th>
<th>Auditorium Plenary Sessions</th>
<th>King's Suite Moderated Posters</th>
<th>Harewood Suite BACR &amp; Affiliated Groups</th>
<th>Ripley Suite Free Communications</th>
<th>Royal Hall Affiliated Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>08.30 – 10.00</td>
<td>Ablative techniques for treatment of arrhythmia</td>
<td>Challenging the myocardium: papers 203-214</td>
<td>BACR: Practical models of rehabilitation</td>
<td>Myocardial perfusion: papers 215-220</td>
<td>Mobile catheter laboratories</td>
</tr>
<tr>
<td>11.00 – 12.30</td>
<td>The results of the ASPIRE study</td>
<td>Lysis and clotting: papers 270-281</td>
<td>Vascular biology: papers 282-287</td>
<td>Echocardiography: papers 288-293</td>
<td>Treatment of heart failure</td>
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<tr>
<td>12.30 – 14.00</td>
<td>Lunch: Exhibition: Posters</td>
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<tr>
<td>14.00 – 16.00</td>
<td>Practical cardiology</td>
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<td>16.00</td>
<td>Finish</td>
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</table>

13.00-16.00: Prosthetic heart valves
1. Advanced nurse practitioners and the law
2. Heart Start UK
16.30: Annual General Meeting of ABCN
## COMMITTEE MEETINGS

### Charter Suite I (Moat House Hotel)

<table>
<thead>
<tr>
<th>Time</th>
<th>Committee</th>
</tr>
</thead>
<tbody>
<tr>
<td>07.30 – 08.30</td>
<td>Training and Manpower</td>
</tr>
<tr>
<td>13.00 – 14.00</td>
<td>RITA II Steering Committee of Investigators</td>
</tr>
<tr>
<td>17.15 – 18.15</td>
<td>RITA Nurses Get Together</td>
</tr>
<tr>
<td>13.00 – 14.00</td>
<td><em>British Heart Journal</em> Editorial Committee Meeting</td>
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### Charter Suite II (Moat House Hotel)

<table>
<thead>
<tr>
<th>Time</th>
<th>Committee</th>
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</thead>
<tbody>
<tr>
<td>13.00 – 14.00</td>
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</tr>
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<td>RITA Nurses Get Together</td>
</tr>
</tbody>
</table>

### Room VIP7 (Level 7, Conference Centre)

<table>
<thead>
<tr>
<th>Time</th>
<th>Committee</th>
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<tbody>
<tr>
<td>13.00 – 14.00</td>
<td>BPCA</td>
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<tr>
<td>12.30 – 14.00</td>
<td>Joint Audit + Medical Practice</td>
</tr>
<tr>
<td>12.30 – 14.00</td>
<td>Epidemiology + Prevention</td>
</tr>
</tbody>
</table>

### The Green Room (Level 5, Conference Centre)

<table>
<thead>
<tr>
<th>Time</th>
<th>Committee</th>
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<tbody>
<tr>
<td>12.30 – 14.00</td>
<td>SAC</td>
</tr>
<tr>
<td>17.15 – 18.15</td>
<td>BCIS</td>
</tr>
</tbody>
</table>

BPEG Harewood Suite 12.30 – 14.00 Tuesday
BNCG Harewood Suite 13.00 – 14.00 Wednesday
08.00  Conference Centre Entrance Foyer
Registration

08.30 – 10.00  Auditorium
Welcome by the President: Mr John Parker
Plenary session
The hibernating myocardium
Chairmen: Prof Keith Fox and Mr John Parker
The pathophysiology of hibernating myocardium
Prof Gerd Heusch
Imaging the heart for hibernating myocardium
Dr Richard Underwood
The clinical relevance of hibernating myocardium
Prof Roberto Ferrari
King’s Suite
Moderated posters
New ideas and new techniques
Chairmen: Prof Ronnie Campbell
Papers 1–12

08.30 – 10.00  Harewood Suite
British Paediatric Cardiac Association
The myocardium in congenital heart disease
The molecular genetics of the myocardium
Prof Bill McKenna
Growth and development of the ventricle
Dr Yen Ho
Discussion
Appropriate and inappropriate ventricular growth
and hypertrophy
Dr Michael Vogel
Discussion

08.30 – 10.00  Ripley Suite
Free communications
Pacing and arrhythmias
Chairman: Dr Andrew Rae
Papers 13–18

10.00 – 11.00  Exhibition Halls B, C & D
Coffee (B & C)
Poster viewing (B & C) – Posters 19–60
Exhibition viewing (B, C & D)

11.00 – 12.30  Auditorium
Judges’ Choice 1
Chairman: Dr John Cleland
Papers 61–67

King’s Suite
Moderated posters
Clinical and experimental vascular biology
Chairmen: Prof Andrew Henderson and
Dr Patrick Vallance  Papers 68–79

Harewood Suite
British Paediatric Cardiac Association
The conditioning of skeletal muscle
Prof Stanley Salmons
Current status of cardiomyoplasty in the
management of patients with ventricular
dysfunction
Mr Tim Hooper
Discussion

Ripley Suite
Free communications
Pathophysiology: Expression, dynamics and
impact
Chairman: Dr Peter Schofield
Papers 80–85

Royal Hall
British Cardiovascular Intervention Society
UK coronary angioplasty 1995 – For whom, by
whom and where?
The panel: Dr Martin Rothman, Dr Roger Boyle
and Mr John Parker
Viewpoint of the purchaser: Dr Peter Doyle (Senior
Medical Officer, Department of Health)
Viewpoint of the provider: Dr Raphael Balcon
Discussion/comments from the floor

12.30 – 14.00  Exhibition Halls B, C & D
Lunch (B & C)
Poster viewing (B & C) – Posters 19–60
Exhibition viewing (B, C & D)

14.00 – 15.30  King’s Suite
Moderated posters
Heart and lungs: Viability, performance and
replacements
Chairman: Prof Keith Fox
Papers 86–97

Harewood Suite
British Pacing and Electrophysiology Group
Atrial fibrillation
Chairman: Dr Anthony Nathan
How to remain in sinus rhythm
Prof John Camm
Intervention for atrial fibrillation
Dr Wyn Davies
Anticoagulation in patients with atrial fibrillation
Dr Richard Sutton

Ripley Suite
Free communications
Myocardial hypertrophy
Chairman: Prof Philip Poole-Wilson
Papers 98–103

Royal Hall
British Society of Echocardiography
Controversies in echocardiography
Chairman: Dr Mark Monaghan
Two topics will be debated: 14.00 – 14.30
There is no point in making quantitative
measurements of left ventricular function
Chairman: Dr Gordon Williams
Protagonist: Dr Simon Gibbs
Antagonist: Dr Derek Gibson
14.30 – 15.00
Stress echocardiography is not cost effective
Chairman: Dr Geoffrey Richardson
Protagonist: Dr Michael Norrell
Antagonist: Dr Petros Nihoyannopoulos
15.00 – 15.30
Guest Lecture – Speaker: Dr Wolfgang Fehske,
University Hospital of Bonn
Chairman: Dr Mark Monaghan
Current status of 3D echocardiography

15.30 – 16.00  Exhibition Halls B, C & D
Tea (B & C)
Poster viewing (B & C) – Posters 19–60
Exhibition viewing (B, C & D)

16.00 – 17.00  Auditorium
Strickland Goodall Lecture
Patients, persons and populations – potential for
coronary prevention
Prof David Wood

17.15 – 18.15  British Paediatric Cardiac Association AGM

17.15 – 18.15  Harewood Suite
Cardiologists in Training Liaison Meeting
Training and manpower in cardiology – update for
trainees
Chairman’s introduction: Mr John Parker
Introduction of the Unified Training Grade
Dr Roger Boyle (Secretary, SAC in Cardiovascular
Medicine)
Manpower issues
Dr Michael Webb-Peploe (Chairman, Training and
Manpower Committee, BCS)
Summary
Dr Roger Hall (Chairman, SAC in Cardiovascular
Medicine)
Questions
(1) MODERATED POSTER

Percutaneous Transluminal Coronary Ultrasonic Angioplasty: Immediate, 24 hour and six month quantitative angiographic assessment
Clare Wales, J Gunn, J Ahmed, N Woolcock, S Campbell, R Bower, D Oakley, D Croome, D Cumberland. Department of Cardiology, Northern General Hospital NHS Trust, Sheffield

The coronary ultrasound (PTCUA) catheter is of standard rapid-exchange design, delivering 19.5kHz vibrations of 10-20μm amplitude at 20-30 Hz energy via a 1.2 or 1.7mm ball tip. We assessed its efficacy quantitatively and by quantitative angiography (QCA; Phillips) in 56 patients, mean age 57 ± 9 years, 46 male, with good left ventricular function and symptom-free single vessel disease. Mean (range) lesion yield pressure after PTCUA was 3.4 (1.8-4.0) atm. One lesion, undilatable in two previous PTCAcs, yielded after PTCUA at only 2 atm. Two chronic total occlusions, unreachable by conventional means, were easily traversed and dilated after PTCUA. One lesion was highly resistant, bursting four balloons; after PTCUA it was dilated and stented successfully. At 24h, 2 of 7 total occlusions re-occluded without sequelae; a third showed dissection and thrombus pressure. It may have a particular role in chronic total occlusion. MLD appears to be maintained between 24h and 6 months; early data suggest a low restenosis rate by traditional criteria.

![Table]

Pre PTCUA PTC A 24h 6 months
MLD 0.66 1.63 1.98 1.75 1.78
Stenosis 75 60 42 38 37

At 6 months, 5/34 patients needed further invasive treatment; and by the >50% diameter stenosis definition, 24% of lesions were restenosed. Conclusions. PTCUA is safe and effective, with adjunctive balloon dilatation, in the treatment of coronary artery disease. It is associated with a low lesion yield pressure at 2 atm.

(2) MODERATED POSTER

INFLUENCE OF LOCAL THROMBUS FORMATION ON LONG TERM RESTENOSIS FOLLOWING PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY
AG Violaiis, R Melker, PW Serruys. The Thoraxcentre, Erasmus University Rotterdam, The Netherlands

Experimental studies suggest that mural thrombus formation may be involved in post angioplasty restenosis. The aim of our study was to examine the role of thrombus in the clinical situation. The study population comprised 2,950 patients (583 lesions) who were prospectively enrolled into 4 major restenosis trials (MERCATOR, MARCATOR, CAPTURE, PARK) and who had quantitative angiographic (QCA) follow up. As the test compounds demonstrated no angiographic or clinical benefit, data from the active and placebo groups were pooled. The presence of thrombus either before, or after, the procedure was defined as the presence of a generalised haziness or filling defect within the arterial lumen. Restenosis was assessed using both a categorical (>50% diameter stenosis at follow up) and a continuous approach (absolute loss = the change in minimal lumen diameter (MLD) between post coronary angioplasty and follow up, and relative loss = change in MLD corrected for vessel size). The study population included 160 lesions with, and 3423 lesions without thrombus. The categorical restenosis rate was significantly higher in lesions containing thrombus, 43.1% vs 34.9%, p < 0.01, Relative risk 1.28, CI 1.05-1.54, as were the absolute and relative loss (Absolute loss 0.43 ± 0.66 vs 0.32 ± 0.52mm, Relative loss 0.16 ± 0.26 vs 0.13 ± 0.21, both p < 0.05). The higher restenosis in lesions containing thrombus was primarily due to an increased incidence of occlusions at follow up angiography in this group, 13.8% vs 5.7%, p < 0.001, Relative risk 2.639, 95% CI 1.64-4.23. If lesions which went on to occlude at follow up angiography were excluded from the analysis the restenosis rate between the two groups was similar using both the categorical (34.1% vs 30.1%, Relative loss 0.18 ± 0.43 vs 0.13 ± 0.21, Relative risk 1.36, 95% CI 0.83-2.22) and continuous approach (Absolute loss 0.23 ± 0.46 vs 0.24 ± 0.42, p = ns, Relative loss 0.09 ± 0.17 vs 0.09 ± 0.15, p = ns). Conclusion: Our results indicate that the presence of thrombus at the coronary angioplasty site is associated with higher restenosis using both the categorical and continuous approach. This reflects an increased risk of late occlusion and intimal hyperplasia after coronary angioplasty.

(3) MODERATED POSTER

QUANTITATIVE ANALYSIS OF EARLY RECEOLL, DISEASE AND RESTENOSIS FOLLOWING ANGIOPLASTY OF TOTAL OCCLUSIONS
S G Ray, C E Bulter, I M Penn, D R Ricci, M D Mosovich, R Fox. Vancouver Hospital and Health Sciences Centre, Vancouver, Canada and Cardiothoracic Centre, Liverpool

Total coronary occlusions have a high incidence of late restenosis and reocclusion following angioplasty (PTCA). Our objective was to determine the magnitude of early recoil and the incidence of complex dissection occurring within 24 hours of the PTCA to a total coronary occlusion. Thirty three patients with an angiographically successful PTCA of an occluded vessel (median duration 2 weeks) were studied. All remained on continuous intravenous heparin until re-look angiography at a mean of 22.1±2.1 hours. Qualitative and quantitative analysis was performed of pre, immediate post and re-look angiograms.

Results. Procedural variables were: reference segment 2.7±0.69mm, balloon artery ratio 1.0±0.17, inflation pressure 8.7±2.8 atm, inflation time 10.0±4.9.

<table>
<thead>
<tr>
<th>Post</th>
<th>Relook</th>
<th>p</th>
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<tbody>
<tr>
<td>MLD (mm)</td>
<td>1.7±0.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Recoil (%)</td>
<td>38±13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dissection</td>
<td>2/33</td>
<td>&lt;0.01</td>
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(MLD minimum lumen diameter). Six vessels (18%) were occluded by the time of re-look, all clinically silent. Immediate post PTCA recoil did not predict recoil or reocclusion on re-look angiography (p = 0.10).

Summary. We conclude that there is marked immediate recoil after PTCA of total occlusions. Recoil progresses over the 24 hours after PTCA and is associated with worsening dissection. Early reocclusion is common and typically silent. Results immediately after PTCA do not predict findings at 24 hours. Coronary stenting may provide a means to counter these adverse mechanical factors and improve long term patency.

(4) MODERATED POSTER

CLINICAL, PROCEDURAL AND QUANTITATIVE ANGIOGRAPHIC VARIABLES PREDICTIVE OF LUMINAL RE-NARROWING AND RE-OCLUSION FOLLOWING SUCCESSFUL DILATATION OF TOTAL OCCLUSIONS
AG Violais, R Melker, PW Serruys. The Thoraxcentre, Erasmus University, Rotterdam, The Netherlands

We have previously shown that successfully dilated occlusions have a higher restenosis rate compared to matched non-occlusive lesions, predominantly due to a high incidence of re-occlusion at follow up angiography. The aim of our present study was to examine for clinical, procedural and quantitative angiographic predictors of restenosis (using both the categorical (>50% diameter stenosis at follow up) and continuous approach (the absolute loss = the change in minimal lumen diameter between post coronary angioplasty and follow up (mm)) as well as re-occlusion using multivariate analysis. Our study population comprised 266 successfully dilated total occlusions with quantitative angiographic follow up. The overall categorical restenosis rate (>50% DS at fup) was 44.7%. Re-occlusion at the time of follow up angiography occurred in 19.2% of cases. Multiple logistic regression analysis suggested the number of diseased vessels (p = 0.034) and the percentage stenosis post-PTCA (p = 0.049) to be positively related and the duration of angina (days) (p = 0.032) to be negatively related with the probability of the occurrence of restenosis using the categorical (>50%DS at fup) definition. When multiple linear regression analysis was used to evaluate the continuous measure of restenosis, the absolute loss, of the variables assessed total inflation time (sec) (p = 0.0004) and the presence of thrombus (p = 0.021) were both found to be positively related to absolute loss. When examining reocclusion at follow up angiography, multiple regression analysis of all available variables suggested the total inflation time (sec) to be positively related (p = 0.002) and the reference diameter post-PTCA (mm, p = 0.009) negatively related to reocclusion at follow up angiography. Conclusion: Our data suggest that a number of clinical, procedural and angiographic variables can influence the likelihood of restenosis and reocclusion following successful PTCA of total occlusions. Measures aimed atameliorating restenosis and reocclusion in this group of lesions should be focused in this direction.

*Papers presented at ARDS, 1 May 1995. Downloaded from the BMJ website.
BLOOD FLOW REDUCTIONS AFTER STENT IMPLANTATION ARE UNAFFECTED BY ASPRIN AND HEPARIN

RK Aggarwal, RS More, MD Ezekowitz, DP de Bono, AH Gerickel
Department of Cardiology, University of Leicester and Yale University, New Haven, CT, USA.

Cyclical blood flow reductions (CFRs), resulting from platelet aggregation, are known to occur in stented coronary arteries and following angioplasty. To investigate the occurrence of CFRs following stent implantation, we implanted 21 commercially available stainless steel stents into the iliac arteries of 13 New Zealand White male rabbits. A 2mm angioplasty balloon, introduced via a femoral arteriotomy, was inflated at 8 atm. for 60s to induce deep arterial injury prior to insertion of a 3mm diameter stent at the same site. Following this, superficial femoral artery ligation reduced blood flow through the stent (mean [sd] reduction 56.5±16.2%). Flow was measured continuously for 120 min using a transit-time perivascular flowprobe (Transonic Systems, NY). Arterial occlusion was defined as flow <0.2 ml/min for >10min, flow variation as a return to flow >0.2 ml/min within 10 min. Three groups of animals were compared. Gr. A received no antiplatelet or anticoagulant drugs. Gr. B aspirin (ASA) 6mg/kg/day for 5 days prior to stenting and Gr. C ASA and heparin 300u/kg. Results:

<table>
<thead>
<tr>
<th>Gr</th>
<th>No. stents</th>
<th>T(time) mean (sd)</th>
<th>Tflow variation (hr-1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>6 of 9</td>
<td>36.6±16.7</td>
<td>26.8±21.7</td>
</tr>
<tr>
<td>B</td>
<td>7 of 9</td>
<td>50±11.9</td>
<td>28±14.1</td>
</tr>
<tr>
<td>C</td>
<td>2 of 3</td>
<td>60±14.1</td>
<td>32±10.6</td>
</tr>
</tbody>
</table>

(Differences between the 3 groups in each category not significant). CFRs occurred in all 15 (100%) stented arteries that had occlusive thrombus at t=120 min compared to only 2 of 6 (33%) vessels that did not (P<0.01). Conclusion: CFRs following stent insertion suggest that periodic platelet thrombus formation plays a central role in stent thrombosis. Aspirin and heparin do not reduce the incidence or frequency of flow variation after stent implantation in a deep arterial injury in vivo model. More potent antiplatelet agents are needed to reduce stent related thrombosis.

RESULTS OF STENT IMPLANTATION FOR SEVERE PULMONARY ARTERY STENOSIS IN CHILDREN LESS THAN THREE YEARS OF AGE

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Endovascular stents have been used with success in the treatment of branch pulmonary artery (PA) stenosis in older children. We investigated the feasibility of placing such stents in children <3 years of age. 22 children had a total of 28 stents placed in the branch pulmonary arteries between April 1991 and October 1993. Age ranged from 1 to 34 months (median 16 months) and weight from 2.7 to 17 kg (median 9.6 kg). The general indication for stent placement was a haemodynamically significant branch PA stenosis which persisted following balloon dilation. A significant increase in the diameter of the stenotic area was achieved in all cases (mean ± SD; pre = 3 ± 1.1 mm and post 6.3 ± 1.9 mm; p < 0.001). In 2 patients the proximal portion of an articulated stent detached and embolised to the main PA. 7 Lobar vessels were covered by a stent with diminution of flow in 2 cases. In one of these there was no antegrade flow in the covered vessel 10 months later. Angiographic improvement in the area of stenosis was maintained at follow up of between 5 and 25 months. The stent was redilated after an interval of between 5 and 25 months in 10 patients achieving an increase in diameter of between 0.6 to 3 mm.

Transcatheter placement of stents is technically feasible in small children. Clinical and angiographic improvement is maintained in the intermediate term but the success of redilation more than 24 months post implantation remains to be determined.

LASER VALVOTOMY WITH BALLOON VALVOLAPSY AS PRIMARY TREATMENT FOR PULMONARY ATRESIA WITH INTACT VENTRICULAR SEPTUM: INTENTION TO TREAT ANALYSIS OF 4 YEARS' EXPERIENCE

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Since 1991 we have used laser valvotomy with balloon dilatation as primary treatment for pulmonary atresia with intact ventricular septum and trispirate right ventricle. The procedure was attempted in 7 infants aged 1-70 (median 6.5) days with weight of 2.1-4.7 (mean 3.5) kg. Patients were selected for treatment if the right ventricle was trispirate with no more than minor tricuspid valve hypoplasia. Under general anaesthetic a 4 or 5F standard Cobra catheter was positioned below the imperforate pulmonary valve. The orientation of the catheter tip was adjusted using hand injection of contrast and a frozen lateral left ventriculogram showing the pulmonary trunk opacified via the duct. No arterial catheter was used. The valve was perforated using a Tridynex 0.018" laser guide wire with 1-3 continuous wave laser firings of 3-5W of 5-5s duration. The laser wire or an .018" FlexT wire was passed into the pulmonary trunk and then into the right pulmonary artery or the descending aorta via the duct. The valve was dilated with a 3-3.5F coronary angioplasty balloon of 2-4mm diameter and then by a 5-8mm Tyshak or Schneider balloon.

Valvotomy failed in only one patient due to laser breakdown. The only complication was transient RVF in one case. Prostaglandin E2 was stopped immediately in all but one patient who remained dependent on the duct. For the 48 days the only study operation performed was in the one in whom laser valvotomy failed. Right ventricular outflow (RVOT) velocity after duct closure was 2.0-3.8 (mean 2.9+m2) and O2 saturation was 70-90% (mean 77). 2 patients had a repeat balloon dilation at 22 and 16 days after laser valvotomy. At least follow up 23-1720 (median 112) days after valvotomy RVOT velocities were 2.0-4.5 (median 3.2) m/s and O2 saturation ranged from 80 to 97%. One child of 4 in whom a waiting surgery for relief of infundibular stenosis and closure of ASD and one aged 4 months is awaiting repeat balloon dilation. Laser valvotomy with balloon dilation is an effective and safe alternative to surgical pulmonary valvotomy in this group of patients.

Trans-radial cardiac diagnostic and interventional procedures in patients with severe peripheral vascular disease

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Trans-radial cardiac procedures are now possible because of improvements in catheter and balloon technology. We report our experience of this technique in 46 patients with peripheral vascular disease (PVD). There were 34 males and 12 females (mean 66 years, range 47-78 years). Indications for the trans-radial approach were: failed femoral (n=8), previous or impending aortofemoral surgery (n=24), severe intermittent claudication (n=10) and abdominal aortic aneurysm (n=4). Four patients had undergone previous carotid or subclavian surgery. Allen's test demonstrated adequate upper limb circulation prior to the procedure. The radial was attempted in 42 and the left in 4 (indication=previous right subclavian surgery, right axillo-bifemoral graft, left internal mammary grafts [ima] x2). The radial artery was punctured using a 21G needle and a 5F sheath was inserted using the Seldinger technique. Judkins-type 5F catheters were used for diagnostic studies. The radial artery was cannulated in 45/46 (97.8%) and 43 patients had a successful study (overall success 93.4%). In two patients the guide wire did not pass to the aorta and the radial artery could not be cannulated in one patient. Twenty six patients had a standard cardiac catheter, 6 a cardiac catheter plus graft study (including ima), 6 a cardiac catheter and peripheral vascular studies while 5 had a diagnostic study with follow-on PCTA. Patients had three vessel disease (n=30), two vessel disease (n=7) or single vessel disease (n=6). PCTA was performed using a 6F sheath and 6F guiding catheters in 5 patients. Four of the 5 had an insertion of an intra-coronary stent (1 bail out and 3 elective, crimped on Palmaz-Schatz plus monorail balloon). One stent patient had a transfusion because of a spontaneous retroperitoneal bleed, despite the trans-radial approach. The only complication of diagnostic studies was one patient (failed procedure) who developed a forearm haematoma with paraphrenia of the hand, which settled within 3 weeks of conservative treatment. There were no ischaemic complications of the hand. The radial artery was palpable in 34/35 (97%) patients who were assessed one month following the procedure. In conclusion trans-radial diagnostic and interventional procedures (including intra-coronary stenting) can be performed safely, with a low complication rate in patients with severe PVD. This approach should be considered as an alternative to the Sones technique in these patients.
MODERATED POSTER

EVALUATION OF AN ULTRASONICALLY GUIDED VENEPUNCTURE TECHNIQUE FOR THE PLACEMENT OF PERMANENT PACING ELECTRODES

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Placement of permanent pacing electrodes by orthodox subclavian puncture is quickly becoming discredited in the cephalic vein, but is known to carry a higher risk of early complications. There is also evidence that late complications (for example, retrograde venopuncture, may be more likely with this approach. We have evaluated a method of puncturing the subclavian vein in its extrathoracic course using an ultrasound guidance system (Site-Rite, Dymax Corporation). Fifty consecutive patients requiring permanent single or dual chamber pacemakers were included in the study. The method was successful in 37 (74%) cases (13 dual chamber systems, 24 single chamber systems) and unsuccessful in 13 (26%) cases (1 dual chamber system, 12 single chamber). The time taken to achieve a successful cannulation of the vein was similar to that taken with orthodox subclavian venepuncture, the average time taken being 32 seconds (range 5-130 seconds). There appeared to be a slight "learning curve" effect, and in many cases it would have been possible to identify patients in whom the method might not have been appropriate beforehand. There were no significant complications. The extrathoracic approach means that there is no risk of pneumo/haemothorax. Brusing observed in a higher proportion of cases than when using other techniques, but this was thought to be as a result of increased venopuncture attempts at the puncture site, as the tissues penetrated using this method are less dense than when using the orthodox approach. Extrathoracic subclavian venepuncture using the Site-Rite scanner in an easy technique to learn. Puncturing the subclavian under direct vision makes it an appropriate method for inexperienced operators, with a lower incidence of immediate complications and possibly fewer long term problems.

MODERATED POSTER

THE SIGNAL AVERAGED P WAVE IN ATRIOVENTRICULAR BLOCK: EVIDENCE FOR ABNORMAL ATRIAL CONDUCTION.

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The increased incidence of atrial fibrillation in patients paced with single chamber ventricular demand units is not exclusively confined to those with sinus node dysfunction. In patients with atrioventricular block (AVB) at the time of implantation, for example, it may include retrograde VA conduction and asynchronous atrial contraction. To assess whether atrial fibrillation may also be related to concurrent abnormality in atrial activation we performed signal averaged P wave (SAPW) recordings in 15 patients with dual chamber pacemakers compared to 21 control patients of similar age and sex ratio. The patient group comprised 11 males and 4 females with a mean(range)of 69(53-80) yrs. Controls comprised 12 males and 9 females with a mean age of 60(31-78) yrs. Ablation of an atrioventricular block (AVB) potential was performed in 10 patients who were functionally pacing in VDD mode at the time of study. SAPW recordings were performed using a selective P wave averaging system that ensured high fidelity of the signal average. Quantitative analysis comprised measurement of P wave duration after high pass filtering at 40 Hz and of low and high frequency energy after Fourier transformation of the P wave signal. We found increased P wave duration and energy in patients with AVB compared to controls.

AVB Controls

- Dur (ms): 146(6) 34(27)
- P20 (p20) 36.7±6.2 33.4±4.8
- P50 (p50) 61.3±10.7 51.3±7.9
- P80 (p80) 193.2±36.1 133.4±26.1

Spontaneous ectopy is a legitimate target for ablative therapy. We studied 5 females (mean age 45 years), with idiopathic non-radiated RVT VT and 3 patients with AVB. The clinical tachycardia with LBBB and inferior axis, was sustained in 3 patients and non-sustained in 2. All patients were syncopal or presyncopal. Spontaneous ventricular ectopy of identical 12 lead morphology was seen at rest in all patients. Resting ECG, echocardiography, right and left ventriculography and coronary angiography were normal in all patients. All had failed one or more antiarrhythmic agents. To confirm the identical morphology of ectopy and clinical arrhythmia, sustained or non-sustained VT was induced once using isoprenaline infusion and the RVT VT origin of the arrhythmia crudely localised with a decapolar catheter. Isoprenaline was discontinued and activation mapping of the monomorphic ectopy performed in the drug-free state in all cases. The onset of surface QRS complex and right ventricular endocardial signals were used as fixed references and onset local digital and on-line digital timer automatically recorded the timing of signals from a roving ablation catheter in the RVT. Results: The target arrhythmia was successfully ablated in all cases, with a mean of 4.1 RF pulses. All successful ablation sites were on the septal RVT VT wall where local electrodes proceeded references by up to 35 msec. No ectopy or VT could be induced post ablation. All patients are asymptomatic and free of arrhythmia on no therapy at a mean follow-up of 16 months. Conclusions: (i) patients with idiopathic RVT VT frequently display ectopy of identical morphology to the clinical VT (ii) this ectopy is a lesser manifestation of the symptomatic VT (iii) such ectopy is a legitimate target for RF ablation (iii) RF ablation of ectopy also abolishes sustained and non-sustained VT (iv) by avoiding the need for repeated VT induction, this technique improves ablation catheter positioning and patient comfort.
NEW INSIGHT INTO AN ARRHYTHMOMEGIC MECHANISM IN THE ISCHAEMIC HUMAN HEART.

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Departments of Academic and Clinical Cardiology, UCL Hospitals, Departments of Physiology, Charing Cross Hospital, London and University of Leeds.

Regional variation in the activation time (AT) between action potentials across the ischaemic border may initiate arrhythmia by local current flow. We present evidence in the human heart that ischaemia alters the normal relationship between APD and cycle length in a manner which may greatly facilitate arrhythmogenesis by a premature beat. Monophasic action potentials were recorded in 14 patients (23 sites) from the right ventricular septum during angioplasty of a mid left anterior descending coronary artery lesion. A test pulse sequence with shorter and longer coupling intervals was incorporated. Under control conditions test beats with the shortest coupling interval had the shortest action potential duration (APD) and test beats with the longer coupling interval had a longer APD. This resulted in a rising curvilinear relationship between increasing APD and increasing diastolic interval. During ischaemia the APD dependence on cycle length was minimised thereby flattening the curve: eg, at shortest intervals APD shortening (control 16.7±1.7ms; ischaemia 0.14±1.2ms; P<0.0001) and at long intervals APD lengthening (control 5.5±2.0ms; ischaemia 0.5±1.0ms; P<0.05).

Using best fit curves we calculated the AT delay required for action potential repolarisation in the ischaemic zone to be delayed until after repolarisation in the adjacent normal zone. This fulfilled experimental criteria for local current flow to reexcite across the ischaemic border: eg, for a 40ms shortening of the steady state (SS) APD (cycle length 600ms) the AT delay required for a premature beat of cycle length 500ms to reexcite was 19.6ms: and for a premature beat with cycle length 400ms the AT delay was 1.4ms. We conclude that: (1) the cycle length dependence of APD in the human heart, (2) calculated AT delay required for a premature beat to generate a voltage gradient sufficient to reexcite across a border zone was minimised at short coupling intervals and maximised at long coupling intervals.

DIASTOLIC MAPPING OF REENTRANT CIRCUITS IN POST-INFARCT VENTRICULAR TACHYCARDIA IN MAN

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Ventricular tachycardia (VT) in the post-infarct setting in man is thought to be due to a reentrant mechanism, but there is little objective evidence for this. This study examined the ability of diastolic mapping to confirm the presence of a "hardwired" VT circuit in patients undergoing intraprocedural multipoint mapping of VT.

Seven patients were mapped using simultaneous recordings from 224 endocardial and epicardial points, by means of balloon and sock multi-electrode arrays. A total of 14 figure-8 VTs were induced and mapped. A definite or putative reentrant tract (with deficit in continuity of diastolic activity of <100ms temporally and <10mm spatially) was sought.

Diastolic activity was found in 7% electrograms, and most of this was located endocardially. Definite or putative reentrant circuits could be defined for 4 VTs (29%). Diastolic potentials closely adjacent to the site of earliest endocardial activation were seen in 8 VTs (57%), but only half of these formed part of a complete reentrant circuit. Electrograms at these points showed diastolic potentials immediately preceding systolic activation which was more than 40 ms ahead of VT onset on the surface electrocardiogram. The systolic component at these sites was often non-sustained and fragmented stellate. Conclusion: Diastolic mapping demonstrates the entire "hardwired" VT circuit in a modest number of patients. This confirms that reentry is the causal mechanism in a sizeable minority of post-infarct VTs in man. Diastolic potentials are found in relation to earliest systolic activation in very few electrograms. These findings have important implications for the intra-operative and catheter ablation management of VT.

THE HAEMODYNAMIC IMPACT OF VENTRICULAR TACHYCARDIA: PREDICTING THE OUTCOME

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Remarkably little is known about ventricular tachycardia (VT) haemodynamics, yet they have importance for both management and prognosis. Aims: To characterise VT haemodynamics and to predict collapse. Methods: 48 VT patients were grouped by symptoms - cardiac arrest (n=11), presyncpe (n=22) or asymptomatic (n=15). VT rate, ejection fraction, age and cardiac disease were recorded. Data were compared by Mann-Whitney U tests. VT was induced in a subset of 18 patients; intra-arterial blood pressure (BP) was recorded continuously. Synchronous arterial pacing was added during VT in 2 patients.

Results: The cardiac arrest group had a faster median VT rate (239 bpm) than either the presyncpe group (182 bpm p<0.01) or the asymptomatic group (160 bpm p<0.001). However, there was overlap: all groups included patients with a VT rate between 175-220 bpm (17 patients in total). In patients with myocardial infarction (MI), age, ejection fraction, number of MIs, and extent of coronary disease did not predict symptoms. Patients with prior MI, however, were more likely to be symptomatic than patients without MI (odds ratio = 3.94). VT was induced by programmed stimulation in 18 patients - 13 patients were 'stable' and conscious; 5 patients lost consciousness and required urgent VT termination. Not surprisingly, this VT effect was dependent upon BP. The eventual outcome, however, was predicted by BP as early as 15 seconds after VT initiation. Stable patients had a systolic BP consistently above 40 mmHg at 15 seconds. Anecdotally, BP increased markedly in 1 of 2 patients who received synchronous atrial pacing during VT.

Conclusion: 77% (37 of 48 patients) 'tolerated' VT and did not suffer cardiac arrest. 31% (15 of 48 patients) had no cerebral or cardiac symptoms. Rate alone did not predict VT haemodynamics, as prior MI was also influential. Within just 15 seconds, systolic BP identified patients who tolerated VT (>40mmHg) from those who would require urgent attention (<40mmHg). This could have important implications for the operation of implantable defibrillators and other non-pharmacological antiarrhythmic strategies.

A HAEMODYNAMIC VERIFICATION SYSTEM FOR AN AUTOMATED EXTERNAL DEFIBRILLATOR

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Automated external defibrillators use ECG analysis algorithms to identify ventricular fibrillation (VF) and ventricular tachycardia (VT). VT can be associated with a wide range of blood pressures and currently automated defibrillators determine the need for DC shock based on the heart rate alone. The incorporation of a haemodynamic sensor may improve the accuracy of an automated defibrillator. The impedance cardiogram (ICG) has been used to non-invasively measure cardiac output and its peak value, dI/dt(dmax), correlates well with aortic blood flow. A system has been developed whereby the ICG can be recorded at cardiac arrests through the same two ECG/defibrillator pads, placed in an antero-apical position, that are used to monitor or shock the patient. At 111 cardiac arrest calls and in 20 healthy volunteers (C) the ICG was recorded for a period of at least 10s without CPR artefact: 9 records were rejected because of poor quality. The rhythms were divided into VF, asystole (As), agonal rhythm (Ag), electromechanical dissociation (EMD), VT requiring DC shock (VTs) and VT not requiring DC shock (VTn). The ICG tracings were ensemble averaged to remove any electrical noise and dI/dt(dmax) was measured. The results are tabulated:

<table>
<thead>
<tr>
<th>ds/dt(dmax)</th>
<th>C VTs</th>
<th>VTs EMD</th>
<th>Ag</th>
<th>VF</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean/Ds</td>
<td>0.622</td>
<td>0.413</td>
<td>0.191</td>
<td>0.178</td>
</tr>
<tr>
<td>SEM/Ds</td>
<td>0.058</td>
<td>0.041</td>
<td>0.032</td>
<td>0.022</td>
</tr>
</tbody>
</table>

Number | 20 20 7 22 20 | 14 19 |

p<0.01 compared with the control group, 1 p<0.01 compared with non-shockable VT. Mean ds/dt(dmax) in the control group was significantly greater than for all other groups. Mean ds/dt(dmax) with VTs was significantly greater than with the pulseless rhythms EMD, Ag, VF and As. There was a significant difference between VTs and the pulseless rhythms. Thus the ICG is a potential haemodynamic sensor for an automated external defibrillator.
(17)

SHOULD FLECAINIDE NOW BE THE FIRST CHOICE DRUG FOR SUPPRESSION OF INFANT SUPRAVENTRICULAR TACHYCARDIA?
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Supraventricular tachycardia (SVT) in early infancy is potentially life-threatening. Natural history studies suggest only 62% will have early recurrence but it is common practice to treat all. From 1986 to 1993, 39 infants presented with atrioventricular re-entry tachycardia at age 1-330 days (median 12). Once sinus rhythm was restored (using ice in 29, adenosine in 6 and DC shock in 4), all patients received prophylactic treatment. Digoxin was effective in 16/35 (46%). Flecainide was effective in 19/19 (100%) of those failing digoxin treatment and in 22/22 (96%) overall. The initial dose of flecainide was 3.2-13.5 mg/kg/day. The dose was adjusted in 11 patients because of low or high blood concentrations or to improve SVT control. Blood concentrations were >1000 ng/ml in 5 without untoward effect but the dose was reduced. The table illustrates the dose-concentration relationship.

<table>
<thead>
<tr>
<th>Plasma concentration ng/ml</th>
<th>&lt;300</th>
<th>300-800</th>
<th>&gt;800</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose mg/kg/day</td>
<td>4</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>≤ 6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-8</td>
<td>2</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>≥ 8</td>
<td>1</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>

Comparison with earlier natural history studies suggest that digoxin is ineffective in prophylaxis of infant SVT. Oral flecainide is safe and effective and may now be preferred as primary prophylaxis. Flecainide dosing is not easily predicted and needs careful monitoring.

(19) POSTER

EFFECTS OF INHIBITION OF NITRIC OXIDE SYNTHESIS IN PROXIMAL AND DISTAL SEGMENTS IN PATIENTS WITH CORONARY ARTERY DISEASE
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Inhibition of nitric oxide synthesis causes a decrease in basal diameter of distal epicardial coronary arteries in patients with normal coronary arteries. The effects of inhibition of nitric oxide synthesis with Nω-nitro-L-arginine methyl ester (LNAME) in atherosomar coronary arteries was evaluated in 13 patients with chronic stable angina (aged 57±7 years, 11 males) due to angiographically documented coronary artery disease and in 8 patients (aged 50±5 years, 4 males) with angiographically normal coronary arteries. LNAME was infused intracoronary at 4, 8 and 16 µmol/min each for 4 minutes. In response to low LNAME, 4 µmol/min, there was a significant (p=0.05) reduction in luminal diameter of both proximal (from 3.40±0.28 to 3.35±0.28 mm) and distal (from 1.3±0.07 to 1.2±0.06 mm) segments in patients with normal arteries. In patients with atherosomar arteries there was a reduction in diameter of the distal segments (from 1.44±0.06 to 1.3±0.07 mm) but no change occurred in the proximal segments (from 2.95±0.16 to 2.89±0.16 mm). In response to high LNAME, 16 µmol/min, there was a significant (p=0.01) reduction in luminal diameter of both proximal (from 2.53±0.27 to 2.33±0.26 mm) and distal (from 1.10±0.06 to 0.95±0.06 mm) segments in the patients with normal arteries. In the patients with atherosomar arteries the distal segments decreased in diameter (from 1.3±0.07 to 1.17±0.06 mm) but no change occurred in the proximal segments (from 3.1±0.12 to 3.08±0.14 mm). The magnitude of the distal vessel constriction was similar in both the patients with normal and in those with atherosomar arteries (-9.6±2.1% and -10.9±2.6% respectively, p=N.S.). In patients with chronic stable angina due to coronary artery disease inhibition of basal nitric oxide synthesis causes distal epicardial coronary artery vasoconstriction but it has no effect on proximal segments.

(18)

ACUTE GRADIENT REDUCTION DOES NOT PREDICT FUNCTIONAL OUTCOME AFTER DDD PACING IN OBSTRUCTIVE HYPERTELESTROPHIC CARDIOMYOPATHY
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Dual chamber pacing with complete right ventricular capture to improve symptoms in drug refractory hypertrophic obstructive cardiomyopathy (HOCM) has been guided by acute assessment of gradient reduction. The functional outcome of DDD pacing in relation to this acute evaluation remains uncertain.

56 patients, (34 male, mean age 48±17 yrs, range 16-79) with mean symptom duration 7.0 yrs and refractory symptoms (angina: Class II n = 22, III n = 19, NYHA: Class II n = 12, Class III n = 42, Class IV n = 1, syncope: n = 22) were assessed with transient dual chamber pacing. Subsequent implantation took place in 53 patients who exhibited left ventricular outflow tract gradient reduction of >30% as assessed by Doppler Echocardiography.

Results: The mean outflow tract gradient prior to pacing was 78±31 mm Hg. At temporary study the mean outflow tract gradient reduced to 38±24 mm Hg. After a mean follow-up of 11±1 months (range 1-70), 52 patients remained alive. Outflow tract gradient at FU was 36±25 mm Hg [p <0.001] which correlated with the observed acute reduction (r=0.69, p <0.0001). Symptoms improved as follows: syncope was eliminated in all but 2 patients with 1 patient developing syncope after implant, angina improved in 39 (75%) but was unchanged or worse in 10 patients and NYHA class was unchanged in 9 patients. There was no correlation between magnitude of gradient reduction, age, duration of symptoms that distinguished the group of non-responders from those who improved.

Conclusion. DDD pacing is provides symptomatic benefit in 80% of patients. Acute assessment of gradient reduction does not predict functional outcome.

(20) POSTER

INTRAVENOUS L-ARGININE RESTORES VASCULAR REACTIVITY IN THE CONDUCT ARTERIES OF YOUNG HYPERCHOLESTEROLAEMIC ADULTS
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Hypercholesterolaemia is associated with loss of endothelium-dependent dilatation in the coronary and systemic circulation in young pre-clinical subjects and those with atherosomar arteries. These effects may be due to interference with nitric oxide (NO) produced from L-arginine. In the coronary and systemic microvasculature this can be reversed by the intravenous (IV) administration of L-arginine, but the effects on the conduit arteries of young asymptomatic subjects has not been examined. We studied vascular reactivity in 6 hypercholesterolaemic subjects and 6 controls (LDL-cholesterol 4.76±0.75mmol/l vs 2.25±0.62mmol/l, p <0.005). All subjects (age 29±2 yrs; range 22-36) were clinically well, lifelong non-smokers, non hypertensive, non diabetic and on no cardiovascular medication. Five of the hypercholesterolaemic subjects and 3 of the controls had been on cholesterol lowering medication (Simvastatin). Using high resolution ultrasound, we measured brachial arterial diameter at rest, in response to reactive hyperaemia (endothelium-dependent dilatation) and to sublingual glyceryl trinitrate (endothelium-independent dilatation). Flow mediated dilation (FMD) was assessed before and after IV infusion of L-arginine (10mg/kg body weight) and the effect compared to a 5% Dextrose (placebo) infusion. Serum L-arginine levels increased >20 fold, without change in heart rate or blood pressure in any subject. L-arginine produced no change in baseline vessel diameter in either group, which suggests that it is not acting as a direct vasodilator. However FMD, which was impaired in the hypercholesterolaemic subjects after IV administration of L-arginine (FMD from 1.1±0.7% to 0.8% p <0.001) compared to controls where there was no change (FMD from 3.6±0.7% to 3.2±0.9%; p=N.S.). No significant change in FMD were observed after placebo infusion and all subjects had dilatation to GTN (Hypercholesterolaemica 19.1±4.6% vs 18.4±1.5% in the controls). Intravenous L-arginine improves endothelium dependent-dilation in hypercholesterolaemic young adults but has no effect in normals. This may provide an important anti-atherogenic strategy if chronic oral administration of L-arginine demonstrates the same effect.
IS L-ARGININE INDUCED VASODILATATION REALLY DUE TO PROVIDING STEREOSPECIFIC SUBSTRATE FOR NO SYNTHASE?
P Rhodes, C Barr, A D Struthers. Department of Clinical Pharmacology, Ninewells Hospital, Dundee, UK.

Nitric oxide is synthesised by L-arginine being a stereospecific substrate for NO synthase. This has led to the use of intravenously infused L-arginine in the forearm as a specific probe for NO synthase in disease states where NO production is thought to be defective. To examine whether this is a valid technique, we have compared the effect of forearm vasodilatation of infusion L-arginine, D-arginine, L-Lysine, D-Lysine, L-Ornithine and D-Ornithine. In other studies, we examined whether the osmolality of the infusate per se could have produced vasodilatation. In the latter study, we infused NaCl at varying osmolalities and showed a clear dose response curve with 40% vasodilatation produced at a NaCl osmolality of 0.58 mosm/Kg. The vasodilatation seen with D- and L-ornithine was very similar to NaCl, demonstrating a clear vasodilatory effect of increased infused osmolality. However, Arginine and Lysine both produced vasodilatation over and above that due to hyperosmolality. Interestingly, the vasodilatation due to L-Arginine was very similar to that of L-Lysine. However the most interesting finding was that the vasodilatation due to the D-isomers was significantly greater than that of the L-isomers and this was true for both arginine and lysine. In summary, our observation that D-arginine, which is not a substrate for NO synthase, produces more vasodilatation than L-arginine casts doubt over the use of intravenous L-arginine as a pharmacological tool for investigating NO. This doubt is enhanced by the fact that a similar amino acid, Lysine, causes the same vasodilatation as Arginine.

VASCULAR AND HORMONAL EFFECTS OF ARGinine IN HEALTH AND HYPERTENSION: PROVISION OF SUBSTRATE FOR NITRIC OXIDE (NO) OR NON-SPECIFIC EFFECTS?
Clinical Pharmacology, St George's Hospital, London, SW17 ORE.

L-arginine is the substrate for NO synthesis. Some reports show local arginine increases responses to NO-dependent dilators and systemic arginine lowers blood pressure (BP) in normals and hypertensives. However, results are inconsistent and it is not clear if NO mediates the responses. Arginine also stimulates pithitary hormone release, which could be NO-mediated, and might contribute to the vascular effects reported. We have studied the vascular effects of local arginine in normals and hypertensives, and the vascular and hormonal effects of systemic arginine in normals. L- and D-arginine were infused locally into the brachial artery of normals (n=7) and hypertensives (n=7) and the effect on the forearm blood flow (FBF) response to acetylcholine (ACH) measured using venous occlusion plethysmography. Systemic intravenous (iv) L- or D-arginine (10g) was given and BP and heart rate (HR) measured supine (n=8) and after 30s of 70° tilt (n=5). Hormone levels were measured 20min after iv arginine. Neither basal FBF nor ACh response differed between normals and hypertensives (basal FBF 3.7±0.6 vs 4.2±0.4; ACh response (AUC) 346±19.3 & 346±42.2 respectively); neither basal FBF nor ACh response was affected by L- or D-arginine. Supine BP and HR did not change after L- or D-arginine. Pulse pressure and HR increased after 70° tilt, arginine had no effect on the response. Arginine infusion increased plasma arginine from 0.077±0.013 to 1.8±0.14mmol/l (L-arg; n=5) and 2.5mmol/l (D-arg; n=3); L- and D-arginine significantly increased prolactin (135±34±70±37.6 mU/mL), glucagon (10.6±2.1 to 18.3±2.2 pmol/l) and insulin (40.4±1.3 to 99.5±25.5 pmol/l) levels. Thus a 20-fold rise in arginine does not alter basal FBF, or responses to NO-dependent dilators in normals or hypertensives, or lower blood pressure. The hormonal changes could contribute to vascular effects reported previously but are not stereospecific and so are unlikely to be NO-mediated.

L-ARGININE CAN ACUTELY REDUCE THE VENTILATORY COST OF CARBON DIOXIDE EXCRETION IN CHRONIC HEART FAILURE?
AP Banning, BD Prendergast, S Elbourne, D Tyler, AH Henderson. Cardiovascular Sciences Research Group, University Hospital of Wales, Cardiff.

Patients with chronic heart failure (CHF) have an increased ventilatory cost of CO2 excretion during exercise (the linear VE/VCO2 slope, m) reflecting mismatch of perfusion to ventilation (Q/V) during exercise. We have suggested that this may be due to pulmonary microvascular dysfunction. Endothelial dysfunction is impaired in systemic arteries in CHF and may be improved by L-arginine, (ARG) (substrate for endogenous nitric oxide) (NO). We enrolled men (n=11) with stable NYHA class II or III CHF into a cross-over study of iv ARG (0.5g/kg over 30 mins) vs. sublingual nifedipine (NIF) (10mg) (a control for the non-specific vasodilator effect of ARG). Other known causes for endothelial dysfunction were absent and no patient had indocuble myocardial ischaemia. All were receiving ACE inhibitors and diuretics. Exercise tests were performed 15 min pre and immediately post infusion. In the 5 patients with peak VO2<15ml/kg/min and increased slope m, ARG reduced m (412±7 to 345±7; p<0.05), but NIF did not (375±5 to 386±6), neither treatment altered a normal m in patients with peak VO2 >15ml/kg/min. Small, non significant differences of ARG and NIF on heart rate and blood pressure, at rest and during exercise did not differ. These findings imply that exercise related Q/V mismatch in severe CHF is improved by ARG, supporting the hypothesis that it is mediated at least in part by endothelial dysfunction.

RESPIRATORY MUSCLE STRENGTH AND CARDIOPULMONARY EXERCISE VARIABLES IN CHRONIC HEART FAILURE T P Chua, S Anker, P Ponikowski, A J S Coats Royal Brompton National Heart & Lung Institute, London

Respiratory muscle weakness is recognised in chronic heart failure (CHF) but its relation to cardiopulmonary exercise variables is not known. We investigated mouth pressures during maximum static inspiratory (Pmax) and expiratory (Pmin) effort in 7 healthy controls (means±SEM: age 52±5.4 years; 3 men) and 17 CHF patients (age 60.5±1.7 years (P=NS); all men; radionuclide left ventricular ejection fraction 26.1±3.4%). We confirm that there is respiratory muscle weakness in CHF patients as seen in the reduction of Pmax at functional residual capacity (FRC) (62.4±7.3 vs 89.3±8.6 cm H2O, P=0.03), Pmax at FRC (91.1±7.0 vs 128.1±9.1 cm H2O, P=0.009) and Pmax at total lung capacity (TLC) (122.4±9.9 vs 159.3±13 cm H2O, P=0.04). Pmax at residual volume was also reduced in CHF but this was not significant (78.5±7.7 vs 91.3±14 cm H2O, P=0.45).

All subjects underwent cardiopulmonary exercise testing and the relationship between maximal oxygen consumption (mVO2) and various indices of respiratory muscle strength above was assessed. Similarly, the relationship between the slope relating minute ventilation (Ve) and carbon dioxide production (VCO2), which is a measure of ventilatory response to exercise, and these indices of respiratory muscle strength was also assessed. We found Pmax at TLC to correlate significantly with both mVO2 (r=0.7, P<0.001) and Ve/VCO2 slope (r=0.44, P=0.03). There was no correlation between Pmax or Ve/VCO2 slope.

We conclude that respiratory muscle weakness is seen in CHF and it may play an important role in exercise intolerance. The strong relationship between inspiratory muscle weakness and the two objective variables of cardiopulmonary exercise testing suggests that inspiratory muscles may especially be relevant.
(25) POSTER
RELATIONSHIP BETWEEN ALVEOLAR-CAPILLARY MEMBRANE FUNCTION, PULMONARY HAEMODYNAMICS AND EXERCISE PERFORMANCE IN CHRONIC HEART FAILURE
S Puri, DP Dutka, L Baker, CM Oakley, JMB Hughes, IGF Cleland Department of Medicine (Clinical Cardiology), RPMJ, Hammersmith Hospital, London

Transient elevation of transcapillary pulmonary vascular pressures has been shown to cause disruption of alveolar epithelium and pulmonary endothelium in animal models. In chronic heart failure (CHF), pulmonary pressures may also be elevated. The aim of this study was to explore the relationship between alveolar-capillary membrane gas exchange, pulmonary haemodynamics, and exercise capacity. Alveolar-capillary membrane diffusing capacity (Dm) was determined using the Roughton and Forster method of partitioning the pulmonary diffusing capacity for carbon monoxide (DLco) using a single breath technique at varied inspired oxygen concentrations. 15 male patients with stable CHF were studied (age 55±11 years, EF 30±10%). All subjects performed symptom limited bicycle exercise tests with respiratory gas analysis to determine maximal oxygen consumption (MV02). Resting pulmonary haemodynamics and cardiac output were assessed by standard right heart catheterisation (cardiac index 2.3±0.7 L/min/m2, pulmonary artery pressure 30±14mm Hg, pulmonary capillary wedge pressure 21±7mm Hg, pulmonary vascular resistance=2.9±2 Wood units). Alveolar-capillary membrane resistance correlated significantly with PVR (r = 0.72, p = 0.002) and MV02 (r = 0.7, p = 0.004), but not with other haemodynamic variables. We propose that measurement of Dm provides a non-invasive and more sensitive measure of pulmonary microvascular damage than conventional haemodynamic indices.

(26) POSTER
GROWTH HORMONE ABNORMALITIES IN SEVERE HEART FAILURE.

The physiological effects of Growth Hormone (GH) in the regulation of myocardial function is poorly understood.
Somatropin (SH) has been shown to increase myocardial contractility in normals and to stimulate the synthesis of myofibrillar proteins. In pts with GH deficiency and dilated cardiomyopathy improvement in cardiac function has been documented following treatment and there are several anecdotal reports of the beneficial use of SH in heart failure (HF). The mechanisms are not clear and the aim of this study was to assess growth hormone metabolism in severe HF. The study group consisted of 9 pts with dilated cardiomyopathy NYHA Class III or IV, age range 53-72 years and the control group was matched for age, sex and BMI, pts with known endocrine disease were excluded. Each sample was analysed for Glucose, Insulin like Growth Factor-1 (IGF-1) and Insulin Growth Factor Binding Protein (IGFBP-3). HF pts had similar mean fasting glucose levels to the controls but the levels of IGF-1 were markedly depressed (80.1±25.8 v.160.2±282.0 mg/dl, p=0.01). In addition all HF pts had IGF-1 levels well below the normal range (113-194 ng/ml). Binding protein levels IGFBP-3 were elevated in the HF group raising the possibility of peripheral resistance to IGF-1. We postulate that the deficiency of IGF-1 may contribute to the progressive ventricular dysfunction seen in heart failure and suggests an alternative approach to treatment in these pts with the use of SH. A prospective trial is in progress.

(27) POSTER
HIGH-DOSE LISINOPRIL IS MORE EFFECTIVE THAN LOW-DOSE IN SUPPRESSING ALDOSTERONE IN PATIENTS WITH CHRONIC HEART FAILURE
NC Davidson, WJ Coutie, AD Struthers. Department of Clinical Pharmacology, Ninewells Hospital and Medical School, Dundee

The optimal dose of ACE inhibitor for the treatment of heart failure is highly controversial and it is uncertain whether the neurohumoral suppression produced by these drugs is dose-dependent. We therefore compared the effects of low-dose and high-dose lisinopril therapy on plasma levels of aldosterone, which causes several important adverse effects independently of angiotensin II, including hypokalaemia, hypomagnesaemia and stimulation of myocardial fibrosis. These effects of residual aldosterone activity are sufficiently harmful to have prompted a mortality study (RALES) of the effects of spironolactone in addition to ACE inhibition. We studied 19 patients with NYHA class II-III congestive heart failure and LVEF<45% who were on chronic ACE inhibitor therapy. Patients were given lisinopril 5mg o.d. and 20mg o.d. for two weeks each in a double-blind, randomised order with a two week run-in period and a wash-out period on 10mg o.d. At the end of each treatment period plasma aldosterone levels were measured after 30 minutes bed rest, at 0 hours(pre-dose), 6 hours(peak effect), 13.5 hours and 22 hours (trough effect) after the dose of lisinopril. The areas under the curve(AUC) for plasma aldosterone concentrations on each dose were compared using paired t-tests. Plasma aldosterone levels (ng/ml) (mean+/SEM):

<table>
<thead>
<tr>
<th>Dose</th>
<th>Measured AUC(ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5mg o.d.</td>
<td>315.4±176.5</td>
</tr>
<tr>
<td>20mg o.d.</td>
<td>434.1±285.6</td>
</tr>
</tbody>
</table>

The AUC for plasma aldosterone concentration was significantly lower on high-dose than on low-dose lisinopril treatment(p<0.001). The plasma levels were significantly lower at both peak (p<0.001) and at trough effect (p<0.01). We have shown that the suppression of aldosterone activity during chronic ACE inhibitor therapy in patients with heart failure is dose-dependent. This provides further evidence that ACE inhibitors should be routinely prescribed in high doses.

(28) POSTER
HEART RATE VARIABILITY IN IDIOPATHIC DILATED CARDIOMYOPATHY: RELATIONSHIP TO DISEASE SEVERITY AND PROGNOSIS
Y Gang, PJ Keeling, JH Goldman, J Huang, L Fei, S Bent, WJ McKenna, M Malik. Department of Cardiological Sciences, St. George’s Hospital Medical School, London, UK

To assess the value of heart rate variability (HRV) in patients with idiopathic dilated cardiomyopathy (IDC) at different stages of disease, analysis of HRV was performed in 30 patients with IDC (pts) compared with 30 patients with myocardial infarction (MI) who were matched for age and sex. The pts with IDC had a mean age of 45±11 years, 22 men, 18 relatives with left ventricular enlargement (LVEF<50%, age mean 41±14, 11 men). During mean 24 month follow-up, 11 patients suffered from progressive heart failure (PHF; 12 underwent heart transplant). Three non-spectral measurements of HRV (SDNN, the standard deviation about the mean; SDANN, standard deviation of 5-minutes time mean normal to normal intervals; RMSSD, root-mean-square of difference of successive normal to normal intervals) were derived from Holter monitoring recordings using Marquette software. Result: All measurements of HRV were markedly reduced in patients with IDC compared to CON (p<0.01). There was significant difference in SDNN and SDANN between IDC and LVE (p<0.01), but no difference were found between LVE and CON (p=NS). The measurements of HRV were more depressed in patients with IDC who developed PHF compared to those remained clinically stable (p<0.05) and a weak but significant correlation was found between HRV measurements and left ventricular ejection fraction (r=0.5; p<0.05). Measurement of SDNN>50ms occurred more frequently in patients with IDC and PHF compared with those remained clinically stable (5, 33% vs 1, 7%; p=NS) but this was not seen in LVE or CON at all. Conversely, more CON and LVE have SDNN measurement >100 ms compared to patients with IDC who remained stable or suffered PHF (16, 88%; 11, 66% vs 8, 53%; 4, 27%: p=0.007). There was a significant difference in SDNN between PHF and IDC (p=0.007). There was a significant difference in SDNN between PHF and IDC during a year between patients with SDNN>50ms and those with SDNN<50ms (33% vs 92%; p=0.005). Conclusion Depressed HRV is related to the severity of IDC and the measurement of HRV reduces the risk of mortality in patients with IDC. Significantly reduced HRV, in particular SDNN measurement, may be a non-invasive marker of patients who are at increased risk of clinical deterioration. The finding that LVE is not abnormal in IDC suggests that reduced HRV appears late in natural history of IDC and HRV analysis did not aid identification of early IDC during family screening.
(29) POSTER

FIRST DEGREE HEART BLOCK IS AN INDICATION FOR PACING IN HEART FAILURE
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Harefield Hospital, Harefield, Middlesex, UK.

First degree heart block (1°HB) is not considered to be an indication for pacemaker insertion, and is unlikely to improve cardiac output significantly in patients with normal left ventricular (LV) function. However, in heart failure it may critically reduce a compromised cardiac output. In addition, recent studies have suggested that patients with heart failure benefit from dual chamber pacing with a short atrioventricular delay (AVD). The aims of this study were to determine whether patients with heart failure and first 1°HB should be paced and the optimum AVD.

15 patients with heart failure and 1°HB were studied following dual chamber pacemaker insertion, mean age 61±7 years, baseline PR interval duration 242±33 ms and QRS interval duration 140±24 ms. The underlying aetiology was ischaemic in 12 and dilated cardiomyopathy in 3.

Radioisotope ejection fraction (REF), echocardiography and cardiopulmonary exercise testing were performed in sinus rhythm and with AVD of 100, 150 and 200 ms in a randomised sequence. Patients were studied after a month at each AVD and in sinus rhythm. The REF increased from 24.8% to 30.11% with optimal pacing (p=0.05). The optimal REF values were obtained with an AVD of 150 ms in all but one of the patients. The REF for the different AVD were as follows: 100 ms 23.8, 150 ms 27.5 and 200 ms 24.6%. There was no significant difference between these though a trend was seen (p=0.09) for the EF at 200 ms to be worse than 150 ms (paired t-test). Peak oxygen uptake was significantly higher with AVD of 150 and 200 ms than at 100 ms and baseline. Racing occurred in an increase in left ventricular filling time from 357 to 460 ms and ‘normalisation’ of the mitral inflow pattern from a summation wave to discrete E and A velocities.

In conclusion, normalisation of the PR interval (AVD 150 ms) results in significant haemodynamic benefit in patients with impaired left ventricular function and first degree heart block.

(30) POSTER

OPEN ACCESS ECHOCARDIOGRAPHY; EXPERIENCE IN A DISTRICT HOSPITAL
J C Rodger, R Shanks , R A Hamill
Monklands Hospital, Airdrie, Lanarkshire

Our hospital serves a population of 160,000. We have given general practitioners (GPs) direct access to echocardiography. Prosthetic valves are not accepted, referrals are otherwise unrestricted. Echocardiograms are recorded and reported by a technician. When appropriate, a medical comment is added following review of the video. In the first ten months, 64 GPs requested 222 echocardiograms. Patients’ ages ranged from ten months to 87 years (mean 59 years). The main reasons for referral were investigation of possible heart failure (54%) and investigation of a cardiac murmur (28%). 26 of the 118 patients investigated for possible heart failure had echocardiographic evidence of left ventricular (LV) systolic dysfunction; of the remainder, 23 had a normal echocardiogram, 30 a trivial valve lesion, 26 LV hypertrophy and six right ventricular dilatation. Of the 62 patients with murmurs for assessment, seven had significant aortic stenosis, two a floppy mitral and 35 a trivial valve lesion; the echocardiogram was normal in six. GPs have been asked about the outcome of each echocardiogram. The first 131 questionnaires returned have shown that as a result of the echocardiogram, there were 41 changes to drug therapy and 13 hospital referrals (five directly to a nearby cardiac centre). 97 investigations were considered to have saved an initial clinic referral. The number of GP requests for echocardiography is similar to the number for Holter monitoring (to which GPs also have access). They account for 15% of our cardiac department’s total echo workload; the corresponding figure for Holters is 23%.

(31) POSTER

"OPEN ACCESS CARDIOLOGY" : IS IT THE WAY FORWARD?
S Khandekar, J J Murphy
Department of Medicine, Darlington Memorial Hospital, Co. Durham

Cardiology departments are under increasing pressure to provide more "open access" to cardiac investigations. This would make the GPs more appropriate if general practitioners (GPs) were to select appropriate tests and act upon the results obtained. This survey examines the former. 100 consecutive referrals to a cardiology clinic at a district general hospital were studied. Following receipt of the referral letter, a questionnaire was sent to the relevant GP. They were asked whether they would have opted for direct access investigations if available, rather than a consultation. The investigations on offer were: an exercise ECG, echo-cardiography and 24-hour ECG monitoring. More than one test could be selected if appropriate. Replies to the questionnaire were received on 53 patients (age range 17-78 years, 41 men and 12 women). The main clinical problems were chest pain in 42 (45%), a suspected cardiac arrhythmia in 31 (33%), a cardiac murmur in 8 (9%), hypertension in 8 (9%) and suspected heart failure in 7 (8%). If open access tests had been available, 52/93 (56%) would have been referred for these initially. Of these, the GP would have been happy to manage the patient in 29, and in the remaining 23 would have referred the patient on for further consultation if abnormalities on screening had emerged. GPs’ views were then compared to the patients’ management following assessment in the cardiac clinic. Only 8/28 of the exercise tests were considered appropriate, 6/19 of the echo-cardiograms. Echocardiograms were performed in a further 6 patients not requested by GPs. Selection of patients for open access was not altered by fundholder status or years since qualification.

Conclusions: GPs are keen to have open access for cardiac investigations. This will result in a major increase in workload, due to a large number of inappropriate tests being performed. Without appropriate education and clinical guidelines, GPs should not have direct access to these investigations.

(32) POSTER

A NORMAL ELECTROCARDIOGRAM PREDICTS NORMAL LEFT VENTRICULAR SYSTOLIC FUNCTION IN PATIENTS WITH SUSPECTED HEART FAILURE
C M Francis, A Davie, G R Sutherland and J J V McMurtry
Cardiology Department, Western General Hospital, Edinburgh

Identifying patients in general practice with impaired left ventricular systolic function (LVSF) is difficult and requires referral for echocardiography. The value of an electrocardiogram (ECG) in determining which patients should be referred was assessed in this study. We recently established an open access echocardiography service to help the primary care management of patients with suspected heart failure. All patients who were referred had an ECG and an echocardiogram. 406 patients have been evaluated. LVSF was assessed as normal or impaired and the ECG as normal or abnormal ("minor" abnormalities were discounted). The results are summarised below:

<table>
<thead>
<tr>
<th></th>
<th>Normal LVSF</th>
<th>Impaired LVSF</th>
</tr>
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<tbody>
<tr>
<td>Normal ECG</td>
<td>182</td>
<td>2</td>
</tr>
<tr>
<td>Abnormal ECG</td>
<td>149</td>
<td>73</td>
</tr>
</tbody>
</table>

A normal ECG has a positive predictive value of 99% in predicting normal LVSF whereas an abnormal ECG only has a positive predictive value of 33%. The negative predictive value of a normal ECG is 99% and the negative predictive value of an abnormal ECG is 67%.
A COMPARISON OF THREE DIFFERENT NATRIURETIC PEPTIDES AS MARKERS OF LEFT VENTRICULAR SYSTOLIC DYSFUNCTION
NC Davidson, AA Naas, WJ Coutie, AD Struthers
Department of Clinical Pharmacology, Ninewells Hospital and Medical School, Dundee

Accurate assessment of left ventricular function is vital to decide which patients will benefit from treatment with ACE inhibitors. It has been suggested that raised plasma levels of natriuretic peptides (NP) may identify patients with LV dysfunction but it is not known which NP provides the most diagnostic information. We have performed the first direct comparison of Atrial Natriuretic Peptide (ANP), B-type Natriuretic Peptide (BNP) and N-Terminal Pro-Atrial Natriuretic Peptide (N-ANP) in identifying patients with LVEF ≤ 35%, as measured by radionuclide MUGA scan. Venous blood samples were taken from an unselected group of 87 patients who had been referred for assessment of ventricular function. ANP-like immunoreactivity (ANP-II), BNP-II and N-ANP-II were measured by radioimmunoassay using commercial kits. Receiver operating characteristic (ROC) analysis was used to provide objective assessment of the diagnostic performance of the assays. There were significant negative correlations between the LVEF and plasma levels of each peptide: ANP-II (r = 0.50), BNP-II (r = 0.56) and N-ANP-II (r = 0.48) (p < 0.01 for each peptide).

The areas under the ROC curves for BNP (0.880) and N-ANP (0.832) were not significantly different from each other but were significantly greater than the value for ANP (0.761): ANP vs BNP p < 0.01; ANP vs N-ANP p < 0.05. The optimum sensitivity and specificity of each assay for the detection of patients with LVEF ≤ 35% was:

<table>
<thead>
<tr>
<th>ANP concentration</th>
<th>BNP concentration</th>
</tr>
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<tbody>
<tr>
<td>31-67 pmol/l</td>
<td>9.8 pmol/l</td>
</tr>
<tr>
<td>31-67 pmol/l</td>
<td>9.8 pmol/l</td>
</tr>
<tr>
<td>31-67 pmol/l</td>
<td>9.8 pmol/l</td>
</tr>
</tbody>
</table>

Plasma concentrations of BNP and N-ANP provide sensitive indicators of ventricular dysfunction; both peptides are objectively superior to ANP for the identification of patients with LVEF ≤ 35%. These simple tests could be used to screen patients with suspected ventricular dysfunction to determine the need for further investigation and treatment. In this way the burden on echocardiography services could be reduced.

PLASMA NATRIURETIC Peptide CONCENTRATIONS IN THE ASSESSMENT OF CHRONIC DysPNEOA
PM Clarkson, CM MacLeod, WJ Coutie, TM MacDonald
Department of Clinical Pharmacology, Ninewells Hospital and Medical School, University of Dundee, Dundee

In a primary care setting the recognition of impaired left ventricular systolic function (SHF) can be problematic, and as such the majority of patients in Britain with SHF do not receive angiotensin-converting enzyme inhibitors. Since elevation of plasma atrial (ANP) and brain natriuretic peptides (BNP) occurs in SHF we assessed the value of measuring these peptides in 52 consecutive echocardiographic patients with unexplained shortness of breath referred directly from general practice for open access echocardiography. On the basis of echocardiographic and spirometry findings 8 of the 52 patients were classified as having SHF, 20 as having a cardiac (CA) cause of breathlessness (SHF, mitral regurgitation, or left ventricular hypertrophy), 12 as lung disease (LD) and 20 with no apparent cause (N). Results are expressed as mean values ± SEM. Patients with SHF and CA were compared with other groups (p < 0.01, *p < 0.001).

<table>
<thead>
<tr>
<th>ANP concentration</th>
<th>BNP concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>(pmol/l)</td>
<td>(pmol/l)</td>
</tr>
<tr>
<td>SHF</td>
<td>3.4.7 (13.1)**</td>
</tr>
<tr>
<td>CA</td>
<td>3.4.8 (6.1)*</td>
</tr>
<tr>
<td>LD</td>
<td>6.9 (3.3)</td>
</tr>
<tr>
<td>N</td>
<td>17.8 (17.9)</td>
</tr>
</tbody>
</table>

Plasma BNP concentration accurately reflected the diagnosis of SHF (75% sensitivity, 95% specificity when BNP > 25 pmol/L). Our data suggests that measurement of ANP and BNP in patients with chronic dyspnoea can aid diagnosis of cardiac disease. This may be of particular relevance in the primary care setting where many patients with dyspnoea are inadequately evaluated.

SEVERITY OF CONGESTIVE CARDIAC FAILURE CAN BE DETERMINED BY MEASUREMENT OF PEPTIDES DERIVED FROM ATRIAL NATRIURETIC FACTOR
P Kelly1, E Macaulay-Hunter2, P Lowry3 and E J Perrins1
Department of Cardiology, General Infirmary at Leeds1 and Department of Biochemistry, Reading University2

The clinical assessment of patients with congestive cardiac failure (CCF) is often subjective, for example the New York Heart Association (NYHA) classification. Atrial natriuretic peptides (ANP) are produced from a 126 amino acid precursor, proANP. Plasma levels of α-human ANP (99-126) increase in CCF, but this has a short half-life and is difficult to measure. To assess the effect of CCF on plasma levels of peptides 31-67 and 79-98 derived from proANP, 44 patients with CCF and 15 control subjects were studied. Blood samples were taken at rest, supine, and before medication. New assays were developed to measure all 3 peptides. Biochemical analysis was independent of clinical assessment of heart failure severity.

<table>
<thead>
<tr>
<th>NYHA class</th>
<th>Peptide</th>
<th>Peptide</th>
<th>Peptide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>31-67</td>
<td>79-98</td>
<td>99-126</td>
</tr>
<tr>
<td>Control</td>
<td>143 ± 16</td>
<td>587 ± 83</td>
<td>8.5 ± 1.1</td>
</tr>
<tr>
<td>I</td>
<td>271 ± 36</td>
<td>853 ± 119</td>
<td>11.7 ± 1.1</td>
</tr>
<tr>
<td>II</td>
<td>1111 ± 356</td>
<td>3471 ± 932</td>
<td>22.5 ± 3.4</td>
</tr>
<tr>
<td>III</td>
<td>4167 ± 667</td>
<td>9043 ± 887</td>
<td>51.6 ± 6.3</td>
</tr>
<tr>
<td>IV</td>
<td>5858 ± 1200</td>
<td>15955 ± 4710</td>
<td>276 ± 47</td>
</tr>
</tbody>
</table>

All 3 peptides showed significant differences between classes I and II, p < 0.01 and II and III, p < 0.01.

Conclusions: The functional classification of CCF can be predicted by plasma concentration of peptides derived from proANP, including, for the first time, peptide 79-98. Peptides other than α-human ANP may have a role in monitoring severity of CCF and response to treatment.

HAEMOSTATIC AND HAEMODYNAMIC ABNORMALITIES ARE ASSOCIATED WITH LEFT ATRIAL THROMBOSIS IN ATRIAL FIBRILLATION
R M Happeil, "K E Berkii, *J M McLenachan, J Davies Division of Medicine, and *Department of Cardiology, General Infirmary at Leeds, Leeds

Left atrial thrombosis is a likely source of the increased risk of stroke in non-rheumatic atrial fibrillation (NRAF). To evaluate the role of haemostatic and haemodynamic parameters in left atrial thrombosis, we performed transoesophageal echocardiography (TOE) in 72 patients with NRAF, not on anticoagulants. Peak blood velocity was measured at three sites in the left atrium (LA) using pulsed wave Doppler. Venous blood was sampled for coagulant proteins, and markers of haemostatic activation. Patients were grouped by the presence or absence of LA thrombus identified by two observers at TOE. LA thrombus was identified in 12 patients (17%), in all the left atrial appendage (LAA). Patients with thrombus had reduced peak LAA velocity compared to those without (0.17 vs 0.25 m/s, p < 0.02), but no significant reductions in peak Mid-LA or LA outflow velocity. These patients had increased levels of beta-thromboglobulin (β-TG, a marker of platelet activation) (58 vs 34 IU/ml, p < 0.004), von Willebrand Factor (proposed as a marker of endothelial dysfunction) (1.96 vs 1.4.5 IU/ml, p < 0.004) and the coagulant protein Factor VIII (C. 2.05 vs 1.89 IU/ml, p < 0.02). Multiple logistic regression identified FVIII:C (p = 0.02), β-TG (p = 0.04) and LAA velocity (p = 0.04) as independent associated of LA thrombosis. Both haemostatic and haemodynamic abnormalities are associated with the presence of LA thrombus in NRAF, and may help stratify thromboembolic risk.
### ROLE OF CONTINUOUS INFUSION OF PROSTANOGEN (PGI2) AS TREATMENT OF PRIMARY PULMONARY HYPERTENSION (PPH)

A Yazdani Butt, George Cremona, Linda Sharples, Tim Higenbottom.

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We have examined the effect of continuous infusion of PGI2 and conventional therapy (CT) on survival of 71 patients with primary pulmonary hypertension. Severity of disease was determined by a mixed venous oxygen saturation (SvO2) and patients were categorized into group 1 (SvO2 > 60%) and group 2 (SvO2 < 60%) at diagnostic right heart catheterization. Patients were treated with PGI2 (n=37) or CT (n=34) in anticoagulants with or without oral vasodilators. Endpoint of the study was either death or heart-lung transplantation.

<table>
<thead>
<tr>
<th>Group 1 (n=36)</th>
<th>Group 2 (n=35)</th>
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<tr>
<td>Age (Y)</td>
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<td></td>
<td>Age (Y)</td>
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<tr>
<td></td>
<td>34.0±13.1</td>
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<td>Sex F/M</td>
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<td></td>
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<td>PAC (mmHg)</td>
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<td>RV (mmHg)</td>
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<td></td>
<td>12.7±6.4*</td>
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<tr>
<td>CI (L/min/m2)</td>
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<td>1.82±0.47*</td>
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</table>

Mean ± SD; * p < 0.05

In group 2 patients treated with PGI2 (n=24) there was a trend towards greater survival in comparison to CT (n=11) (median survival: 653 days with PGI2 vs 428 days with CT, p=0.07, 95% CI). In group 1 effect of PGI2 was less marked (median survival: 2088 days with PGI2(n=13) vs >1275 days with CT(n=23), p=0.77). Applying the equation proposed by the national registry of PPH patients using PAPm, RAPm and CI (D'Alonzo et al: Ann Intern Med 1991,115:343-349), actual 3 year survival of PGI2 treated patients was 49.9% vs expected survival of 36%. Continuous PGI2 may have a role in the treatment of selected patients with severe PPH.

### DIURNAL VARIATION OF TRANSPIRMONARY ENDOTHELIN-1 LEVELS IN PATIENTS WITH PULMONARY HYPERTENSION

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The vasconstrictor peptide endothelin has been implicated in the pathogenesis of primary and secondary pulmonary hypertension. We have previously shown diurnal variations in pulmonary vascular resistance in these patients. Changes in endothelin levels were measured in 8 patients with pulmonary hypertension (5 primary, 2 secondary to thromboembolic lung disease, 1 secondary to ischaemic heart disease) over a 24 hour period. Blood samples were taken from the radial and pulmonary arteries, and endothelin-1 measured by specific radioimmunoassay. The mean levels of endothelin varied between 11.9 ± 2.3 pg/ml to 26.6 ± 7.4 pg/ml in arterial samples and 15.2 ± 3.2 pg/ml to 25.9 ± 7.9 pg/ml in pulmonary artery samples. The levels of endothelin in both arterial and pulmonary artery samples increased at midnight, and returned to the previous value (8am) by the following morning (8am) (Figure 1). The rise of endothelin levels during the night could have implications with regard to understanding the pathophysiology of the disease and possibly targeting therapy.

### RATE AND LOAD DEPENDENCE OF PULSUS ALTERNANS IN THE ANAESTHETISED PIG HEART

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Pulsus alternans can be feature of cardiac dysfunction due to a variety of aetiologies. It is known to follow sudden perturbations such as rate changes and premature beats. Pulsus alternans can also be produced by sudden reductions in loading and sudden increases in loading. We studied the interaction between heart rate and load in the generation of pulsus alternans. A snare was placed around the proximal aorta in eight open chested pigs anaesthetised with 1% Halothane in a 1:1 mixture of oxygen and nitrous oxide. Fluid filled catheters inserted into the left ventricle (via apex) and aorta (via left carotid) measured ventricular and arterial pressures respectively. The proximal aorta was occluded transiently during steady state right atrial pacing at cycle lengths of 450,400,350, and 300 milliseconds. Occlusions resulting in ectopic beats were not analysed. A total of 47 occlusions produced an average rise in peak left ventricular pressure of 70% (40-90%) and lasted a mean of 6 seconds (5.7-7.7s). At 450ms cycle length no pulsus alternans was seen before or during atrial output. However, pulsus alternans was transiently induced during 25% of occlusions at 400 ms cycle length, during 40% at 350ms cycle length and during 67% at 300s cycle length. Transient increases in myocardial loading produce pulsus alternans in a rate dependent manner. Increased myocardial loading has the effect of reducing the rate threshold for pulsus alternans. This may in part explain the occurrence of spontaneous pulsus alternans in situations of abnormal myocardial loading e.g congestive cardiac failure and aortic stenosis.
INCREASED MYOCARDIAL WORK IMPAIRS LEFT VENTRICULAR SYSTOLIC FUNCTION BEFORE SYSTOLIC FUNCTION IN PATIENTS WITH ANGINA

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Left ventricular diastolic abnormalities precede systolic impairment during ischaemia, subendocardial perfusion is affected early during acute ischaemia with a predominant effect on left ventricular long axis function. Localized diastolic dysfunction (defined by decreased myocardial long axis velocity. Nine volunteers without a history of cardiovascular disease (7 male, mean age 38 range 28-56) and 24 patients with angina (mean age 58, range 36-78) with a previous myocardial infarction 3 with no evidence of reversible ischaemia) were studied at rest and during low (5 or 7.5 mg/kg/min) and high (15 mg/kg/min) dose dobutamine infusion. Peak systolic and early diastolic long axis velocity were correlated between baseline and dobutamine stress. Controls increased peak systolic long axis velocity over baseline during dobutamine infusion, median (25th, 75th centile) increase from baseline to low was 71% (57, 75), and from baseline to high was 118% (104, 138). This was accompanied by an increase in diastolic velocity in all but one control, increase from baseline to low was 23% (10, 38) and baseline to high was 21% (16, 35). A reduction of mean systolic or diastolic velocity below baseline was defined as abnormal. Five patient studies could not be analysed because of artefact. All patients increased systolic long axis velocity over baseline during low dose dobutamine, 43% (32, 82). All but one increased systolic long axis velocity during high dose infusion, 65% (35, 101). The patients with reduced systolic velocity had reversible ischaemia without myocardial infarction. Of 15 patients with effort angina 10 had reduced diastolic long axis velocity during stress, change at low dose was 56% (43, 83) and at high dose -8 (-17, 10). Patients without effort angina did not develop impaired diastolic long axis velocity, change at low dose was 52 (31, 75) and at high dose 64 (42, 79). In conclusion, increased workload impaired diastolic wall velocity developed without impairment of systolic wall velocity in 9 of 15 patients with reversible ischaemia, but not in any patient without effort angina. The diastolic abnormalities reflected impaired transition of stored elastic energy into wall motion due to ischaemia induced impaired myocyte relaxation. MR velocity mapping during dobutamine infusion provides useful insights into the effects of increased myocardial workload on left ventricular wall motion.

HOW IMPORTANT ARE IMAGE DISTORTION ARTIFACTS WHEN USING MECHANICAL INTRAVASCULAR ULTRASOUND TRANSDUCERS?

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Nonuniform rotation of mechanical intravascular ultrasound transducers may give rise to geometric distortion of the ultrasound image. Localised distortion of the image may influence the interpretation of wall motion and wall thickness. We have measured the influence of catheter shaft angulation on image morphology has not previously been reported and the quantitative impact of such distortion is not known. A circular perspex 4 mm internal diameter, 2 cm long probe was used in central and eccentric positions using nine (3 new and 6 old) 3.5 F, 30 MHz Boston Scientific 'Sonicath' catheters connected to a Hewlett Packard Sonos Intravascular. The shaft of each catheter was angulated outside the phantom to varying degrees and in different combinations at different points along its length in a 21 part protocol involving over 200 measurements per catheter. Major and minor diameters, cross-sectional area and circumference of the phantom lumen were measured. Visually apparent geometric distortion was graded from 1 (absent) to 4 (severe). Phantom lumen shape distortion was evident only when the catheter was eccentrically placed and was significantly greater in old catheters than in new ones (grade 1.68±0.86 vs. 2.43±1.09, p<0.001). Distortion was present in only 34% of images acquired with new catheters but in 88% of those acquired with old catheters. Only catheter tip bends, multiple distal angulations or 360° distal and mid catheter loops gave rise to significant quantitative changes. In the case of maximum distortion, the mean minor diameter decreased by <10%, and maximum diameter and lumen area increased by 4% and 6% respectively. Reduction in minor diameter dimensions was less in new catheters (2% vs. 4%). In conclusion, quantitative effects of RAA were small. Catheters performed significantly better than old catheters, producing less shape distortion and less quantitative changes. Most geometric distortion and quantitative change were associated with catheter tip bends and distal loop formation.

MAGNETIC RESONANCE IMAGING PLANES FOR THREE DIMENSIONAL RECONSTRUCTION OF HUMAN CORONARY ARTERIES

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Magnetic resonance imaging (MRI) has the potential to obtain noninvasively three dimensional (3D) images of coronary arteries. However, because of their small size and mobility, 3D images of only the proximal segments of the coronary arteries have been obtained in vivo. In this in vivo study was performed to develop a simplified strategy that would allow acquisition of sufficient data for 3D reconstruction of each of the main coronary arteries, and would be applicable in vivo. A 2.4T, 31cm bore magnet was used for MRI imaging. Various spin and gradient echo sequences were assessed to maximise the contrast between coronary arteries and the surrounding fat. The image matrix was typically 256 by 256 giving a maximum resolution of 400 μm. Seven cadaveric human hearts obtained from patients who had died from noncardiac causes were pressure perfused with formalin to maintain coronary artery patency. A series of tomographic planes were devised based on the longitudinal and transverse axes of the heart which allowed imaging of each of the main coronary arteries in cross-section and longitudinally. Initial coronary anatomy was then defined by imaging the coronary sinuses in the transaxial plane and once located they provided consistent anatomical landmarks from which further imaging planes could be derived. The left main(LM), left anterior descending(LAD) and posterior descending arteries were visualised from planes which were parallel to the transverse plane joining the coronary ostia. Imaging of the circumflex and right coronary artery(LCA) and mid and distal segments of the right coronary artery(RCA) employed longitudinal planes which were perpendicular to a line joining the posterior edges of the coronary ostia. A further series of consecutive oblique planes parallel to a line joining the posterior edges of the coronary ostia allowed imaging of the proximal right coronary artery. Images were then reconstructed into a 3D image using commercial software. The LCA, LAD and RCA could be visualised to a maximum of 10 mm, 24 mm, 31 mm and 50 mm respectively. We have developed an imaging protocol which allows 3D reconstruction of the main coronary arteries in vivo using a series of markers that are readily detected in vivo. An equivalent approach may be applicable to the systematic imaging of human coronary arteries in vivo.

TECHNICAL ASPECTS OF 3-DIMENSIONAL IMAGE RECONSTRUCTION OF TRANSOESOPHAGEAL ECHO (TOE) IMAGES IN THE ASSESSMENT OF MITRAL VALVE MORPHOLOGY

J Radwan, SA Livesey, CL Lawson, DM Walker, and IA Simpson
Wessex Regional Cardiac Centre, Southampton

Three-dimensional echocardiography using TOE imaging (3-DTOE) has been shown to offer the potential for accurate spatial definition of valve morphology, but methodologic guidelines required for optimal data acquisition in a clinical setting have not been described. The evaluation of mitral valve prolapse (MVP) presents a uniquely 3-dimensional problem and requires exact anatomical definition. We therefore studied 8 patients (age 56 ± 5 years) (mean±SD) with MVP, using pseudo-real time dynamic 3-DTOE, to define the technical parameters required for optimal imaging. Imaging data was obtained at 2 frames/s, automatically integrated and reconstructed using commercially available equipment (Tomtec, GMGH). 16 scans were performed in the 8 subjects, for diagnostic reasons and in an intra-operative setting. Results: 3-DTOE acquisition was considered optimal in 62%. 3-DTOE did not alter overall assessment of valve morphology from 2-D studies, but 3-D TOE accurately reflected the shape of MVP when the 3-D TOE images included the entire valve annulus and leaflets, and offered enhanced spatial evaluation. Technical prerequisites for optimal imaging were: 1) Depth and centering of the ultrasound cone was set to include both edges of the mitral valve ring with the annulus at its widest. 2) The probe was held in a completely fixed position by the operator during real time tomographic recording, and remained fixed during data recording. 3) The 3-D TOE images included the entire valve annulus and leaflets. 4) Sufficient image quality was achieved for reliable identification of the valve edges. 5) The image acquisition was set to allow the greatest depth of field possible. Observations: 1) Whilst 3-DTOE is in its infancy, the potential value of this new technology merits early evaluation and discussion. 2) 3-DTOE offers the potential for new quantitative and functional indices in MVP, particularly as an adjunct to mitral reconstructive surgery.
USE OF TRANSTHORACIC ECHOCARDIOGRAPHY FOR NONINVASIVE ASSESSMENT OF LEFT INTERNAL MAMMARY ARTERY GRAFT PATENCY
J J Crowley, A Kenny, L M Shapiro
Regional Cardiac Unit, Papworth Hospital, Cambridge

A noninvasive means of assessing coronary artery bypass graft patency would be useful for clinical diagnosis and long-term follow-up of graft outcome. Transthoracic high frequency combined two-dimensional and Doppler echocardiography allows visualisation of the distal left internal mammary artery (LIMA) anatomy and blood velocity profile when imaged using a modified left parasternal approach. In this study we assessed this technique for the evaluation of LIMA graft patency in patients with previous coronary artery bypass surgery admitted for further assessment of new onset angina. A total of 37 consecutive patients (32 males and 5 females, mean age 67 ± 6 years) admitted for coronary angiography were studied. All patients had coronary artery bypass graft surgery 9 ± 2 years prior to admission using the LIMA graft to the left anterior descending coronary artery. The LIMA and its blood velocity profile were visualised in 33 (89%) of the 37 patients. Two distinct patterns of blood flow were seen. In 25 patients who had angiographically proven normal LIMA grafts a biphasic flow velocity pattern with diastolic predominance was seen. In 8 patients who had total occlusion or severe (> 75%) stenosis of the LIMA by angiography, a systolic predominant pattern was seen. A diastolic/systolic peak velocity ratio of < 0.5 predicted severe left internal mammary artery graft stenosis with a sensitivity and specificity of 100% and 80% respectively. We conclude that Doppler echocardiography provides a noninvasive means of detecting significant stenosis of LIMA grafts in patients with recurrence of angina after coronary artery bypass surgery.

BRITISH NUCLEAR CARDIOLOGY GROUP: SURVEY OF UK NUCLEAR CARDIOLOGY PRACTICE 1993
DJ Pennell, J Caplis, E Pruklovich
On behalf of the British Nuclear Cardiology Group

In mid-1994, questionnaires were mailed to 218 departments practising nuclear cardiology in the UK, requesting data on current practice of nuclear cardiology. To date 132 (61%) have replied, and the following total figures have been adjusted for this proportion. The estimated total number of nuclear cardiology scans in 1993 was 40,300, of which 24,900 were myocardial perfusion imaging (MPI) and 14,100 were ventriculograms. On a national basis this represents respectively approximately 0.5 and 0.3 scans/1000 population per year. The stress used for MPI was exercise 45%, dipyridamole with exercise 20%, IV dipyridamole 16%, adenosine with exercise 16%, adenosine 2%, dobutamine 2%, oral dipyridamole 0.2%, and ice 0.2%. Thallium was used in 66% and MIBI in 33%, with a strong preference for the 2 day protocol (86%). Tomography was used in 77% and planar in 33%. Ventriculography was performed with an equilibrium technique at rest 81%, equilibrium at rest and stress 11%, first pass at rest 5%, and first pass at rest and stress 3%. Workload for cardiac scans was reported as rising, steady or falling in 58, 44, and 1 centres respectively. The use of MPI has more than doubled since 1988, but ventriculography has slightly decreased. This reflects the growing clinical acceptance of perfusion imaging, but also the preference of cardiologists to gauge ventricular function from echocardiography. Although progress has been made in greater performance of MPI, which is increasingly matched with tomographic equipment, the UK still lags very far behind the US (average 1.8 MPI/1000/year). For all nuclear cardiology scan, the UK is also still far behind the USA (4 scans/1000/year). The anticipated increasing workload for nuclear cardiology is encouraging, but improved provision of services is required.

ASSessment of Gastroepiploic Artery ByPass graft blood flow with H130 and Dynamic Position Emission Tomography
N Spyrou, F Sogliani, R Foale, R de L. Stanbridge, PG Camici
MRC Clinical Sciences Centre, Royal Postgraduate Medical School, Hammersmith Hospital and St Mary's Hospital, London.

In view of the favourable results of coronary artery bypass grafting (CABG) using the internal mammary artery other arterial conduits have been sought. The gastroepiploic artery (GEA) has often been used. However, the assessment of this method of revascularisation has proved difficult. The aim of this preliminary investigation was to assess whether coronary revascularisation using the GEA is effective in relieving ischaemia in patients with coronary artery disease. Regional myocardial blood flow (MBF, ml/min/g), at baseline and following dipyridamole infusion (Dip, 0.56mg/kg over 4 minutes), was measured with H130 and dynamic positron emission tomography (PET) in 5 patients with coronary artery disease before and after GEA bypass. All operations where carried out by the same surgeon. The GEA was attached to the inferior wall, in 4 cases using the posterior descending artery and in 1 case the distal circumflex artery. Baseline MBF was corrected for the rate pressure product (RPP) using the following formula: cMBFbas = MBFbas/RPP x 10. Coronary flow reserve ( CFR), was calculated as MBFdip/cMBFbas.

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<th>Post-op</th>
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<tr>
<td></td>
<td>MBFbas</td>
<td>MBFdip</td>
</tr>
<tr>
<td></td>
<td>MBFbas</td>
<td>MBFdip</td>
</tr>
<tr>
<td>Pt 1</td>
<td>1.13</td>
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<tr>
<td>Pt 2</td>
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<tr>
<td>Pt 3</td>
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<tr>
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<td>1.37</td>
<td>1.35</td>
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<tr>
<td>Pt 5</td>
<td>1.00</td>
<td>0.93</td>
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In conclusion: 1) All five patients showed a substantial increase of MBFdip and CVR following GEA bypass; 2) PET allows the noninvasive assessment of effectiveness of GEA coronary bypass.

SAFETY AND EFFICACY OF SECONDARY PACEMAKER IMPLANTATION IN PATIENTS WITH IMPLANTABLE CARDEOVERTOR DEFIBRILLATORS
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Background: The automatic gain control feature in implantable cardioverter defibrillators (ICD) is designed to allow detection of ventricular fibrillation (VF), when the amplitude of the electrogram on the rate-sensing lead may be considerably smaller than that seen in sinus rhythm. There are concerns that if a pacemaker continues to pace during VF, detection of the arrhythmia by the ICD can be inhibited by resetting of the gain at each paced spike. Aim: This study examines the safety and efficacy of secondary pacing in patients with ICD's.
Methods: Patients in whom a pacemaker was secondary implanted underwent VF induction during which VF sensing by the ICD was carefully observed. Spontaneous episodes of VF were also telemonitored and examined for sensing dropout. Results: Five patients had pacemakers implanted (Medtronic Activitrax VVR, Teletronic Refex DDD, Siemens DDD, Medtronic Minuet DDD and Medtronic Theris DDD) in addition to an ICD ( CPI P2, CPI Prorx2, Ventex Circitena and Medtronic Jewel (2 patients)). The mean number of induced VF episodes was 2.8 (range 2-4), and the mean number of spontaneous episodes was 3.8 (range 0-15). No problems with VF sensing occurred in any of the patients despite continued pacing by the pacemaker during both the induced and spontaneous episodes. Furthermore, telemetry of pacemaker after shock delivery demonstrated that none had been reset. The only pacemaker /I CD interaction observed was T wave sensing by the ICD following V pacing from the pacemaker in one patient, which was easily corrected. Conclusions: Secondary implantation of a pacemaker is safe and does not interfere with VF sensing by an ICD. Continuous ventricular pacing from the ICD may reduce its longevity by up to 18 months. Implantation of a pacemaker may therefore be an extremely cost-effective way to ensure pacing in patients with ICD's.
OPTIMAL PACING HAEMODYNAMICS

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A 3 phase relation has been shown between increasing cardiac output (CO) and heart rate (HR) with CO initially increasing phase I, a plateau phase II and finally decreasing CO phase III as the HR increases. Inappropriate rate response programming could lead to detrimental haemodynamics. The maximum CO at a given rate is achieved if the heart fills at the fastest rate throughout the whole of the filling time. The Active Time (AT) is defined as the total time that would elapse from the beginning of the cardiac cycle to the end of the filling phase providing that the ventricles are refilled at this rate. This AT can be calculated from waveform data derived from the Capintec VEST as shown below.

20 patients with CHF have been studied under constant exercise conditions at 3 different work loads either 75, 50, 25 and 0 watts, during VVI pacing. After 3 minutes of exercise the pacing rate was increased at 1 minute intervals, until in excess of their maximum sinus rate. The AT was then calculated at each HR for each work load and converted into a heart rate (ATHR) and plotted against the paced rate. The Maximum Haemodynamic Sensor Rate (MHSR) is defined as the HR above which their will be a compromise of cardiac function which is the intersection of the paced rate and the ATHR. The mean MHSR at 75 watts was 115 bpm (95% confidence intervals (CI) 102-128), at 50 watts 106 bpm (95% CI 100-112, p<0.003), 25 watts 97 bpm (95% CI 92-101, p<0.007, 90 bpm (95% CI 87-93, p<0.002). A plot of CO against HR was derived from the same data and the MHSR was shown to lie within phase II. In conclusion, a sensor able to limit the maximum rate to the MHSR will mean that phase III is never entered and optimal pacing haemodynamics will be achieved.

AUDIT OF THE CURRENT PRACTICE AND COMPLICATIONS OF TEMPORARY TRANSCUTANEOUS CARDIAC PACING

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Despite an established role in the management of bradycardia, the practice and complications of temporary pacing have received little attention. This paper reports the first survey of temporary cardiac pacing in district general hospitals. 18 of the 20 acute hospitals in the Northern Region participated in this 6 month prospective study. 194 temporary pacings were reported, the mean age of patients being 71 years (range 33-88), 123 (64%) were performed by Senior House Officers, 49 (25%) by Registrars, 9 (5%) by Senior Registrars and 11 (6%) by Consultants (with 2 done by anaesthetists). In total, Consultants were involved (by supervising or performing) in only 28 (14%), 110 (57%) were performed between 9 am and 6 pm, 56 (29%) between 6 and 12 pm and the remaining 28 (14%) between midnight and 9 am. 129 (66%) had complete heart block and in 102 (53%) cases, pacing was performed to manage the complications of acute myocardial infarction. For venous access, the right subclavian vein was chosen in 132 but proved unsuccessful in 22 (17%). In 36 the right internal jugular was chosen but was unsuccessful in 3 (8%). Immediate complications were reported in 12 (6%): ventricular tachycardia/fibrillation requiring DC shock in 6, arterial puncture in 3, pneumothorax in 2 and possible brachial plexus injury in 1. These last three complications occurred following attempted subclavian puncture. Late complications were reported in 22 (12%): ventricular arrhythmia requiring DC shock occurred in 10, proven sepsicaemia in 7 (Staphylococcus aureus in 6, Streptococcus in 1), possible sepsicaemia (but negative blood cultures) in 3 and wound infection in 2. 38 (17%) pacing wires required repositioning, 33 in the first twelve hours and 5 complications were found in 11 patients (3.5%). Of the 194 patients, 11 died within one hour of the procedure and a further 55 (28%) during the hospital admission. 72 (37%) required inotropic support, 96 (50%) were returned to the ward after a trial of pacing and 20 (10%) required permanent pacing.

Conclusion: Problems and complications with temporary pacing remain common. Pacing is generally performed by junior medical staff and consultants are involved infrequently. The timing of most procedures is such that greater consultant involvement is feasible. Whether this would reduce the complication rate is unknown.

BUDGETARY IMPLICATIONS OF IMPLEMENTING THE BPEG PACING GUIDELINES: FIVE YEAR STUDY OF 1600 IMPLANTS

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In 1991 the British Pacing and Electrophysiology Group (BPEG) published guidelines recommending a substantial increase in the proportion of permanent pacing systems providing 'physiological' pacing. Despite concerns about costs, to date only projected data on the fiscal consequences of physiological pacing programmes have been available. In a 4.5 year audit involving a total of 1600 procedures at a major implanting centre, the number of systems implanted annually increased by 16% from 332 in 1990 to 385 in 1993 but total annual expenditure on pacing increased by 69% from £300,139 to £508,417. Over the study period the proportion of patients receiving 'physiological' pacing systems increased progressively from 22.9% in 1990 to 64% (36.9% dual chamber) in 1994. In 1994 83% of patients aged <80 years received pacing systems in accord with BPEG guidelines. Thus, the cost/implant also increased progressively from £393 in 1990 to £537 in 1994, a 70% increase. Corrected for inflation this represents a 47% increase in the cost/implant. The average cost of implantation over the study period was £2030 for dual chamber systems, £1401 for VVI and £812 for VVI. Suprisingly, the actual and projected longevity of individual units was similar irrespective of pacing mode: over the study period the mean generative life was 7.2 years for dual chamber systems, 7.0 years for VVI and 7.2 years for VFI. Thus, the mean cost per year of pacing was £277 for dual chamber systems, £182 for VVI and £112 for VFI.

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of Implants</th>
<th>Physiological (%)</th>
<th>Dual Chamber (%)</th>
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<th>Cost/Unit (£)</th>
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<tr>
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<td>332</td>
<td>22.5</td>
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<td>300</td>
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<td>1991</td>
<td>357</td>
<td>28.2</td>
<td>10.5</td>
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<td>1992</td>
<td>361</td>
<td>41.0</td>
<td>19.1</td>
<td>429</td>
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<tr>
<td>1993</td>
<td>385</td>
<td>51.5</td>
<td>26.8</td>
<td>508</td>
<td>1319</td>
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<tr>
<td>1994</td>
<td>(7/12)</td>
<td>65.0</td>
<td>39.9</td>
<td>639</td>
<td>1537</td>
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In conclusion, following the BPEG guidelines for the majority of patients requiring permanent pacing has resulted in a 47% real increase in the annual cost of service provision. This is due primarily to a greater initial outlay on pacing hardware and not reduced unit life. Additional 'hidden' costs which merit consideration include more complex follow-up and longer implantation time.

PERMANENT PACEMAKERS AFTER CARDIAC TRANSPLANTATION: COST EFFECTIVE AUDIT?

ND Holt, G Parry, M Tynan, JH Dark, JM McComb
Department of Cardiopulmonary Transplantation, Freeman Hospital, Newcastle upon Tyne.

An audit in 1990 of permanent pacemaker (PPM) usage in cardiac transplant (CTX) recipients revealed that no patient who had a pacemaker before the 16th day after CTX had been pace long term. As a result of this, our policy was changed from early implantation (day 8 to 21) on a prophylactic basis when resting heart rate was below 70 beats/min (period 1), to later implantation such that only recipients with bradyarrhythmias that persisted at the 21st day post CTX received a PPM (period 2). The cost-effectiveness of this change was assessed using 1994 cost figures. In period 1, 16 PPM were implanted in 152 recipients (10.5%) compared with 13 in 148 recipients (8.8%) in period 2. Three patients have had PPM implantation at a late stage, 1 in period 1 and 2 in period 2. None had indications for pacing at 2 or 3 weeks and are therefore not included. Mean in-patient stay following CTX in PPM recipients in period 1 was 13.63 days compared with 23.69 days in period 2. The cost of this extended hospital stay is approximately £55,570 excluding cost of cyclosporin (mean cost of in-patient stay on the transplant ward is £440/day, mean cost of cyclosporin per patient is £15.50/day). Had the implantation policy not been changed, an estimated excess of 3 PPM would have been implanted during period 2. Mean cost of PPM per patient implanted is £2025. Cost of PPM implantation has been reduced therefore by adoption of pacing change in PPM implantation policy has therefore resulted in increased expenditure of £49,495 assuming that PPM implantation was the only reason for the extended hospital stay. This should, however, be balanced with the potential risks of permanent pacemaker implantation.
CHAMBER AND SUBTYPE SELECTIVE Β-ADRENOCEPTOR DOWNREGULATION IN THE SYMPTOMATICALLY DENERVATED HUMAN HEART: AN ENDPOINT OF IDIOPATHIC DILATED CARDIOMYOPATHY

M R Chester, D B Barnett. Cardiological Sciences Dept, St George's Hospital and the Department of Pharmacology, Leicester Royal Infirmary.

Studies in humans and experimental models of heart failure have demonstrated the importance of sympathetic innervation to β-adrenoceptor regulation. These observations are consistent with the prevailing view that β-adrenoceptors are mostly regulated by sympatoadrenergic activity. However, this hypothetical mechanism has not been previously tested in humans. The failing transplanted human heart provides a unique opportunity to assess the effect of heart failure on cardiac β-adrenoceptors in the absence of sympathetic innervation. We therefore assessed the effect of cardiac failure on β-adrenoceptor density in 5 transplanted (sympathetically denervated) human hearts and 5 normal controls using radioligand binding techniques. Results. Right ventricular total and subtype β-adrenoceptors in the denervated hearts were downregulated compared to the controls. β1-adrenoceptors were selectively downregulated in the right ventricle compared to the left ventricle of the denervated hearts. Tissue levels of noradrenaline confirmed sympathetic denervation in the transplanted hearts. Conclusion. The study shows that sympathetic innervation is not necessary for chamber and subtype selective downregulation. Control of the sympatoadrenergic pathway is potentially important in the management of heart failure and further research should continue to be directed towards selectively regulating β1-adrenoceptors at the post synaptic membrane.

QT INTERVAL DISPERSION PREDICTS CARDIAC DEATH IN PATIENTS WITH PERIPHERAL VASCULAR DISEASE.

NC Davidson, D Darbar, J Luck, G Main, TH Pringle, GP McNell, AD Struthers, Departments of Clinical Pharmacology and Cardiology, Ninewells Hospital and Medical School, Dundee.

Patients with peripheral vascular disease (PVD) often have coincidental, asymptomatic coronary artery disease (CAD) and are therefore at risk of cardiac death. Identifying patients at risk has previously involved an exercise test, a thallium scan or coronary angiography. We examined whether QTc interlead dispersion, the difference between the longest and the shortest corrected QT interval in a standard resting 12 lead ECG, was able to identify prospectively those patients who would subsequently suffer a cardiac death. Forty-nine patients with no signs or symptoms of cardiac disease were followed for 5 years after baseline investigations of coronary angiography, radionuclide ventriculography and QTc dispersion. The patients were divided into 3 groups: survivors(S), n=34, cardiac death(CD), n=12, and non-cardiac death(NCD), n=3. The left ventricular ejection fractions were similar in all three groups: S 46(95%CI 42-50%), CD 44(39-49%), and NCD 45(33-58%). QTc dispersion was significantly prolonged (p=0.0008) in the CD group (mean131ms±17[95%CI 78,3-184]) as compared to S (53[51.8-61.1]). The standard deviation of the QTc between leads was significantly greater(p=0.0001) in the CD group(mean42.8) than in the S group(19.3). A QTc dispersion ≥90ms/c had a 92% sensitivity and a 95% specificity for the prediction of cardiac death. Although coronary angiographic findings in terms of normal, 1, 2, or 3 vessel CAD did not correlate significantly with either QTc dispersion or cardiac death, QTc dispersion in those patients with diffuse CAD was significantly greater (p=0.05) than in the other groups. We have found a strong link between QTc dispersion and cardiac death in patients with PVD who have neither symptoms nor signs of cardiac disease. Indeed QTc dispersion was a much better predictor of cardiac death than coronary angiographic findings. We also found that QTc dispersion was significantly greater in those patients with diffuse CAD than in those with discrete, exclusive CAD. QTc dispersion is therefore a cheap and non-invasive method of cardiac risk stratification in patients with peripheral vascular disease.

QT DISPERSION AND RR VARIATION ON 12-LEAD ECGS IN PATIENTS WITH CONGESTIVE HEART FAILURE SECONDARY TO IDIOPATHIC DILATED CARDIOMYOPATHY

Lu Fei, J H Goldman, K Prasad, P J Keeling, K Reardon, W J McKenna, A J Camm. Cardiological Sciences, St George’s Hospital Medical School, London.

Background: Data on QTd in patients with congestive heart failure are scarce.

Methods: In this study, conventional 12-lead ECGs were recorded in 135 consecutive patients with congestive heart failure secondary to idiopathic dilated cardiomyopathy. Seventy five patients were excluded due to one or more of the following reasons: (1) low amplitude of the T wave(n=3), (2) atrial fibrillation(n=26) and (3) bundle branch block (n=46). QTd was evaluated in the remaining 60 patients. QTd was calculated as (1) QT-range: the difference between the maximum and minimum QT intervals on any of the 12 leads and (2) QT-sd: the standard deviation of the QT interval in all the 12 leads. RR intervals were measured in leads II, aVL, V2 and V5.

Results: QT-ad (20.8±4.50 ms) was significantly (p=0.8997, p<0.001) related to QT-range (65.6±15.77 ms), but not to the QT interval. Neither QT-range nor QT-sd was significantly related to age, left ventricular dimensions, left ventricular and diastolic pressure, left ventricular ejection fraction or left ventricular wall thickness. There was no significant difference in QTd between survivors and those who died (n=8) or were transplanted (n=9) during 34±23 month follow-up. No significant difference in QTd was observed between patients with and without ventricular tachycardia (a 3 consecutive beats) detected on 24-hour Holter ECGs. RR interval variation was significantly lower in patients who died compared with survivors (standard deviation: 36.0±24.3 vs 10.3±4.6, p<0.001, coefficient of variation: 4.5±6.4% vs 1.8±7.0%, p<0.001).

Conclusions: These data suggest that QTd in congestive heart failure is not significantly related to either QT interval or cardiac size and function and does not predict death. The application of QTd assessment is limited by the commonly encountered atrial fibrillation and bundle branch block in this patient population. It seems that reduced RR variation on standard 12-lead ECGs has important prognostic implications in these patients.

EXERCISE INDUCED VENTRICULAR ARRHYTHMIA IS ASSOCIATED WITH INCREASED QT DISPERSION

S. Aggelakas, A. Dritsas, A. Michailidis, P. Toutouzas, D.V. Cokkinos, Onassis Cardiac Surgery Center and University Cardiology Department, Hipokration Hospital, Athens, Greece.

Increased QT dispersion (≥50ms, defined as the difference of maximum QT across the 12 leads of a standard ECG) is observed in patients (pts) with propensity to ventricular arrhythmias (VA). We examined its correlation with exercise-induced VA, in 48 pts (mean age 62±9 years) with angiographically documented coronary artery disease. All underwent a treadmill exercise test on the Bruce protocol and were divided into 2 groups according to the presence (Group 1, n=25) or absence (Group 2, n=23) of high grade VA (Lown grade>IIIB) during exercise.

Mean age 58±10 vs 62±10 yrs, history of myocardial infarction (52% vs 50%) and rate corrected maximal QT (QTc, 426±39 vs 421±34) were similar in the 2 groups. QTc dispersion at rest was greater in Group 1 (42±12 ms) compared with Group 2 (44±13 ms, p<0.01). Heart rate expressed by the RR interval was not different between the two groups both at rest (75±12 ms vs 81±13 ms) and at peak exercise (42±17 ms vs 46±27 ms, respectively). QTc dispersion increased significantly during exercise compared with baseline both in Group 1 (55±17 ms vs 41±12 ms, p<0.01) and Group 2 (51±20 ms vs 44±13 ms, p<0.05). QTc dispersion at peak exercise was greater in Group 1 (55±17 ms) compared with Group 2 (31±20 ms, p<0.01).

Thus, QT dispersion derived both at rest and at peak exercise can distinguish patients prone to high grade VA induced by exercise. These findings provide further support to the concept that it is a simple non-invasive arrhythmogenic marker.
REGRESSION OF LEFT VENTRICULAR HYPERTROPHY IS ACCOMPANIED BY A REDUCTION IN QT DISPERSION
J Mayet, M Shah, K McGrath, V R Pooler, P S Spenn, D W Davies, S A McG Thom, R A Foale, St. Mary's Hospital, ICSTM, London

We have previously found that left ventricular hypertrophy (LVH) is positively correlated with QT dispersion. However it is difficult to separate this relationship from those involving blood pressure, E/A ratio, isovolumic relaxation time (IVRT) and age, which are all also related to QT dispersion. In order to assess which factors are most important in determining QT dispersion a prospective regression study was undertaken. 24 previously untreated hypertensive patients underwent 2 dimensional and Doppler echocardiography to determine left ventricular mass index (LVMI), E/A ratio and IVRT. Additionally from a 12-lead ECG examination QT length was measured for each lead and corrected for heart rate (QTC). QTC dispersion was determined as the difference between the maximum and minimum QTC interval. Patients were then treated with Ramipril with the addition of Felodipine if necessary. Investigations were repeated after 6 months of BP control and again after a 2 week washout period.

QTC dispersion decreased from 82.8 to 63.4 ms after treatment, and after drug washout was 66.4 ms (F=4.9, p<0.01). The change in LVMI over this period was 144.1, 121.1, 124.4 g/m² (F=13.6, p<0.01). Systolic BP decreased from 175 to 144 mmHg and increased again to 164 mmHg after drug washout (F=22.5, p<0.01). E/A ratio (0.97, 1.02, 1.02, P=0.37, P=0.69) and IVRT (111, 112, 112, F=0.03, P=0.97) remained unchanged through the 3 assessment points.

In conclusion, QTC dispersion decreased in parallel with LVMI, even though the parameters of left ventricular relaxation (E/A ratio and IVRT) remained the same. QTC dispersion remained decreased after a 2 week washout period when BP increased again; this would seem to exclude a direct effect of BP reduction. These data add weight to the suggestion that QTC dispersion is intimately related to LVH.

SHORTENING OF THE QT INTERVAL IMMEDIATELY PRECEDING THE ONSET OF IDIOPATHIC SPONTANEOUS VENTRICULAR TACHYCARDIA
Lü Fei, A J Camm. St George’s Hospital Medical School, London

Background A prolonged QTC interval is generally believed to be associated with a propensity to ventricular tachyarrhythmias. Whether there is a change in the QT interval immediately preceding the onset of ventricular tachyarrhythmias episodes is unknown.

Methods In this study, the QT interval was evaluated on ambulatory Holter electrocardiograms in 10 patients with idiopathic ventricular tachycardia (5 men and 5 women, aged 38 ± 16 years) in a drug free state. Three consecutive QT intervals immediately prior to the onset of 60 episodes of ventricular tachycardia were measured on ECG strips from 24-hour Holter recordings and were compared to those recorded at the same heart rate approximately 40 minutes previously.

Results: There was a significantly higher heart rate immediately preceding the onset of ventricular tachycardia compared with mean heart rate over the 24-hour period (93 ± 12 vs 77 ± 12 beat per minute, p < 0.01). The QT interval was significantly shorter prior to the onset of ventricular tachycardia compared to that occurring 40 minutes before at the same heart rate (342 ± 43 vs 353 ± 35 ms, p < 0.01) (Figure). A shortened QT interval existed before the onset of most of the ventricular tachycardia episodes (75%).

Conclusions We conclude that a transiently shortened rather than prolonged QT interval may play an important role in the pathogenesis of idiopathic ventricular tachycardia.


Patients with the congenital long QT syndromes (LQTS) have a tendency to life threatening ventricular arrhythmias, particularly during conditions of stress. Differential timing of repolarisation between neighbouring areas of myocardium, which may be reflected by increased QT dispersion on the surface ECG, provides a possible substrate for these arrhythmias. The prognosis in this condition is improved by beta-blockade. In this study we evaluated the effect of beta-blockade on the dynamics of the QT interval and of QT Dispersion in 7 LQTS patients. QT intervals were measured from the beginning of the QRS complex to the return of the repolarisation wave to the TP baseline (including U waves where present) in at least 11 leads of a simultaneous 12 lead ECG recording. QT intervals were corrected for heart rate using Bazett's formula (QTC), but non-rate-corrected values were used for dispersion analyses. Exercise QT intervals were measured when the patient's heart rate was approximately 120 beats per minute in all cases. Data were compared using the paired t-test and are expressed as mean ± SD.

Results: Resting QTC values were not significantly different before and after beta-blockade (0.58±0.07 vs. 0.55±0.06, p=0.18). However, QTC values during exercise were significantly reduced after medication (0.59±0.03 vs. 0.53±0.06, p=0.01). QT dispersion, defined as the difference between maximum and minimum QT intervals for the 12 leads, tended to increase during exercise on no medication (0.08±0.03 to 0.09±0.03), while dispersion decreased during exercise after beta-blockade (0.10±0.06 to 0.06±0.02). These differences did not reach statistical significance. Similar results were observed for the standard deviations of QT intervals from the 12 leads 0.22±0.07 increasing to 0.02±0.01 on no medication and 0.01±0.02 decreasing to 0.02±0.006 on beta-blockers. Conclusion: These results suggest that beta-blockade may protect against stress induced arrhythmias in the LQTS by improving rate adaptation of the QT interval and may also prevent an abnormal rise in QT dispersion during exercise.

SPATIAL CORRELATION OF INFARCT SITE AND QTc
Q Fang, JC Doig, TPM Gumbrilie, AFN McDermott, JP Bourke, SS Furniss, RWP Campbell. Academic Cardiology, Freeman Hospital and University of Newcastle upon Tyne.

QT and QT dispersion are affected by myocardial infarction (MI). Both may be a marker of arrhythmogenic risk. Little is known of how MI causes QT effects.

Aim: To determine whether MI has a global QT effect or has an ECG lead spatial effect.

Method: 12 lead ECGs were obtained from 20 acute MI patients (first MI;10 anterior; 10 inferior; 1-6 hours from symptoms) and from 15 healthy individuals. QT was measured by digitizer in 2 consecutive cardiac cycles in each of the 12 leads. QTc values were plotted in an ECG lead arrangement which reflected vectorial spatial characteristics.

Results: QTc was longer in MI patients (both anterior and inferior) than controls (p<0.01). The QTc curve of normals was relatively flat across the ECG (normal QTc dispersion (QTcmax - QTcmin)=50ms). By contrast, QTc curves of MI patients showed fluctuations. The QTc dispersion of anterior MI (mean = 68 ms) was larger than controls (p<0.05) as was QTc dispersion of inferior MI (p=ns). Anterior and inferior MI QTc curves were similar in the V leads and AVR but QTc rose in AVF and II in anterior MI and fell markedly in these leads of inferior MI.

Conclusion: Infarction, particularly anterior, creates QTc dispersion. There are spatial correlations of myocardial damage with specific ECG leads. This new finding (QT mapping) adds yet another dimension to QT analysis.

Conclusion: Infarction, particularly anterior, creates QTc dispersion. There are spatial correlations of myocardial damage with specific ECG leads. This new finding (QT mapping) adds yet another dimension to QT analysis.
PERIOPERATIVE ASSESSMENT OF MYOCARDIAL STUNNING USING TRANSESOPHAGEAL ECOCARDIOGRAPHY COMBINED WITH HIGH-FIDELITY VENTRICULAR PRESSURE

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Royal Brompton Hospital, National Heart & Lung Institute, London SW3

Detecting and quantifying of myocardial stunning is essential for optimal clinical management early after cardiac surgery. To compare the significance of changes in haemodynamics with those in regional myocardial function and perfusion early after aortic valve replacement (AVR), we studied 27 pts (age 62±12 (M±SD) yrs, with normal coronary arteriogram) during induced AVR (cardioplegia time 10±1.8 min) due to stenosis (n=20) or regurgitation (n=7). Transoesophageal Doppler echocardiogram with simultaneous high fidelity left ventricular (LV) pressure and cardiac output was recorded before bypass and 0.5, 6, 12, 20 hours after reperfusion. Regional stroke work (SWaw) per cubic centimetre myocardium of anterior wall was derived from continuous measures of LV cavity pressure, dimension and wall thickness. 5MHz pulsed Doppler was used to measure the flow velocities in the proximal left descending coronary artery (LAD), and the time integral of flow velocity per beat (VTLAD) was determined. Results: After 30 minutes reperfusion and off bypass, LV stroke volume index and cardiac index were unchanged compared with preop. However, the SWaw fell from 3.0±1.4 to 1.6±0.7 mJ.cm-3, and did not recover until 20 hours (2.2±0.7 mJ.cm-3), p<0.001; Simultaneously, VTLAD increased from 6.2±0.9 to 4.2±0.7 cm, and subsequently returned (23±11 cm) to baseline, p=0.006; The ratio of SWaw to VTLAD fell from 0.18±0.10 to 0.07±0.05 mJ.cm-4, and had not fully recovered at 20 hours (0.12±0.07 mJ.cm-4), p<0.001. Thus, myocardial stunning is characterised by reduced myocardial mechanical work, and increased coronary flow velocity. The ratio of function to coronary flow velocity is a more sensitive index of myocardial stunning than global hemodynamics. However, its relevance to clinical outcome need to be studied further.

MORTALITY IN ACUTE MYOCARDIAL INFARCTION: DO YOUNG PATIENTS REALLY FAIR SO WELL?

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London Chest and Newham General Hospitals

It is well established that the risk of death in acute myocardial infarction (AMI) is affected importantly by age, younger patients faring better than the elderly. Assessing as this may be for the younger patient, it says nothing of his or her risk relative to the general population. We have attempted to define 2 age group, (ii) the all-cause mortality rate per 1000 person-years, and (iii) the standardized mortality ratio (SMR), using 1991 England and Wales mortality rates by 5 year age group and sex. The main results are summarized below:

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Relative risk</th>
<th>Mortality rate/1000/year</th>
<th>SMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>1.0</td>
<td>32.0</td>
<td>13.3</td>
</tr>
<tr>
<td>50-69</td>
<td>1.29</td>
<td>(0.54-3.07)</td>
<td>(28.8-57.4)</td>
</tr>
<tr>
<td>70+</td>
<td>4.56</td>
<td>(1.95-10.7)</td>
<td>(146.0-226.103)</td>
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</tbody>
</table>

Thus, in the youngest age-group the absolute risk of death was about 3% a year, but the risk of death in comparison with the general population the same age was very high. In contrast, patients 70 had an absolute risk of death of about 15% a year, but the excess risk compared with their contemporaries was much lower. Indeed, those well enough to be discharged within a week had an SMR of only 1.67. In conclusion, prognosis measured by SMR in young patients with AMI is particularly bad and justifies a more aggressive approach in terms of risk stratification and revascularisation in this group.

SLOW RECOVERY DOES NOT PRECLUDE A GOOD RESULT

L Holmes, S Treasure, S Gallivan
St. George's and UCL, London

THE PROBLEM: Cardiac surgical patients who have a lingering postoperative course present ethical, logistic, and economic dilemmas.

AIM: To define the outcome a year after surgery for these patients.

METHODS: All adult cases under the care of ten surgeons, in three units, were registered during a 12 month period. Those who spent more than 48 hours in ICU were followed for a year and the survivors assessed with the Index of Health Related Quality of Life (IQHL), Euroqol (also an index), and the Nottingham Health Profile (NHP). A reference population of 365 patients operated upon within the same time frame, but with <48 hours ICU stay, were similarly studied.

RESULTS: Of 2256 cases, 162 (7.2%) met the criterion of >48 hours in ICU. They included a higher than usual proportion of emergencies (21%) but 44% were elective cases. 115 survived to leave ICU; 98 were alive at one year (100% follow up). One declined assessment. He was at work.

Index Study N=97 Reference N=365
IQHL (IGR) 0.77±0.96 0.62±0.97 (NS)
Euroqol (IGR) 0.32±1.0 0.43±1.0 (NS)

In the NHP, the study group were significantly more impaired in only two domains, social interaction and mobility, while the risk of death (<48 hour ICU) were used to construct a 5%–95% reference range. Of the study patients only 109 by IQHL and 78 by Euroqol fell within this reference.

CONCLUSIONS: Of the relatively small number of patients in ICU >48 hours the majority (98/162, 60%) were alive, at home, and independent at one year, with measured QOL not significantly worse than other cardiac surgical patients.

THE ROLE OF ENDGENOUS BRADYKININ IN HUMAN CORONARY VASOMOTOR CONTROL

PH Groves, S Kurz, H Just, H Drexler
Department of Cardiology, University of Freiburg, Germany.

Bradykinin (BK) causes vasodilation through the stimulated release of endothelium-derived nitric oxide, prostaglandins and hyperpolarizing factor. We have investigated the endogenous activity of BK in 125 men undergoing elective coronary angiography. In 100% coronary lumen was determined using an IC. Doppler flow wire and ECG was measured by quantitative coronary angiography at baseline, after IC. acetylcholine (Ach, via infusion catheter; 0.03, 0.36, 3.6 mg/min) and after 10 mic of lcu. HOE 140 (via guide catheter; 200 mg/ml). Flow-dependent dilation (FDD) was assessed before and after HOE 140 (IC. papaverine 8mg). Ach caused vasodilation in 5 patients and vasoconstriction in 5. HOE caused an increase in coronary vascular resistance - mean±SEM (2.92±0.31) to 3.57±0.33 mmHg/ml/sec, p<0.005) and a decrease in CBF (40.31±2.92 to 33.51±2.18 ml/min, p<0.01). Following HOE there was a reduction in CBF in both the intramural (9.03±1.12 to 7.57±1.04, p<0.001) and mid vessel (4.48±0.56 to 3.82±0.52 mm2, p<0.001). FDD was significantly inhibited by HOE 140 (2.43±6.94 to 3.93±6.01, p<0.001). This inhibitory influence of HOE on FDD was also apparent in patients with angiographic narrowing. These data provide the first evidence that endogenous BK plays an important role in mediating basal and stimulated vasomotor responses in the human coronary circulation.
DO THE ENDOTHELINS CONTRIBUTE TO PERIPHERAL VASCULAR DILATION IN CHRONIC HEART FAILURE? M.P. Love*, W.G. Haynes, D.J. Webb & J.J.V. McMurray*. Departments of Cardiology* and Medicine, Western General Hospital, Edinburgh.

The endothelins have potent vasoconstrictor, anti-natriuretic and mitogenic properties which have implicated them in the pathophysiology of chronic heart failure (CHF). Mutant endothelins are generated from its biologically inactive precursor big endothelin by endothelin converting enzyme (ECE). Current evidence suggests that the ETA receptor is the major endothelin receptor subtype mediating endothelin induced vasoconstriction in humans. We investigated the contribution of the endothelins to peripheral vasoconstriction in CHF by examining the effects of phenolamine (a combined ECE and endothelinatepeptidase inhibitor), thiorphan (a selective neutral endopeptidase inhibitor) and BQ-123 (a selective ETA receptor antagonist) in CHF patients (mean age 66 years, NYHA II-IV) already treated with a diuretic and ACE inhibitor. Drugs were infused into the left brachial artery for one hour while forearm blood flow was measured by venous occlusion plethysmography. Phosphoramidon (30 nmol/min) was administered to 10 patients and caused a 52.3 ± 10.1% increase in forearm blood flow (p<0.0006). Thiorphan (30nmol/min) was administered to 8 patients and caused a 15.8 ± 6.0% decrease in forearm blood flow (p=0.0034). BQ-123 (100 nmol/min) was administered to 10 patients and caused a 31.3 ± 5.6% increase in forearm blood flow (p=0.002). Heart rate and blood pressure did not change significantly in any study confirming that drugs had no systemic haemodynamic effects. The reduction in forearm blood flow observed with thiorphan is presumably secondary to reduced breakdown of small peptides such as angiotensin II and endothelin itself. This in turn indicates that the vasodilatation observed with phosphoramidon (which is equipotent with thiorphan as an inhibitor of neutral endopeptidase) is secondary to inhibition of ECE. We have shown that significant arterial vasodilatation results from ECE inhibition and ETA receptor blockade in patients with CHF. Importantly, this haemodynamic benefit is additional to that already obtained with an ACE inhibitor. Anti-endothelin strategies are exciting new therapeutic prospects in CHF.

MODERATED POSTER

PRESERVED ENDOTHELIAL FUNCTION IN THE BRACHIAL ARTERY IN PATIENTS WITH PREMATURE ATHEROSCLEROSIS N Stephens M J Brown M Miceli A Parsons P M Schofield. Cardiac Unit, Papworth Hospital and Cambridge University, UK.

Endothelial dysfunction, seen as loss of arterial flow-mediated dilatation (FMD) is held to be an early sign and pathogenic event in atherosclerosis. We have tested this hypothesis in subjects with proven coronary atherosclerosis (26 on angiography, 5 with Q wave MI), but who have none of the risk factors known to influence FMD. All were men <45 yrs or women <55 yrs, non-smokers with no history of diabetes or CHF. Patients and 19 healthy controls were studied after discontinuation of vasoactive drugs for 48 hrs. Baseline brachial artery diameter was measured with a 7MHz linear array ultrasound transducer (mean of 5 enddiastolic values), and then measured again after 4 minutes forearm ischaemia. This ischaemic stress produces a reflex vasodilatation in the normal brachial artery which is endothelin-dependent.

**Known CAD Controls P**

<table>
<thead>
<tr>
<th>Age/yr: mean ± sd</th>
<th>43.1 ± 7.4</th>
<th>33.7 ± 5.6</th>
<th>&lt;0.0001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male female</td>
<td>20:11</td>
<td>12:7</td>
<td>NS</td>
</tr>
<tr>
<td>Lipoprotein(a):</td>
<td>mean ± sd/mg/dL</td>
<td>31.1 ± 35.5</td>
<td>-</td>
</tr>
<tr>
<td>Chol; mean ± sd/mmol/L</td>
<td>6.23 ± 1.8</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>SBP; mean ± sd/mmHg</td>
<td>133 ± 23</td>
<td>125 ± 14</td>
<td>0.178</td>
</tr>
<tr>
<td>Vessel diam; mean ± sd/mm</td>
<td>4.42 ± 0.60</td>
<td>3.62 ± 0.65</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

FMD; mean ± sd/mg/dL 4.43 ± 5.67 7.23 ± 7.96 0.153

There is a trend towards a reduction of FMD in atherosclerosis (perhaps explained by greater vessel size), but the most striking finding in this study is its preservation in 21/28 patients. This finding questions the premise that "global" endothelial dysfunction is a fundamental early event in the development of coronary atherosclerosis.

MODERATED POSTER

ARTERIAL ACTIVITY IS IMPAIRED IN YOUNG HEALTHY SUBJECTS WITH A FAMILY HISTORY OF PREMATURE CORONARY ARTERY DISEASE INDEPENDENT OF OTHER CORONARY RISK FACTORS P Clarkson, R Henry, A E Donald, J A Powe, D S Celermajer, J E Deanfield. Great Ormond Street Hospital for Children NHS Trust, London, UK.

A family history of premature coronary artery disease (CAD) in first degree relatives is a risk factor for coronary disease. Genetic and environmental influences may both be responsible and interact, but their relative importance is unclear. We studied endothelial function in 44 first degree relatives (30 men, 14 women, median age 28 years, range 15-40) of young patients (men<55years, women<55years) with CAD, proven angiographically or with myocardial infarction. All subjects were well, lifetime non-smokers, not diabetic, not hypertensive and took no medications. Using high resolution external ultrasound we measured brachial artery diameter at rest, in response to reactive hyperaemia (endothelium-dependent vasodilatation) and to sublingual glyceryltrinitrate (GTN, an endothelium-independent dilator). Vascular responses were compared with those of 44 healthy controls matched for age, sex and brachial artery size. Flow mediated dilatation (FMD) was impaired in the family history group (5.30±1.0% vs Controls 8.2±5.6%, p<0.005). In contrast GTN caused dilatation in all subjects (family history 16.9±1.0%, controls 19.1±1.0%; p<NS) suggesting that reduced FMD was due to endothelial dysfunction. FMD in the family history subjects was not related to age, blood pressure or LDL-cholesterol. The family history subjects were divided into 3 groups: A-those with an elevated cholesterol (serum LDL-cholesterol >4.2 mmol/L) (10 subjects), B-those with a normal cholesterol whose affected relative had coronary risk factors (22 subjects), C-those with a normal cholesterol whose affected relative was free of such risk factors (12 subjects). While vascular responses were abnormal in all groups compared to controls, the subjects in Group C had the most impaired FMD despite absence of risk factors in their relatives or themselves (5.5±1.2% vs Group B 6.6±1.2%, p=0.1). Thus healthy young adults with a family history of premature coronary heart disease may have impaired endothelium-dependent and independent function of other risk factors. This implies an inherited abnormality of vascular function which may be an early manifestation of atherosclerosis. Early detection should permit identification of subjects who might benefit from interventional strategies.

MODERATED POSTER

GROSSLY ELEVATED SERUM LIPOPROTEIN(a) CONCENTRATIONS IN YOUNG WOMEN WITH ENDOMETRIOSIS D Crook, M Sidhu, R Howell, DK Edmonds, JC Stevenson. Wynn Institute for Metabolic Research & Dept of Obstetrics and Gynaecology, Queen Charlotte’s & Chelsea Hospital, UK.

Serum lipoprotein(a) [Lp(a)] has been implicated in the formation of atherosclerotic plaques, perhaps by interfering in fibrinolysis. Case-control studies show higher Lp(a) levels in subjects with CHD, but recent epidemiological studies do not support a causal role in the disease. This conflict would be explained if Lp(a) is an acute-phase protein, a role supported by the demonstration of functional interleukin-6 regulatory elements in the apo(a) gene promoter.

Women with endometriosis, a common disorder in which endometrial tissue is found outside of the lining of the uterine cavity, have high concentrations of activated macrophage products in their peritoneal fluid. We studied 39 non-obese women with untreated endometriosis and 39 healthy matched controls. Serum concentrations of lipid, lipoproteins and apolipoproteins were similar in the two groups except for five-fold higher concentrations of lipoprotein(a) in women with endometriosis (median 15.0 mg/dl [range 0.05-87.3 mg/dl] vs. 3.0 mg/dl [0.05-29.0 mg/dl] in controls; P<0.001). This difference remained highly significant after adjustment for differences in age, height, adiposity and cigarette smoking.

This study provides further evidence that Lp(a) is an acute phase reactant and challenges the view that serum Lp(a) levels will provide useful information about a healthy individual’s CHD risk.
(73) MODERATED POSTER

NITRIC OXIDE MEDIATES PACING-DEPENDENT EPICARDIAL CORONARY ARTERY VASODILATION BUT NOT FLOW CHANGES

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Epicardial coronary artery dilation occurs in response to an increase in heart rate by atrial pacing. Inhibition of basal nitric oxide synthesis causes a decrease in basal diameter of normal distal epicardial coronary arteries. It is not known whether the dilation of angioographically normal and diseased human epicardial coronary arteries during atrial pacing is nitric oxide-dependent. The effects of an intracoronary infusion of N\(^-\)monomethyl-L-arginine (LNMMMA), an inhibitor of nitric oxide synthesis, 4\(\mu\)mol/min for 8 mins, was studied in 11 male patients with coronary artery disease and in 3 male and 2 female patients with normal coronary arteriograms. In all patients atrial pacing up to 140 beats/min was performed during normal saline and during LNMMMA infusion. The diameter of angiographically normal coronary artery segments and stenoses was assessed by quantitative angiography and changes in blood flow velocity were measured with a Doppler catheter. A significant increase in luminal diameter of the proximal (7.02±1.1 and 5.7±1.0%, p<0.01) and distal (10.4±2.2 and 10.0±1.4%, p<0.01) segments of both normal and diseased arteries occurred during atrial pacing performed during the saline infusion. No change in luminal diameter occurred in either group during atrial pacing with the LNMMMA. A significant coronary blood flow velocity with atrial pacing was similar during saline infusion (3295±9%) and LNMMMA infusion (298±8.1%) in patients with coronary artery disease, but not in normals during LNMMMA (37±12.4%) infusion compared to saline infusion (272±8.4%, p<0.05). In conclusion, in patients with chronic stable angina and in normal subjects distal epicardial coronary artery segments during atrial pacing is inhibited by LNMMMA. Pacing induced blood flow increases are not inhibited by LNMMMA in patients with coronary disease and only slightly inhibited in normals. These findings suggest that epicardial coronary artery dilation, but not microvascular dilation during atrial pacing is dependent on nitric oxide synthesis.

(74) MODERATED POSTER

MODULATION OF LEFT VENTRICULAR FUNCTION IN HUMANS BY PARACRINE RELEASE OF NITRIC OXIDE FROM CORONARY ENDOTHELIUM

* A M Shah, ** P J Vantrimpont, # W J Paulus
*Department of Cardiology, University of Wales College of Medicine, Cardiff & **Cardiovascular Center, Aalst, Belgium

Previous studies in isolated hearts have shown that both exogenous nitric oxide and nitric oxide released from coronary endothelium exert direct effects on left ventricular (LV) contractile function. In normal human subjects, intracoronary infusion of the nitric oxide-donor sodium nitroprusside, enhanced LV relaxation and increased diastolic distensibility, independent of systemic vasodilatation. In this study, we investigated the effects of intracoronary infusion of substance P (20 pg/min for 5 min), which releases nitric oxide from endothelial cells, in 8 normal subjects with atypical chest pain and 8 transplant recipients free of rejection or graft vasculopathy (ages 30-68). Measurements were made of high-fidelity LV pressure, LV dp/dt and right atrial pressure. Sequential LV angiograms before and after substance P infusion were obtained in 11 patients, from which LV volumes were calculated. Biocoronyar artery substance P reduced the LV peak systolic pressure in normals (147±16 to 139±15 mmHg; p<0.05) and in transplant recipients (147±25 to 141±22 mmHg; p<0.05) and decreased the time to onset of isovolumic relaxation (time to dp/dtmax) by 0.07 ms, but did not alter LV dp/dt or the time constant of isovolumic relaxation. LV end-diastolic volume increased from 127±5 to 128±52 ml (p<0.5), despite a fall in LV end-diastolic pressure (144±8 to 125±5 mmHg; p<0.07), consistent with increased end-diastolic distensibility. Heart rate, stroke volume and ejection fraction were unchanged. Creation of biocoronyar artery substance P infusion resulted in a rebound increase in peak LV pressure to 154±18 mmHg in normals and to 152±20 mmHg in transplant recipients (both p<0.05 cf baseline). Right atrial infusion of substance P (60 pg/min) in 14 patients (8 normals, 6 transplant recipients) failed to alter LV systolic pressure or LVEDP. Thus, substance P-mediated stimulation of coronary endothelium modulates LV systolic and diastolic function in humans; this pathway may be important both physiologically and in disease states.

(75) MODERATED POSTER

CHANGES IN ENDOTHELIAL AND INDUCIBLE NITRIC OXIDE SYNTHASE ACTIVITY FOLLOWING BALLOON INJURY?

AP Banning, L Butter*, J Wharton, RAD Rutherford*, P Black, J Polak*, MJ Lewis. Cardiovascular Sciences Research Group, University Hospital of Wales, Cardiff and Dept Histchemistry*, Hammersmith Hospital, London.

Nitric oxide (NO) inhibits platelet aggregation and leukocyte adhesion and potentially vascular smooth muscle cell (VSMC) proliferation. We studied the effect of balloon injury on endothelial (e) and inducible (i) NO synthase (NOS) activity using immunohistochemical staining and \(^{3}H\) labelled nitro-L-arginine (\(^{3}HL-NOARG\)) autoradiography. Pigs underwent bilateral carotid angioplasty and were sacrificed at 4hrs, 5 days, 7 days or 21 days (n=4 each). Proliferating cell nuclear antigen (PCNA) expression indicated active VSMC division. eNOS and iNOS activities were measured using simultaneous release of L-arginine and L-arginine-\(^{3}H\), and aortic endothelial cell NOS antisera. Uninjured arteries exhibited dense \(^{3}HL-NOARG\) binding and strong uniform endothelial staining for eNOS along the whole luminal endothelium but no iNOS activity was detected. 24 hrs after injury eNOS was generally absent at the luminal surface, iNOS activity was detected in the media. 5 days after injury, patchy eNOS activity at the lumen and iNOS activity in the media and forming neo-intimal layer were detected. At 7 days (time of maximal intimal proliferation detected by PCNA) eNOS covered most of the luminal surface, with iNOS activity in the neointima. By 21 days (time of maximal intimal growth detected by cross sectional planimetry) \(^{3}HL-NOARG\) binding and eNOS staining were as in uninjured arteries with little iNOS activity. This study shows that eNOS activity follows the time course of endothelial denudation and regeneration following balloon injury and that iNOS is prominently expressed in the forming neointima. NO released by eNOS and iNOS may be the mechanism responsible for limiting neointimal growth following balloon injury.

(76) MODERATED POSTER

ARTERIOVENOUS SELECTIVITY OF NITRIC OXIDE (NO) DONORS IN HUMANS. CAN NO DELIVERY BE TARGETED?

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Clinical Pharmacology, St George's Hospital, London, SW10 1RE.

The arteriovenous potency in humans in vivo of 4 NO donors with different methods of bio-transportation to NO (glyceryl trinitrate GTN; sodium nitroprusside SNP; lisinidmine SIN-1; S-nitrosothioglutathione GSNO) was studied. GTN is metabolised to NO within smooth muscle; SNP & SIN-1 release NO spontaneously. GSNO has selective effects on platelets possibly due to preferential metabolism by platelets. 22 healthy subjects took part, all gave informed consent. The study was approved by the local ethical committee. Drugs were infused locally into the dorsal hand vein and vein size measured using a linear displacement probe, or into the brachial artery and forearm blood flow (BFB) measured using venous occlusion plethysmography. In veins, equi-effective infusions of GTN, SNP, GSNO, SIN-1 were 2, 4, 16 & 160mol/min respectively, which caused 58±9, 19±2%, 52±±11±6%, 46±3±11±6%, 35±2±12±3% vasodilatation respectively. In arteries, equi-effective infusions of GTN, SNP, GSNO, SIN-1 were 5, 5, 5, & 200mol/min respectively which increased FBF to 249±37%, 249±57%, 233±36%, 199±32% of control respectively. The arterio-venous index (AVI) relative to GTN was calculated. SNP and SIN-1 were similar to GTN (AVI not significantly different from unity). In contrast, GSNO was significantly more arterioselective than GTN in vivo (AVI = 0.13±0.04; p<0.05). The findings suggest arterial GSNO to NO more effectively than veins in humans in vivo. Nitrosodithiols including GSNO occur endogenously, thus the stability of NO and its activity on different tissues could be altered by interaction with thiolis in vivo. It is possible that NO donors are to be developed to replace the apparent deficiency of NO that occurs in hypertension, diabetes and cardiovascular disease. This may reduce the incidence of vascular occlusion in these disorders, there may be advantages in delivering NO to specific vessel types or specific tissues. The selective effect of nitrosothiols on different vessels in vivo offers such a possibility.
INCREASED CHEMOSENSITIVITY TO HYPOXIA AT REST AND DURING EXERCISE IN CHRONIC HEART FAILURE
T P Chan, A Amadi, A L Clark, D Harrington, A J S Coats
Royal Brompton National Heart & Lung Institute, London

The mechanisms underlying exercise breathlessness in chronic heart failure (CHF) are not fully understood. We studied the resting chemosensitivity of 30 CHF patients (mean±SEM: 27 men; age 60.5±1.5 years; radiouclide left ventricular ejection fraction 26.6±2.6%) and 14 healthy controls (10 men; age 55.4±3.2 years; P=NS) by assessing the ventilatory response to hypoxia using transient pure nitrogen inhalation and to hypercapnia using single breaths of 13% carbon dioxide in air. The ventilatory response to hypoxia was significantly increased in CHF compared with normal subjects (0.695±0.089 vs 0.287±0.059 l/min%/SaO2, P=0.0004) but not to hypercapnia (0.369±0.043 vs 0.276±0.041 l/min/mm Hg CO2, P=NS). Mean maximal oxygen consumption on cardiopulmonary exercise testing was 16.2±0.9 vs 21.0±2.0 ml/min/kg (P<0.001) and the slope relating minute ventilation (V02) and carbon dioxide production (VCO2) was 36.1±4.7 vs 26.8±1.6 (P<0.001). The hypoxic ventilatory response correlates with both maximal oxygen consumption (r=0.32, P=0.038) and V02/VCO2 slope (r=0.41, P=0.007).

Fourteen of the CHF patients and all the controls also underwent chemosensitivity testing during mild exercise on a bicycle ergometer at 25W for 10 minutes. There was an augmentation of hypoxic ventilatory response (1.56±0.29 vs 0.657±0.12 l/min%/SaO2, P=0.01) by a mean factor of 2.7 and 3.1 (P=NS) in CHF patients and controls respectively compared with resting values. Hypercapnic ventilatory response was also augmented during exercise (0.538±0.084 vs 0.509±0.056 l/min/mm Hg CO2, P=NS) but there was no significant difference between the two groups.

In conclusion, there is increased chemosensitivity to hypoxia both at rest and during exercise in CHF and this may contribute to the mechanisms of exercise breathlessness in this condition.

APOTOPSIS OF VASCULAR SMOOTH MUSCLE CELLS IS REGULATED BY MULTIPLE GENE PRODUCTS.
M R Bennett, GJ Evans* and SM Schwartz
Department of Pathology, University of Washington, Seattle, USA and *Imperial Cancer Research Fund, London

Although apoptosis (programmed cell death) has been demonstrated in normal human arteries, atherosclerotic plaques, and arteries following injury, little is known about apoptosis in vascular smooth muscle cells (VSMCs) are mostly unknown. To study the molecular mechanisms which control apoptosis in VSMCs, we have used aortic VSMC from high levels of the proto-oncogenes c-myc, bcl-2, adenosine EIA, and the tumour suppressor gene p53, both singly and in combination. These genes have all been implicated in the regulation of apoptosis in some cell types. Apoptosis was assessed and quantified by time-lapse videomicroscopy and electron microscopy. C-myc and EIA induced apoptosis in VSMCs in low-serum conditions (36.4%±4.5) and 43.1%±(5.0)(Mean, SEM) of cells died over 24 hours respectively. Wild type or mutant type p53 expression had no effect on apoptosis when expressed alone, but wild type p53 increased apoptosis in a-cmyc and EIA infected cells to 54.8%±(5.5) and 65.6%±(7.2) respectively. EIA and c-myc both increased expression of p53 protein expression on Western blotting approximately 10 fold, but did not increase p53 mRNA levels on Northern analysis. Co-expression of mutant p53 (which inhibits endogenous wild type p53) suppressed apoptosis induced by c-myc and EIA. Co-expression of bcl-2 suppressed c-myc and EIA-induced apoptosis to 2.5%±0.3 and 11.4%±(1.3) respectively, but did not affect expression of c-myc mRNA or p53 mRNA or protein. We conclude that VSMC apoptosis is controlled by the interaction of multiple gene products. EIA and c-myc induce apoptosis by a similar mechanism involving an increase in p53 protein expression; apoptosis in these cells is mediated by a dependent upon p53. Bcl-2 suppresses apoptosis induced by EIA and c-myc, but does not act via p53. Thus, p53 and bcl-2 may be critical regulators of VSMC apoptosis, acting at separate points on a final common pathway.
Reduction in Exercise Threshold To Post-Prandial Angina Is Due To Its Carbohydrate Content And Occurs Independently Of Myocardial Oxygen Consumption.

RR Baliga, L Burden, J S Koonen
Division of Cardiology, Hammersmith Hospital and Royal Postgraduate Medical School, London

We investigated the role of food constituents in mechanisms contributing to post-prandial angina (PPA). Studies were performed in 8 males (ages 60±3 yrs), with reproducible PPA, after an overnight fast, off all medications (except GTN) for 3 days. HR, BP, rate pressure product (RPP), time to onset of angina (TA) and 1mm ST depression (TST), plasma nonadrenaline (NOR, nmol/l) and adrenaline (AD, nmol/l), were measured before, during and after infusion of water (WM), liquid carbohydrate (CM), fat (FM), and protein (PM) meals, and during exercise (Bruce protocol). Meals were isocaloric (1000 cal), isonitrogenous, and administered in random order, on separate days.

Results
HR, BP, and RPP increased to similar levels 30 min after CM, FM and CM, compared to WM. During exercise TA, TST and ED were reduced after CM, but not FM or PM, compared to WM (*p<0.05). RPP was unchanged after CM, but increased after FM and PM, and compared to WM. Plasma NOR rose after CM (3.4±0.4 to 4.9±0.4* nmol/l) and FM (3.1±0.3 to 4.2±0.2*), but not after FM compared to WM. Plasma AD did not rise after meals.

TIME TO ANGINA

<table>
<thead>
<tr>
<th>TIME</th>
<th>ANGINA</th>
<th>TST (sec)</th>
<th>RPP*10^3</th>
<th>TIME</th>
<th>ANGINA</th>
<th>TST (sec)</th>
<th>RPP*10^3</th>
</tr>
</thead>
<tbody>
<tr>
<td>WM</td>
<td>141±20</td>
<td>162±1.0</td>
<td>315±51</td>
<td>WM</td>
<td>141±20</td>
<td>162±1.0</td>
<td>315±51</td>
</tr>
<tr>
<td>CM</td>
<td>106±17*</td>
<td>121±1.0</td>
<td>146±3*</td>
<td>CM</td>
<td>106±17*</td>
<td>121±1.0</td>
<td>146±3*</td>
</tr>
<tr>
<td>FM</td>
<td>157±21</td>
<td>172±1.0</td>
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<td>FM</td>
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<td>172±1.0</td>
<td>203±2.1*</td>
</tr>
<tr>
<td>PM</td>
<td>149±22</td>
<td>182±2.4*</td>
<td>227±2.1</td>
<td>PM</td>
<td>149±22</td>
<td>182±2.4*</td>
<td>227±2.1</td>
</tr>
</tbody>
</table>

Summary
Decrease in time to angina, 1mm ST depression and peak exercise occur after carbohydrate, but not fat or protein, as compared to water. RPP did not rise after CM, unlike FM and PM. Reduced exercise threshold to post-prandial ischaemia after carbohydrate meals occurs independently of increased myocardial oxygen consumption, suggesting 'steal' mechanisms contribute.

Does stunning cause prolonged myocardial dysfunction after exercise induced ischaemia?

N D Masani, P G Averly, R A Jones, E Jones, R J C Hall
University Hospital of Wales, Cardiff, U.K.

Prolonged abnormalities of left ventricular wall motion (WMA) occur frequently following exercise-induced angina. It is postulated that the underlying mechanism is myocardial stunning. We studied 12 men with angiographically proven coronary artery disease. A novel protocol combining echocardiography (ECHO) and 99-Tc sestamibi SPECT was used to study wall motion and myocardial perfusion simultaneously. Each patient underwent: (i) resting sestamibi SPECT (treadmill) exercise test with sestamibi injected at peak ischaemia (iii) exercise test with sestamibi injected 15 minutes (Group 1, n=8) or 30 minutes (Group 2, n=4) after peak stress. ECHO was performed before and at 15 minutes intervals after exercise. SPECT was performed 60 minutes after sestamibi injection. In all patients, chest pain and ECG changes resolved within 9 minutes of peak stress. 10 patients (83%) developed prolonged WMA (≥30 minutes) after both exercise tests. Quantitative ECHO data (measured pre-exercise, 15 and 30 minutes post-exercise are shown below: *(p<0.005 vs pre-ex; SF=shortening fraction)

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of patients</th>
<th>peak stress</th>
<th>MIBI perfusion defect</th>
<th>15 min post ex</th>
<th>30 min post ex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>global ejection fraction (%)</td>
<td>61.2±4.3</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>yes</td>
<td>no</td>
<td>MIBI perfusion defect</td>
<td>yes</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>yes</td>
<td>yes</td>
<td>MIBI perfusion defect</td>
<td>yes</td>
</tr>
</tbody>
</table>

In conclusion, normalisation of perfusion after exercise-induced angina may be delayed despite the resolution of angina and ECG changes. 15 minutes after exercise 2 groups of patients were identified: those in whom reperfusion had occurred in the dysynchronous regions (indicating stunning) and those in whom perfusion defects persisted (indicating delayed reperfusion). 30 minutes after exercise, perfusion had normalised in all cases and WMA were thus due to myocardial stunning.

Enalapril reduces QT dispersion in patients with mild, asymptomatic ventricular dysfunction

CS Barr, NC Davidson, AA Naas, AD Struthers Department of Clinical Pharmacology, Ninewells Hospital and Medical School, Dundee

QT dispersion, the difference between the longest and the shortest corrected QT interval on a standard ECG, has been shown to be a powerful independent predictor of mortality in patients with heart failure. The pathological basis of QT dispersion in the failing ventricle is thought to be patchy myocardial fibrosis which causes repolarisation abnormalities and which potentially could be preventable by early treatment. Forty one patients with mild impairment of ventricular function (mean electrocardiographic fractional shortening 22%) on diuretic therapy (NYHA class I) were randomised to treatment with enalapril 20mg o.d.(E) or placebo(P) in a double-blind manner. QT dispersion was measured manually and with a digitiser pad by an observer who was blinded to the treatment group at baseline, 6 weeks, 4, 8 and 12 months. Baseline QT dispersion was similar in the two groups(mean ± SD): E 93±14, 35.2±5; P 93±14-35.7. Over the treatment period of one year the QT dispersion measured both manually and by digitiser fell significantly in the enalapril group but did not change in the placebo group. QT dispersion at one year: E 59.9±21.5 ms±5, P 87.6±28.2; difference between mean changes from baseline (E-P) -31.1, 95%CI -59.5 to -2.8ms±1, p<.003. The fractional shortening increased significantly in the treatment group compared with placebo: difference between mean changes from baseline (E-P) 3.68, 95%CI 1.3 to 6.06%, p<.003. These results show that in patients with asymptomatic ventricular dysfunction, enalapril treatment reduces QT dispersion, which reflects electrical inhomogeneity in the myocardium and is a surrogate marker for mortality.
NEUROPSYCHOLOGICAL MORBIDITY AMONG SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST

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As a result of the Heartstart Scotland project, increasing numbers of patients are being discharged from our center having survived out-of-hospital cardiac arrest (OHCA). This study examines the prevalence of memory impairment, anxiety and depression in these patients.

Patients and methods: We attempted to trace all 56 patients discharged after OHCA between May 1993 and July 1994. 35 patients agreed to psychological assessment. (5 were deceased, 8 geographically unavailable, 2 refused, 5 were not traced. One patient could not be tested due to psychosis). Patients were assessed at least 2 months (range 2-14, mean 6.7 months) after OHCA. The Rivermead Behavioural Memory Test (RBMT) was used to assess memory function. We used the Hospital Anxiety and Depression (HAD) Scale and National Adult Reading Test to measure affective state and premorbid intelligence.

Results: RBMT profile scores (maximum 24 points) are shown below.

<table>
<thead>
<tr>
<th>RBMT score (deficit)</th>
<th>Number of cases</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>22-24 (normal)</td>
<td>7</td>
<td>20%</td>
</tr>
<tr>
<td>17-21 (mild)</td>
<td>15</td>
<td>43%</td>
</tr>
<tr>
<td>10-16 (moderate)</td>
<td>10</td>
<td>29%</td>
</tr>
<tr>
<td>0-9 (severe)</td>
<td>3</td>
<td>8%</td>
</tr>
</tbody>
</table>

These scores are significantly lower than the published population reference range (Chi^2=60.6, 3DF, p<0.001). RBMT scores did not vary with age or gender. The incidence of “caseness” (>10 points on HAD test) for anxiety and depression was low (4 and 2 cases respectively). The difference in estimated pre-morbid intelligence levels between groups did not account for the extent of memory impairment observed.

Conclusions: The prevalence of clinically significant memory impairment among Heartstart survivors is high. 37% of cases have moderate or severe memory impairment. The memory test findings do not appear to be confounded by anxiety, depression, age or sex. A study of psychological rehabilitation is needed on the basis of these results.

A COMPARISON OF ATRIAL NATRIURETIC PEPTIDE AND B-TYPE NATRIURETIC PEPTIDE AS PREDICTORS OF OUTCOME POST-MYOCARDIAL INFARCTION

NC Davidson, D Darbar, AM Choy, CC Lang, TH Pringle, GP McNeill, AD Struthers. Departments of Clinical Pharmacology and Cardiology, Ninewells Hospital and Medical School, Dundee.

Plasma levels of cardiac natriuretic peptides are increased following acute myocardial infarction (AMI) due to their release from storage granules and increased by production stimulated by raised intracellular pressures. We assessed the prognostic significance, in terms of mortality and the development of heart failure, of the post-infarct levels of ANP and B-type natriuretic peptide (BNP), which is secreted predominantly from the left ventricle. Venous blood samples were taken on day 2-3 post-infarct from an unselected group of 64 patients who presented with AMI. Plasma levels of ANP and BNP were measured by radioimmunoassay. Patients were then followed up for 14-22(mean±18.4) months post-infarct. Echocardiography was performed to assess the left ventricular ejection fraction (LVEF). The baseline plasma levels of ANP and BNP in groups with different outcomes were compared using ANOVA. Patients were divided into three groups at follow up: 1. dead (n=9), 2. asymptomatic(NYHA I; n=12) and 3. symptomatic heart failure(NYHA II-IV; n=44). The baseline plasma levels of both ANP and BNP were significantly higher in group 1 than in the survivors (ANP mean 55.5 ± 30.1 pmol/l, p=0.01; BNP 42.7 ± 18.7 pmol/l, p=0.00001). The levels of ANP at baseline were significantly greater in group 3 than in group 2 (mean 33.8 ± 16.1 pmol/l, p=0.02) but the levels of BNP were not significantly different between these groups. The survivors were also categorised according to LVEF, the baseline plasma levels of both ANP and BNP were significantly greater in the group with LVEFs <40% at follow-up (ANP mean 37.8 ± 24.3 pmol/l, p=0.034, BNP 22.1 ± 16.1 pmol/l, p=0.035). In conclusion the post-infarct plasma level of BNP is a stronger predictor of mortality than the level of ANP; both peptides are predictive of ventricular dysfunction; only the ANP level is significantly associated with subsequent symptomatic status. Routine measurement of both these peptides in the period immediately following an acute myocardial infarction would provide a simple means of risk stratification, with different information gained from each peptide.
(89) MODERATED POSTER

PROPHYLAXIS AND MANAGEMENT OF CYTOMEGALOVIRUS INFECTION FOLLOWING CARDIAC TRANSPANTATION
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There is still a lack of consensus regarding the prophylaxis, management and possible role of CMV disease in cardiac transplantation (CTX). We reviewed a large series of patients managed using an identical protocol. Between May 1985 and May 1994 a total of 285 adult CTx were performed at this centre. All patients received acyclovir (200mg 8 hourly) as prophylaxis for the first three months post transplant. In addition, those patients CMV antibody negative pre-transplant received CMV positive organs were given IV CMV hyperimmune-globulin on days 0, 7, 14, 21, 28 and 49 post CTx or until they acquired CMV IgM. Significant pyrexial episodes were investigated for CMV by investigation and culture of urine, upper respiratory secretions, bronchoalveolar lavage if appropriate and CMV specific IgM. Specific antiviral chemotherapy was instituted when there was evidence of CMV disease affecting more than one organ system or progressive pneumonitis. Those patients who survived more than 28 days post transplant (249) are included in this analysis.

<table>
<thead>
<tr>
<th>CMV Status Pre Transplant</th>
<th>No.</th>
<th>CMV Disease</th>
<th>Treated</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-R-</td>
<td>50(20%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>D+R-</td>
<td>34(13%)</td>
<td>6(17%)</td>
<td>1</td>
<td>26(6%)</td>
</tr>
<tr>
<td>D-R+</td>
<td>104(42%)</td>
<td>7(7%)</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>D+R+</td>
<td>61(25%)</td>
<td>4(7%)</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

The incidence of CMV disease in our series is remarkably low when compared with published data, and confirms that our prophylaxis regime is effective. Additionally CMV disease was not found to be associated with graft rejection but there is an association between CMV mismatch (but not disease) and graft coronary disease.

(90) MODERATED POSTER

CLINICAL STATUS OF PATIENTS THREE YEARS AFTER ORTHOTOPIC HEART TRANSPLANTATION
R M Grocott-Mason, AG Mitchell, N Banner, C O-Brien, A Khaghan, M Yacoub. Harefield Hospital, Harefield, Middx. UB9 6HJ

Orthotopic heart transplantation (OCTx) is an established treatment for end stage heart failure, however, there is little data on the long term clinical outcome. We have reviewed the clinical status of 94 adult patients who survived for at least 1 year following OCTx at Harefield Hospital between Jan 1980 and Dec 1984. After the first year, survival fell by 3.7% per annum. Of the 94 patients who survived the first year were alive 10 years post OCTx. Half of the 32 deaths, more than 1 year after OCTx, were cardiac (4 sudden death, 2 rejection, 6 CHF; 4 following repeat OCTx for CHF); 40.6% were non-cardiac (e.g. infection 5, malignancy 4); and 3 unknown. All patients have been studied annually with right and left heart catheterisation, MUGA scans and exercise tests. LV filling pressures increased with time (e.g. LVEDP 10.2±4.2 vs 13.1±5.9 mmHg and PCWP 9.9±3.5 vs 12.9±4.5 mmHg at the 10 years post OCTx respectively, both p<0.01). Resting ejection fraction measured by MUGA scan fell from 61.1±11% at 1 year to 55±11.8% at 10 years (p<0.01). Development of accelerated coronary disease is an important clinical problem, and its prevalence increases with time of the patients surviving at least 10 years. 61.7% had angiographically detectable coronary disease at 10 years and 9 of these have undergone a revascularisation procedure (9 PTCA and 1 CABG). The functional status of the majority of long term survivors remains good. The mean exercise time 9.9 mins of standard Bruce protocol). A number of complications not directly related to the cardiac graft occur in transplant survivors, many of which are side effects of the immunosuppressive drugs, e.g. hypertension (62% in all patients; 72% those on cyclosporin A (CyA)); renal impairment (Creatinine > 150; 68% patients; 82% those on CyA), osteoporosis, Metabolic bone disease, e.g. hypercalcaemia, hyperuricaemia and gout are common. There is a significant incidence of malignant disease (1094, 10.6%). In summary, compared to quoted annual mortality rates of 20 - 60% for patients in NYHA Classes II and IV, the long term survival rates of OCTx are excellent. However, there remain a number of complications, both cardiac and non-cardiac, which produce significant morbidity and mortality in long term survivors. Newer immunosuppression regimes may further improve results.

(91) MODERATED POSTER

DONOR CARDIAC TROPOIN-I ESTIMATION PREDICTS SUBSEQUENT CLINICAL COURSE FOLLOWING CARDIAC TRANSPLANTATION
J Anderson, M Hosein-Nia, B P Madden, D Holt, A J Murday Department of Cardiothoracic Surgery, St. George's Hospital, London SW17

Relaxation of donor criteria has permitted previously considered unsuitable hearts to be successfully used despite the risk of early allograft failure. Donor hearts are usually deemed suitable for transplantation on haemodynamic function and ECG status rather than assessment of myocardial injury. Cardiac Troponin-I (cTnI) and Troponin-I (cTnT) are specific and sensitive markers of subclinical cardiac injury that have little cross reactivity with skeletal troponins. We measured cTnT and cTnI in 55 cardiac donors that fulfilled our normal criteria prior to procurement and correlated the levels with the clinical course of the recipient.

Results. The mean cTnT was 0.34 ± 0.1 μg/l in all donors (range for normal controls 0.0-0.2 μl). The cTnI was similar in donors with traumatic head injury (n = 23, cTnI 0.27 ± 0.11 μl) and those with subarachnoid haemorrhage ( n = 29, cTnI 0.24 ± 0.1 μl, p = 0.65). Donors requiring dobutamine support had similar levels to those requiring renal dose dopamine or no support at all. Post-operatively, the patients with an unencumbered course who required no adrenergic support had a significantly lower median cTnT compared to those patients with early allograft failure despite mechanical and isotropic support or those requiring prolonged adrenergic support (0.36 μl/g/l ± 0.07 μl/g/l p < 0.005). Patients with a donor TnT > 0.2 μl/g/l had a higher median peak TnT in the post-operative period (4.25 μl/g/l ± 3.22 μl/g/l p < 0.05). Similar findings were seen with cTnI measurements.

Conclusions. Donors with good cardiac function often have subclinical myocardial injury. The finding that a raised donor TnT was associated with a significant increase in echocardiographic support in the early post-operative period suggests that it may be a useful early marker of allograft dysfunction and may influence the decision to use the heart for transplantation. A prior knowledge of TnT level may help in deciding the level and timing of cardiac support if primary organ dysfunction occurs.

(92) MODERATED POSTER

SIGNIFICANCE OF CORONARY FLOW RESERVE FOLLOWING CARDIAC TRANSPLANTATION
MH Cave, J Parameshwar, P Mullins, S Large, J Wall, PM Schofield. Transplant Unit, Papworth Hospital NHS Trust, Cambridge CB3 4RE

Coronary occlusive disease (COD) following cardiac transplantation is characterised by progressive diffuse concentric narrowing of the coronary arteries. The earliest haemodynamic effects of this process occur in the distal capacitance vessels, and a reduction in coronary flow reserve (CFR) might, therefore, be expected to be an early sign of COD. In 1990, coronary angiography and estimation of CFR was performed in 52 heart transplant patients. CFR was defined as the ratio of peak flow velocity to resting flow velocity in the proximal left anterior descending artery measured using a 20 Mhz intracoronary Doppler flow probe. Peak flow was achieved using increasing doses of intracoronary papaverine up to a maximum of 14mg. Low CFR was defined as <3, based on a concurrent study of normal control patients. The most recent coronary angiograms belonging to these patients were reviewed. CFR was estimated a median of 49 (range 3-122) months following transplantation. The median age of the patients was 48 (21-61) years and 48 were male. In 13 patients with evidence of COD on the initial angiogram, mean CFR was 3.0 (SD 1.2). In the remaining 39 patients with no evidence of COD, follow-up angiography was performed a median of 47 (8-51) months later. 6 patients (15%) had developed angiographic evidence of COD. Mean CFR in these patients was 2.9 (1.8) compared to 4.0 (1.2) in patients who did not develop evidence of COD (p=0.002). 4 out of 9 patients (44%) with CFR <3 developed COD, compared to 2 out of 30 patients (7%) with CFR >3 (relative risk of COD 6.7; 95% confidence limits 1.5-30.6). Conclusions. Following heart transplantation, patients with normal coronary angiography who subsequently develop COD have a similar CFR to those who already had evidence of COD. CFR <3 was associated with a low risk of developing angiographically detectable COD during the next 4 years. However, CFR <3 confers a significantly increased risk.
PACED LINKAGE OF THE DONOR AND RECIPENT HEARTS AFTER HETEROPTIC HEART TRANSPLANTATION: ACUTE HAEMODYNAMIC STUDIES.

Harefield Hospital, Harefield, Middlesex, UB9 6HJ

Heterotopic cardiac transplantation is a useful procedure in patients with elevated pulmonary vascular resistance or when there is a weight mismatch between the donor and the recipient. However, the operation is limited by a progressive deterioration in the recipient heart's (RH) left ventricular function and a reduced exercise capacity compared with orthotopic transplantation. We believe that these are related to the competitive contraction of the two hearts. Following computer modelling of several pacing options we have evolved an effective method of linking the two hearts with a pacemaker such that the two hearts contract sequentially (PL). This was investigated systematically involving haemodynamic, metabolic and functional assessment. In eleven patients the mean cardiac output increased from 5.0 to 5.6 l/min (p=0.003) and the wedge pressure decreased from 16 to 12 mm Hg (p=0.003) with PL. PL also significantly increased the ejection period of the RH from 174 to 203 ms (p=0.046) and decreased the pre-ejection period from 181 to 147 ms (p=0.013). As PL increases RH rate to that of the donor we evaluated the possibility of precipitating ischaemia in the RH by measuring coronary sinus flow (CSF) and hypoxanthine (Hx) release - a sensitive marker of ischaemia. Peak CSF of 1.56 to 2.78 mmol (p=0.02) and no increase in Hx release was detected. Finally, pacing was found to increase exercise duration from 7.1 to 7.7 min (p=0.04) in 12 patients during cardiopulmonary exercise testing.

We conclude that HHT the acute haemodynamics can be improved by PL and that these are associated with an improvement in functional capacity. The resulting increase in RH rate does not increase the ischaemic burden as evidenced by increased CSF flow and lack of change in Hx levels. We are now implanting permanent pacemakers to evaluate the long term effects of pacing on quality of life and the deterioration of the RH left ventricular function.

CENTRAL AND REGIONAL HAEMODYNAMIC RESPONSES TO HIGH CARBOHYDRATE AND HIGH FAT MEALS IN CARDIAC TRANSPLANT RECIPIENTS.

Queens Medical Centre Nottingham.

It is well established that patients with pathophysiological or age related autonomic dysfunction show diminished cardiovascular (CV) responses to food, leading to hypotension. We assessed the CV responses to isocaloric (2.4 MJ) high carbohydrate (HC) and high fat (HF) meals in cardiac transplant (CT) recipients, who prior to CT have significant CV and autonomic abnormalities, and post CT have cardiac denervation. CT recipients (mean age 52±2; 8 male) were compared to 9 healthy controls (mean age 52±2; 6 male). Cardiac output (CO) was measured using the indirect Fick method. Blood pressure (BP) and heart rate (HR) were measured using an automated sphygmomanometer. Superior mesenteric artery blood flow (SMABF) was measured using Doppler ultrasound. Fully familiarised, subjects attended the laboratory fasted, on two occasions. After 30 min rest, baseline measurements were taken. Subjects then consumed a HC or HF meal, and measurements were repeated every 30 min for two hours. Results expressed as mean±SE. Controls showed a significant increase in HR after HC (7.6±1.3) and HF (6.2±1.7 p<0.001) a significant increase in CO (HC 1.29 l/min ± 0.18) and HF (0.92 l/min±0.20) p<0.01 and a significant increase in SMABF after HC (128±20 ml/min ± 7) and HF (147±5 ml/min ± 13 p<0.001). BP fell in controls after HC (p<0.01), CT recipients had significantly higher resting HR than controls before both meals (p<0.01), but CO and SMABF were not significantly different. BP was higher before both meals. After both meals CT recipients showed a similar HR response as the controls. The CO response after HC was the same as the controls (1.14 l/min ± 0.25) but after HF, the CO response was significantly greater compared to controls (p<0.001). CT recipients had significantly higher resting HR than controls before both meals (p<0.01). CO was maintained after both meals. Our data show that CT recipients have a normal HR response to meal ingestion. However, the different CO responses to HC and HF and the attenuated SMABF suggest some abnormalities of post-prandial CV homeostasis. Despite this, BP is well maintained post-prandially in CT recipients.
(97) MODERATED POSTER

THE UTILITY OF INHALED PROSTACYCLIN IN PATIENTS WITH SEVERE PULMONARY HYPERTENSION (PHT) AWAITING LUNG TRANSPLANTATION. GW. Middlesex, London SW3 6LY

Patients with severe PHT awaiting transplantation are often unresponsive to I.V. prostacyclin (PGI2). We have studied six such patients. Two patients had primary PHT, one had thromboembolic lung disease, one had Eisenmengers Syndrome and two had PHT secondary to congestive cardiac failure. Inhaled prostacyclin was given in a nebulized form for a period of 20 minutes in increasing doses: 15-50ng/kg/min. The patients subsequently had trials of I.V. PGI2, 1-5ng/kg/min and inhaled nitric oxide (NO) 10-100ppm. The following results were obtained on each of the 6 patients with nebulized prostacyclin.

<table>
<thead>
<tr>
<th>BASELINE</th>
<th>NEBULIZED PGI2</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA</td>
<td>FA PVR AP CO</td>
</tr>
<tr>
<td>Pt 1</td>
<td>86/28</td>
</tr>
<tr>
<td>Pt 2</td>
<td>140/52</td>
</tr>
<tr>
<td>Pt 3</td>
<td>128/50</td>
</tr>
<tr>
<td>Pt 4</td>
<td>77/59</td>
</tr>
<tr>
<td>Pt 5</td>
<td>100/90</td>
</tr>
<tr>
<td>Pt 6</td>
<td>42/21</td>
</tr>
</tbody>
</table>

We conclude that nebulized PGI2 produces a significant drop of PVR in the majority of patients with severe PHT without affecting systemic arterial pressure. The observed effect appeared to be superior to both I.V. PGI2 and inhaled NO. The partial reversibility of PVR and the type of therapy in these patients with advanced disease could have important implications.

(99) MODE OF ACTION OF CARDIAC TROPONIN T MUTATIONS IN FAMILIAL HYPERTROPHIC CARDIOMYOPATHY.

H Watkins, HL Sweeney, WJ McKenna, JG Seidman, CE Seidman. Harvard Medical School, Boston, MA, St George's Hospital Medical School, London, University of Pennsylvania, Philadelphia, USA.

We have recently identified three mutations in the cardiac troponin T (cTnT) gene that cause familial hypertrophic cardiomyopathy (FHC). Two are missense mutations situated in a region of cTnT involved in binding to a troponym. In contrast the third mutation is a G->A transition that inactivates the S' donor splice site of intron 15. This mutation results in two aberrantly spliced mRNAs which are predicted to encode truncated TnT peptides with the loss of the highly conserved carboxyl terminus of an analogous splice donor mutation in Drosophila, spf2, which is functionally null (producing no mature troponin T), is thought to produce a dominant phenotype through an imbalance of sarcromere components. If such a mechanism were involved in FHC this would have important implications for pathogenesis and potential intervention. To test the hypothesis that FHC-causing mutations in cTnT might act as null alleles we have first screened for further mutations in unrelated probands to look for null mutations e.g. premature stop codons. Five more mutations have been identified: four are missense mutations and one a deletion of a single codon without frameshift. Thus these mutations do not appear to be null alleles. To directly investigate the splice site mutation we have investigated the expression of the aberrantly spliced TnT mRNAs at the protein level. Transient expression in Cos cells of the two aberrantly spliced mRNAs revealed truncated but stable TnT peptides by western blot. Stable transfection in a primary quail myocyte culture indicates that the truncated TnT peptides are incorporated into sarcromeres. However, myotubes with truncated TnT peptides generated half the maximum force of contraction seen in cells transfected with normal human TnT.

Conclusions: Mutant cardiac TnT peptides most probably act as 'poison polypeptides' rather than null alleles; once incorporated into cardiac sarcromeres they appear to interfere with force generation.

(98) CATECHOLAMINES CAUSE HYPERTROPHY AND INCREASED EXPRESSION OF ENDOTHELIN-1 (ET-1) mRNA BUT NOT ET-2 OR ET-3 mRNA IN CULTURED VENTRICULAR MYOCYTES; EFFECTS OF THE ETA RECEPTOR ANTAGONIST BQ123

S Kaddoura, J Fireth*, P Poole-Wilson, P Sugden National Heart and Lung Institute, London, *Institute of Molecular Medicine, Oxford

Endothelin-1 (ET-1) has potent effects on cell growth and in experimental models induces myocardial hypertrophy. ET-1 may be generated by myocytes in vivo and act in an autocrine/paracrine fashion. The roles of ET-2 and ET-3 in hypertrophy are unknown. We investigated the effects of the catecholamine a-adrenergic agonist phenylephrine (PEP) on levels of ET-1, ET-2 and ET-3 mRNAs in neonatal rat ventricular myocytes, and the effects of the ETA antagonist BQ123 upon the hypertrophic response. Ribonuclease protection assay and laser densitometry were used to measure the mRNAs for ET-1, ET-2 and ET-3, constitutive GAPDH and ANF, re-expression of which is a marker of hypertrophy in ventricular myocytes. ET-1 mRNA was present in control myocytes. ET-2 and ET-3 mRNAs were not detectable in control or stimulated myocytes. PEP caused a dose-dependent increase in myocyte [ET-1 mRNA] within 1 hour and levels remained elevated for 24 hours. Figure shows the effect of 100ng PEP (mean±sem,n=3, *p<0.05, **p<0.005):

![Graph showing the effect of 100ng PEP on myocyte [ET-1 mRNA]]

ANF mRNA re-expression followed stimulation with PEP; BQ123 reduced this effect.

Conclusions: Ventricular myocytes produce ET-1 mRNA but not ET-2 or ET-3 mRNAs. PEP increases ET-1 mRNA levels in myocytes. PEP-induced hypertrophy may be mediated at least in part by ET-1 generation from myocytes.

(100) RAMIPRIL REVERSES CARDIAC HYPERTROPHY BUT LEADS TO INCREASED COLLAGEN CONCENTRATION IN THE HEARTS OF THE TRANSGENIC (mRen2)27 RATS

Division of Biochemistry and Cell Biology & Division of Cardiology, University College, London; Centre for Genome Research, Edinburgh.*

The circulating and tissue renin angiotensin systems (RAS) have been implicated in the development of interstitial fibrosis in hypertensive left ventricular hypertrophy (LVH). We investigated this association using the hypertensive transgenic rat (TGR) (mRen-2)27 in which there is tissue expression of the murine renin gene. Four week old TGRs were treated with Ramipril (1mg/kg/day) for six weeks. Mean systolic blood pressure (BP) was measured thrice weekly. Animals were killed and the right ventricle (RV) and left ventricle plus septum (LV) separated and weighed. Collagen content and concentration were determined by measuring hydroxyproline levels using an HPLC method. The results are shown in the table below.

<table>
<thead>
<tr>
<th>BP (mmHg)</th>
<th>LV weight (mg)</th>
<th>LV collagen content (mg/g dry tissue)</th>
<th>LV collagen (mg/g dry tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>177±13</td>
<td>975±19</td>
<td>4.14±0.17</td>
</tr>
<tr>
<td>TGR</td>
<td>241±17</td>
<td>1312±34</td>
<td>4.57±0.51</td>
</tr>
<tr>
<td>Ramipril</td>
<td>175±12</td>
<td>821±20</td>
<td>3.81±0.19</td>
</tr>
</tbody>
</table>

Values represent mean±SEM (n=6). *p<0.05 **p<0.001 vs TGR; +p<0.001 vs control.

Hypertension and LVH in TGRs were both blocked by Ramipril. The absence of collagen accumulation in this stage in TGRs contrasts with the marked accumulation reported in rat models of hypertension in which circulating RAS is activated. The increased collagen concentration in treated TGRs may be due to a relatively greater effect of Ramipril on early myocyte hypertrophy compared to collagen deposition. Experiments to further clarify the relative roles played by blood pressure and local RAS in the development of LVH in this model are currently in progress.
### MORPHOLOGICAL AND NUMERICAL CHANGES IN RESISTANCE VESSELS IN PRESSURE OVERLOAD LEFT VENTRICULAR HYPER trophy (LVH)

J Radwan, D O'Gorman, MA Turner, AJ Firth and DJ Sheridan.
Department of Academic Cardiology, St Mary's Hospital, London.

There is conflicting evidence about the degree and time course of vascular proliferation of resistance vessels (ReV) in LVH. This may be because previous studies have assessed changes at a single time point. We investigated the time course of ReV changes in 32 guinea-pigs with LVH induced by aortic banding (H) and 32 sham-operated controls (C). Animals were studied at 50, 100 and 150 days post surgery. Cardiac tissue was perfusion fixed, was embedded and 5-10um sections prepared using stereological technique. A total of 784 ReVs (100-300µm) were assessed using 80 x 1.215mm² fields for each heart with a dedicated image analysis system. ReV density, ReV lumen area fraction (sum of lumen areas measured/area of fields), ReV lumen diameter, wall thickness/lumen ratio and myocyte diameter were assessed.

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>ReV density (m⁻²)</th>
<th>Sham operated</th>
<th>Aortic banded</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>0.40 ± 0.04</td>
<td>0.19 ± 0.03</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>0.45 ± 0.06</td>
<td>0.28 ± 0.02</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>150</td>
<td>0.44 ± 0.05</td>
<td>0.29 ± 0.03</td>
<td>&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

Lumen area fraction

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>Lumen area fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>0.61 ± 0.11</td>
</tr>
<tr>
<td>100</td>
<td>0.56 ± 0.09</td>
</tr>
<tr>
<td>150</td>
<td>0.60 ± 0.08</td>
</tr>
</tbody>
</table>

Heart weight/body weight ratio, myocyte diameter and ReV wall-thickness lumen ratio were significantly greater in H than in C at all time points (p<0.01 for all). Histograms of vessel distribution by lumen diameter confirm no difference with time in C, but there is a shift from smaller to larger lumen diameters in H at 100 and 150 days post surgery. **Conclusions**: 1) ReV wall thickness is significantly increased in LVH 2) ReV proliferation occurs early in LVH, but vessel density remains significantly attenuated with time 3) The impaired vessel density is partly compensated for by an increase in vessel lumen size, resulting in similar lumen area fractions at 100 and 150 days.

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### Differential effects of isoprenaline on ventricular myocytes from normal and hypertrophied guinea-pig hearts.

By WRJ Wallis, R Wu, M Cooklin*, DJ Sheridan*, CH Fry

Institute of Urology & Nephrology, UCL, 67 Riding House St, London W1P 7PN and *Academic Cardiology Unit, St Mary's Hospital, London W2 1PG

Isoprenaline increases L-type calcium current (GCa) and action potential duration (APD90) in isolated ventricular myocytes. Using patch-pipettes such increases are unchanged in myocytes from hypertrophied hearts (50 days) (Wallis et al., 1994), whilst using microelectrodes the effects are blunted. We postulated that this discrepancy between dialysed and non-dialysed cells is attributable to the differential activation of KATP, in intact cells, following application of isoprenaline. To test this hypothesis the effects of glibenclamide (100µM) on the increase of APD90 by isoprenaline (1µM) was assessed.

Guinea-pigs (650-750g) underwent thoracic aortic constriction or sham operation under halothane (2%), N2O (49%) and O2 (49%) anaesthesia. Myocytes were prepared by collagenase dissection after 50 days. Action potentials were recorded using potassium aspartate (1M) filled microelectrodes. ICa was measured using patch electrodes containing (mM): CsCl, 20; aspartic acid, 110; MgCl2, 5.45; Na2ATP, 5.0; Na2GTP-2H2O, 0.1; EGTA, 5.0; HEPES, 5.0; pH 7.2 with CsOH.

Cells were superfused with Tyrode's solution, at 37°C, pH 7.35±0.03.

There was a significant increase in heart/body weight ratio (g/kg) 3.6±0.56, n=18 and 4.6±0.87, n=25, SD, p<0.0001 and cell capacitance (µF) 214±58, n=89 and 272±76, n=83, SD, p<0.0001) 50 days after aortic constriction. Table 1 shows no reduction in the response of ICa to isoprenaline. In contrast microelectrode recordings show the increase of APD90 to be significantly reduced in hyper trophy. Glibenclamide abolishes this differential response. These observations suggest that increased expression of KATP contributes to the smaller increase of APD90 in hypertension. We conclude that changes of intracellular metabolism may contribute to the altered response of myocytes to 8 agonists seen as a result of hypertension.

Table 1 Mean ±SD (n) * p<0.01 from sham group.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Sham 50</th>
<th>Hyper trophy 50</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICa (%)/increase</td>
<td>319±60 (45)</td>
<td>83±71±6 (30)*</td>
</tr>
<tr>
<td>APD90 (%)/increase</td>
<td>110±121±5 (18)</td>
<td>110±121±5 (18)</td>
</tr>
</tbody>
</table>

We thank the BHF for financial support and Mr M Turner for technical assistance.


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### ANGIOTENSIN II RECEPTOR EXPRESSION AFTER MYOCARDIAL INFARCTION

D C Lefroy, J Wharton, T Crake, G A Knock, R A D Rutherford, J M Polak, P A Poole-Wilson

Department of Histochemistry, Hammersmith Hospital, and Department of Cardiac Medicine, National Heart and Lung Institute, London

The heart is a potential site of action for angiotensin II after myocardial infarction. The left coronary artery ligation model was used to evaluate the changes in the myocardial angiotensin II receptor population after myocardial infarction in rats. The regional ventricular angiotensin II receptor density was assessed in myocardial tissue sections by [3H]1(Sar1, Ile8)angiotensin II ([H]-ATII) binding and quantitative autoradiography. The relative expression of the angiotensin II AT1 and AT2 receptor subtypes was characterised using selective antagonists. Collagen deposition was assessed by picrosirius staining and immunostaining for collagen type I. After left coronary artery ligation, the specific [3H]-SIAII binding was unchanged at 18 hours (n=6), but was markedly increased after 7 days in the infarcted region of the left ventricle (73.2±3.2 amol.mm⁻², mean ± SEM) compared both with the non-infarcted region (1.6±0.2 amol.mm⁻², n=7, p<0.0001) and with the left ventricular myocardium of sham-operated control animals (1.3±0.1 amol.mm⁻², n=6, p<0.0001). The increased [3H]-SIAII binding density was still present, but diminished, at 8 months after coronary ligation (49.0±5.7 amol.mm⁻², n=4, p<0.001 vs control, p=0.008 vs 7 day infarcts). The increased binding sites in the infarcted region were of the AT1 angiotensin II receptor subtype. The regional increase in AT1 receptor density was associated with fibroblast infiltration and collagen deposition. In conclusion, this study showed that AT1 angiotensin II receptors are expressed at high concentration in infarcted myocardium. The distribution of the increased receptors suggests a role for angiotensin II in modulating the formation of the scar.
**WEDNESDAY 24 MAY 1995**

<table>
<thead>
<tr>
<th>Time</th>
<th>Location/Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>08.00</td>
<td>Conference Centre Entrance Foyer</td>
</tr>
</tbody>
</table>
| 08.30-10.00 | Auditorium  
Plenary session  
Aortic root disease  
Chairman: Prof Tom Treasure  
Surgical anatomy and surgical pathology of the aortic root  
Speaker: Mr Donald Ross  
Imaging the aortic root  
Speaker: Dr Christoph Nienaber  
Physical properties of the aorta in health and disease  
Speaker: Dr David Lehmann  
Genetics of aortic root disease  
Speaker: Dr Anne Child  
**King’s Suite**  
Moderated posters  
Risk factors, outcomes and management strategies  
Chairman: Dr Richard Wray  
| 12.30 - 14.00 | Exhibition Halls B, C & D  
Lunch (B & C)  
Poster viewing (B & C) – Posters 122–172  
Exhibition viewing (B, C & D)  
| 14.00 – 15.30 | Auditorium  
Judges’ Choice 2  
Chairman: Prof Andrew Henderson  
Papers 179–184  
**King’s Suite**  
Moderated posters  
ACE and heart failure  
Chairman: Prof Stephen Ball  
Papers 185–196  
**Harewood Suite**  
British Nuclear Cardiology Group  
Myocardial perfusion imaging: What is happening in the UK and study interpretation  
BNCG survey results  
Dr Dudley Pennell  
Myocardial perfusion imaging  
(a) Artefacts  
Dr Steve Walton  
(b) Diagnosis  
Dr John Caplin  
(c) Prognosis  
Dr Liz Pruvolovich  
**Ripley Suite**  
Free communications  
Clinical myocardial dysfunction  
Chairmen: Dr Sue Chamberlain and Prof Celia Oakley  
Papers 197–202  
**Royal Hall**  
Technicians’ Day  |
| 15.30 – 16.00 | Exhibition Halls B, C & D  
Tea (B & C)  
Poster viewing (B & C) – Posters 122–172  
Exhibition viewing (B, C & D)  
| 16.00 – 17.00 | Auditorium  
Paul Wood Lecture  
The Master’s Legacy, 1995  
Dr Jane Somerville  |
| 17.00 – 18.30 | Auditorium  
Annual General Meeting  
(members only)  |
| 09.30 | Royal Hall  
‘Technicians’ Day  
For programme see p. 35  |
| 10.00 – 11.00 | Exhibition Halls B, C & D  
Coffee (B & C)  
Poster viewing (B & C) – Posters 122–172  
Exhibition viewing (B, C & D)  |
| 11.00 – 12.30 | Auditorium  
Young Research Workers Prize Final  
Finalists: Dr A Chauhan  
Dr C H Davies  
Dr J Gunn  
Dr N S Jepson  
Judges: Prof Henry Dargie  
Prof Roberto Ferrari  
Prof David Hearse  
Prof John Martin  
Abstracts A–D (p. 36)  
**Ripley Suite**  
Free communications  
Congenital heart disease  
Chairman: Prof Mike Tynan  
Papers 173–178  
**Royal Hall**  
‘Technicians’ Day  |
WEDNESDAY 24 MAY 1995: TECHNICIANS’ DAY PROGRAMME

Back to basics

09.00 – 09.30 Registration

09.30 – 11.00 Extraordinary General Meeting

11.00 – 12.00 “It’s not as simple as EA-SY-GEE”
Professor Peter MacFarlane
Medical Cardiology, Glasgow Royal Infirmary

12.00 – 14.00 Exhibition and Lunch

14.00 – 14.45 Ambulatory ECG monitoring
Dr Douglas Chamberlain
Consultant cardiologist, Royal Sussex County Hospital

14.45 – 15.00 Coffee

15.00 – 15.30 The importance of serial ECGs in cardiac transplantation
Ms Cathy O’Brien
Chief technician in transplant cardiology, Harefield Hospital
**CARDIO-OESOPHAGEAL REFLEX: A MECHANISM FOR "LINKED ANGIOPHAGES" IN PATIENTS WITH ANGIOGRAPHICALLY PROVEN CORONARY ARTERY DISEASE**

A. Chaushan, M C Petch, P M Schofield
Regional Cardiac Unit, Papworth Hospital, Papworth Everard, Cambridge

It has been shown previously that oesophageal acid stimulation can reduce coronary blood flow in syndrome X patients suggesting the presence of a cardio-oesophageal reflex in humans. The presence of such a reflex in patients with coronary artery disease could explain the mechanism of "linked angina". We studied the effect of oesophageal acid stimulation on coronary blood flow in 14 patients with angiographically documented coronary artery disease and 18 heart transplant patients. A fine tube was positioned in the patient's distal oesophagus. A 3.6% intracoronal Doppler catheter was positioned in the proximal left anterior descending coronary artery for coronary blood flow (CBF) measurements. Oesophageal instillation of 0.1M hydrochloric acid and 0.9% saline was performed in random, double blind fashion (60 ml over 5 minutes) and the measurements were repeated after each infusion. The coronary blood flow was significantly reduced by acid oesophageal stimulation in the coronary artery disease group (CBF before 30.9±14.3 ml/min; p<0.01). However, there was no significant difference in the coronary blood flow on saline infusion [73.5±15.3 versus 72.5±14.1 ml/min (p>0.01)].

**Conclusion:** Oesophageal acid stimulation can produce angina and significantly reduce coronary blood flow in patients with coronary artery disease. The lack of any significant effect in the heart transplant group, in whom the heart is denervated, suggests a neural reflex.

**DOES REDUCED CONTRACTION OF INDIVIDUAL VENTRICULAR MYOCYTES CONTRIBUTE TO THE PATHOGENESIS OF HUMAN HEART FAILURE?**

CH Davies, K Davia, PA Poole-Wilson, SE Harding
National Heart and Lung Institute, London

Introduction: Previous work has failed to demonstrate reduced contraction of isolated ventricular myocytes from failing human hearts compared to non-failing controls, although a reduction is shown. In this study we show that high frequency stimulation frequencies reveal an additional contraction defect in cells from failing human hearts. We have used an animal model of beta-adrenoceptor (β-AR) desensitisation to explore the role of cAMP in the frequency response of myocytes. Thapsigargin, an inhibitor of the sarcoplasmic reticulum (SR) Ca²⁺-ATPase, was used to probe SR function in human and guinea-pig myocytes.

Methods: (i) Left ventricular (LV) myocytes were isolated from 16 failing, explanted hearts and 13 LV biopsies (mean weight: 125 mg) from patients with preserved systolic function undergoing coronary surgery. Myocytes were exposed to either maximally activating Ca²⁺ at 37°C or 2 mM Ca²⁺ at 32°C. Contraction was measured using a video-edge-detection system and expressed as % change in cell length (% shortening). (ii) Osmotic minipumps infusing noradrenaline at 1.8 mg/kg/hr were implanted 6 guinea-pigs for 7 days. Myocyte contractile responses to isoprenaline were reduced, confirming β-AR desensitisation, and basal cAMP levels decreased. Results: There was no depression of % shortening in myocytes from failing hearts at 0.1 Hz. The % shortening was reduced in myocytes from failing hearts relative to non-failing controls in both maximal Ca²⁺ from 0.5 Hz (4.1% Vs 8.7%) to 1.4 Hz (4.9% Vs 9.1%) and in 2 mM Ca²⁺ from 0.3 Hz (2.0% Vs 3.3%) to 1.4 Hz (1.7% Vs 4.2%) (ANOVA: p<0.001). Times to peak contraction and to 50% and 90% relaxation in maximal Ca²⁺ were prolonged in myocytes from failing hearts at 0.2 Hz (P<0.01) but only the time to 50% relaxation was significantly prolonged at 1.0 Hz (p<0.05). Thapsigargin (3μM) reduced or prevented the increase in contraction with increasing frequency in control guinea-pig myocytes in 2.5 mM Ca²⁺. Shortening was not affected by thapsigargin at 0.1 Hz (2.1% Vs 2.1%) but was at 1.4 Hz (2.5% Vs 3.8%) (ANOVA: p<0.001). Parameters of relaxation were unchanged. Thapsigargin also reduced the contractile response to increased frequency in myocytes from failing human hearts. β-AR desensitisation produced a similar effect to thapsigargin, with maximum shortening unaltered at 0.1 Hz (5.2% Vs 4.0%) but depressed at 1.4 Hz (4.3% Vs 7.1%) (ANOVA: p<0.001) in cells and diastolic abnormalities in human heart failure. Depression of SR function and reduction of basal cAMP levels in animal models reproduces the contraction defect at high stimulation frequencies, but not the slowing of relaxation, seen in ventricular myocytes from the failing human heart.

**Local delivery of antisense oligodeoxynucleotide to c-myc in vitro and in vivo inhibits vascular smooth muscle cell proliferation.**

Junn, Cathy M Holt, Sheila E Francis, Lynda Shepherd, G H Smith, D C Crossman, D C Cumberland. Sections of Cardiology and Cardiothoracic Surgery, University of Sheffield, Clinical Sciences Centre, Northern General Hospital, Sheffield

Objective Vascular smooth muscle cell (VSMC) proliferation is central to the pathogenesis of atherosclerosis, restenosis after angioplasty, saphenous vein graft occlusion and coronary sclerosis after cardiac transplantation. The expression of cell-cycle related proteo-ondes, including c-myc is involved. Antisense deoxynucleoligonucleotides (AS ODNs) inhibit VSMC proliferation and neo-intima formation in selected animal models. The effect of AS ODN c-myc on porcine and human VSMCs in vitro, and its local delivery in porcine coronary arteries in vivo was tested. Methods An 18-mer AS ODN c-myc was applied to SMCs cultured from human arteries and veins and porcine aorta in culture. Cell proliferation, c-myc mRNA expression and c-myc protein levels were examined. A double-skinned porous balloon catheter (Transport, CardioVascular Dynamics) delivered AS ODN c-myc immediately after high pressure, oversized balloon injury in a porcine model of restenosis. Neo-intimal hyperplasia at four weeks was assessed. Results AS ODN c-myc inhibited the proliferation of human VSMCs from all sources. VSMC activity after incubation with mean (SEM) [³H]-Thy was 497(23) DPM/well after 5μM AS ODN c-myc compared with 472(0.47) after sense control (p<0.005). C-myc mRNA levels were also reduced at 48-96h. Immunocytochemical staining for c-myc protein showed only weak perinuclear staining in cells incubated with AS ODN. The intracoronar accumulation of fluorescent labelled AS ODN was seen at up to 24h. Porcine coronary arteries post angioplasty showed AS ODN deposition in the inner one of the media. There was a reduction in mean (SEM) maximal internal thickness from 22.7% (4.2%) to 10.7% (3.6%) total wall thickness (n=10, p<0.05). Conclusions AS ODN c-myc reduces VSMC proliferation in vitro. Its local intracoronary delivery via the Transport catheter is a feasible and effective method for reducing restenosis after angioplasty.

**CHANGES IN MYOCARDIAL ENERGY METABOLISM IN HUMANS AT ANGIOPLASTY - EVIDENCE FOR PRECONDITIONING.**


Brief periods of myocardial ischaemia and reperfusion paradoxically protect against subsequent prolonged ischaemic insults. This adaptive response termed preconditioning has been observed with successive coronary occlusions at PTCA based on anginal intensity and ECG changes. The aim of this study was to quantify myocardial energy levels in response to repetitive insults at angioplasty. Nine male patients (mean age 59±2) with isolated left anterior descending (LAD) artery stenoses (>70%) and normal left ventricular function were studied. Collateral channels filling the diseased arterial segment were absent on the diagnostic angiogram. PTCA consisted of three inflations separated by 5 minutes of reperfusion. Inflation durations of were; 1) 90 seconds, 2) 90 sec and 3) 180-300 sec. Subjective anginal intensity (0-10) and ST segment shift were recorded at the end of each inflation. Paired arterial and great cardiac venous blood samples were taken before PTCA and immediately after each deflation. Right ventricular endomyocardial biopsies were taken from LAD perfusion area (anterior inter-ventricular septum) in seven patients immediately before and after the first and third inflations. Blood samples and biopsy extracts were analysed by HPLC for hypoxanthine(3H)intranuclear catabolite and sensitive marker of ischaemia), ATP and total adenine nucleotides (TAN). Results: Hypoxanthine arterio-venous differences (mean±SEM) were:

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<th>Hypoxanthine µmoles/litre</th>
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<td>Before PTCA</td>
<td>1</td>
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<tr>
<td>10.0±1.98</td>
<td>-3.4±3.5</td>
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The rate of ATP and TAN depletion were delayed during the prolonged inflation (5.4±2.9% and 58.4±2.1% of control vs 58.7±2.7 and 67.2±2.0% respectively after the initial short inflation). ST segment shift was reduced (13.4±9.7 vs 10±8.6 p<0.04) and angina was unchanged (54±2 vs 54±3 comparing the third to the first inflation). These results indicate an adaptive response by the myocardium to repetitive ischaemia at PTCA, providing evidence preconditioning occurs in the human heart.
(104) MODERATED POSTER
CARDIOVASCULAR RISK FACTORS, CORONARY EVENTS AND ALL CAUSES MORTALITY IN EIGHT YEARS' FOLLOW-UP OF MEN AND WOMEN IN THE SCOTTISH HEART HEALTH STUDY COHORT
In 1984-86 10 359 men and women were studied in the Scottish Heart Health Study. These were a random sample aged 40-59 of those on the lists of 300 general practitioners in 22 local government districts of mainland Scotland. Numerous cross-sectional analyses have been published of the questionnaire and biochemical data, but participants were also flagged for mortality follow-up and gave written consent to surveillance of their medical records. To the end of 1993 712 deaths from all causes have been notified and record linkage through the Scottish SMR1 system has revealed thousands of hospital admissions from which acute coronary events have been extracted.
Combined fatal and non-fatal coronary events, analysed by fifths in each sex, show a similar risk gradient, with strong gradients for cholesterol, cotinine (smoking), and body mass index, and lesser risk ratios for fibrinogen and systolic blood pressure, and a negative gradient for alcohol consumption.
All causes mortality over eight years shows a comparatively flat relationship between fifths of the risk factor distribution and mortality rates for body mass index, cholesterol and alcohol consumption. The two sexes are again consistent with cotinine, fibrinogen and systolic blood pressure showing positive gradients.
The differences in the power of cardiovascular risk factors to predict coronary events versus their failure in all causes mortality pose questions for health promotion and different explanations are discussed.

(106) MODERATED POSTER
INCREASED LATE MORTALITY AND MORBIDITY AFTER FIRST MYOCARDIAL INFARCTION IN SOUTH ASIANS COMPARED TO WHITES
N Shukla, J Lear, S Fletcher, K Wood, D P deBono
Departments of Cardiology and Pharmacology and Therapeutics, University of Leicester, Leicester.
Although South Asians (SA) living in the UK have an increased incidence and prevalence of coronary artery disease (CAD) compared to whites, their outcome after first myocardial infarction (MI) is not known. We compared morbidity and mortality in a consecutive series of 241 SA MI patients (200 men) admitted between January 1987 and August 1993. They were matched with 241 whites for age, sex, date of admission, type and site of MI. Mean(SE) age for SA and white patients was 57.6 (0.7 ) years, follow up period was also similar, 73 (214) months. Hospital mortality was similar but late mortality was increased in the SA patients, 48 deaths (20.4%) at a mean (SE) interval of 18.2 (3.1) months vs 27 deaths (11.6%) at a mean (SE) interval of 22.6 (4.1) for whites, p=0.02. Of the hospital complications the occurrence of left ventricular failure (LVF) was increased in SA patients 73 (30%), compared to 52 (22%) for whites, p=0.03. SA patients also had larger infarcts than whites, as measured by peak creatinine phosphokinase (CPK), p=0.01. Long-term morbidity was also significantly increased in the SA group, with rates of reoccurrence of angina and re infarction almost twice that for whites. Logistic regression revealed the same independent predictors of late mortality in both groups i.e., advanced age, post MI LVF, diabetes, creatinine (>150 umol/l) and CPK (>200 U/I). Increased mortality and morbidity in SA patients after first MI is a worrying finding and requires further investigation.

(105) MODERATED POSTER
CORONARY HEART DISEASE AND THE SOCIO-ECONOMIC ENVIRONMENT IN A SINGLE HEALTH DISTRICT
N Huff, D Gray and J R Hampton.
Department of Geography, University of Nottingham and Division of Cardiovascular Medicine, University Hospital, Nottingham.
Strategies are needed to identify patients at risk to meet coronary heart disease (CHD) targets in ‘Health of the Nation’. We describe a novel method to identify areas of high and low prevalence in our health district.
Data over the last 20 years were retrieved from a) a disease register of patients admitted to hospital with myocardial infarction; b) community deaths from some manifestation of ischaemic heart disease.
Prevalence of CHD can be influenced by social deprivation so we developed socio-economic indices from the last three census returns. Postcodes were used to identify geographical location. Populations were age- and sex-standardised.
From this information, we were able to define a) those socio-economic groups and geographic areas of our health district with the greatest prevalence of morbidity from acute myocardial infarction and death from ischaemic heart disease; and b) trends in prevalence of CHD mortality and morbidity.
Male CHD mortality declined over the last 20 years even in areas of social deprivation, though the decline was most marked in socially-affluent areas of the health district; CHD morbidity rates in affluent and deprived areas declined equally, though morbidity was greater in more affluent areas. Female CHD mortality was associated with relative deprivation in the 1970s while in later years mortality increased in more affluent areas; morbidity events were too few to analyse.
This method facilitates the direction of limited health care resources for health promotion, screening and treatment to those areas and populations with the greatest need.

(107) MODERATED POSTER
REVIEW OF TRIAGE, DIAGNOSIS AND READMISSION RATES IN PATIENTS WITH ACUTE CHEST PAIN
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Department of Medicine, The University of Edinburgh, Accident & Emergency Department, Royal Infirmary, Edinburgh.
Over a four month period, 1297 patients presented to an Accident and Emergency (A & E) Department with non-traumatic chest pain. Detailed, independent review of these cases included discharge data, follow-up investigations and a postal questionnaire to patients discharged directly home. We obtained complete data on 1229 (94.7%) patients. 333 patients were discharged directly, 194 were admitted to CCU and 702 to medical wards. The rate of inappropriate discharge in A & E was very low (3.3%) and no patient with AMI was sent home. We judged the diagnosis to be wrong in 7.2% and no diagnosis was given in 12.0%. By contrast, diagnosis was complete in all patients discharged from CCU and was wrong in only one (0.5%). We judged only one CCU admission to be inappropriate. Of the 702 patients admitted to wards, the discharge diagnosis was wrong in 8.8% and incomplete in 13.7%. The wrong diagnoses included 25 of the 92 (27.2%) cases we judged to have AMI and 8 cases of unstable angina. In the 6 months after discharge, readmission rate was 94/1229 (7.6%) overall. 27/158 (17.1%) ward patients with incomplete or inaccurate diagnosis were readmitted compared with 31/544 (5.7%) others (p<0.001). Readmission was much more likely in patients with IHD (72/691 vs 22/538, p<0.001). 82/105 (78.1%) non-Q wave MIs were admitted to wards while 136/154 Q wave MIs were admitted to CCU (p<0.01). Death and cardiac failure were equally likely to occur in ward and CCU patients with AMI, while arrhythmias were much more likely in CCU patients (39/159 vs 6/110, p<0.01). In conclusion, a significant proportion of patients presenting with acute chest pain will be discharged with wrong or incomplete diagnoses. Readmission rate is high, and more likely if diagnosis is inaccurate. Very few patients are sent home or admitted to CCU inappropriately. Patients with suspected IHD admitted to wards need to be accurately identified.
(108) MODERATED POSTER

PHYSICIAN PREJUDICE INFLUENCES TREATMENT ALLOCATION IN SINGLE VESSEL CORONARY ARTERY DISEASE: AN EXAMPLE OF THE ENTHUSIASM HYPOTHESIS OF HEALTH CARE VARIATION?

RH Stables, C Anastasopolous, B Denne, R Underwood, NP Buller, DM Denison. The Royal Brompton Hospital, London

Single vessel coronary artery disease (SVD) has a generally benign prognosis and many patients with this pattern of disease are managed conservatively. Although coronary artery bypass grafting is sometimes recommended, balloon angioplasty (PTCA) and other interventional procedures provide the principal alternative management strategy. The aim of this study was to identify factors predicting the allocation of SVD patients to medical or interventional treatment and to test the hypothesis that the disposition of the consultant cardiologist, as manifest by the nature of his or her practice, will strongly influence the process. Some 1860 consecutive adult diagnostic catheter procedures were prospectively examined. Patients with previous intervention, acute coronary syndromes or coexisting valvar and myocardial disease were excluded. A final cohort of 75 patients manifesting non-occlusive SVD was identified. These patients were under the care of 11 different cardiologists who were grouped on the basis of whether or not they themselves performed coronary angioplasty (Interventionists(n) = 4; Physicians(n) = 7). There are well established channels for the referral of patients between groups. The baseline characteristics of the patients in the groups were compared and no significant differences with respect to age, risk factor profile, body mass index, anginal symptoms or treadmill exercise test performance. With informed consent, adenosine stress thallium imaging was performed on 60 patients. The extent of reversible ischaemia, quantified by the nine segment method, again, was similar in the two groups. Patients of Interventionists were more than twice as likely to be offered PTCA than patients of physicians (15/27 [56%] vs 12/48[25%]; p < 0.01). A multiple logistic regression analysis was established to examine factors predicting initial treatment allocation. This confirmed cardiologist type to be a significant and independent predictor of treatment allocation (p < 0.001). This study demonstrates that, in patients with SVD, physician prejudice may be an important factor in treatment recommendation and while this may have little influence on the group's uniformly favourable prognostic outlook it has clear implications for individual patients and for resource allocation.

(109) MODERATED POSTER

COMPARISON OF 3991 CORONARY EVENTS IN MEN AND 1551 IN WOMEN IN THE GLASGOW MONICA PROJECT.

ARE HEART ATTACKS IN MEN AND WOMEN DIFFERENT?

H Tunstall-Pedoe, C Morrison, M Woodward, B Fitzpatrick, G Watt. Cardiovascular Epidemiology Unit, Dundee and Scottish MONICA Project, Glasgow

Since 1985 all recognised episodes of non-fatal acute myocardial infarction and of coronary death in residents of North Glasgow aged 25-64 have been subjected to standardized data recording and to WHO MONICA Project diagnostic assessment. Accumulated data from the calendar years 1985-91 allow precise comparison of what happens in 3991 men and 1551 women, and results are compared before and after age standardization. For very many variables there is no significant difference, percentage breakdowns agreeing to less than 1%. However, women have fewer attacks, are more often widowed and more socially deprived. More of them are first seen at home whereas more men go straight to hospital. Compared with men, women take slightly longer to reach hospital. They present with more complicating symptoms and signs, but fewer of them develop myocardial infarction with unequivocal electro-cardiographic Q wave progression and more have lesser ECG findings and raised cardiac enzymes. Proportionately more men die suddenly before reaching hospital and more women after arrival. Differences of presentation and of delay in death lead to some differences in management in hospital. CCU and hospital fatality rates are very significantly different in the two sexes. If deaths outside hospital are added in however, in the differences in 28 day survival between the sexes are abolished and they finish equal.

(110) MODERATED POSTER

HOW OFTEN IS HEART FAILURE A CAUSE OR CONTRIBUTOR TO DEATH?


Since heart failure is usually a syndrome arising from an underlying condition such as coronary artery disease, it should not be recorded as the primary cause of death at the time of certification. Official statistics, by utilising the stated primary cause of death, may therefore substantially underestimate the contribution of heart failure to overall mortality. The General Register Office for Scotland maintain a database of the ICD 9 codes for the primary causes and up to three additional contributory causes of all deaths in Scotland. We carried out a retrospective, computer-assisted analysis of death certificates in Scotland between 1979 and 1992 for which congestive heart failure, left heart failure, heart failure (unspecified), primary cardiomyopathy, alcoholic cardiomyopathy or secondary cardiomyopathy were specified as either the primary or a contributory cause of death. From a total of 883,622 deaths in Scotland between 1979 and 1992, heart failure was recorded as the primary cause of death in 13,685 people (1.5%) and as a contributory cause in 126,073 people (14.3%). Heart failure therefore caused or contributed to a remarkable 137,892 deaths (15.6% of all deaths) between 1979 and 1992. Ischaemic heart disease was responsible for a total of 251,661 deaths over the same period (28.5% of all deaths) and of these, heart failure was recorded as a contributory factor in 36,923 (15.5%). These data confirm that heart failure as a major health problem and suggest that in Scotland, mortality statistics may considerably underestimate the extent of the problem. Attempts to reduce mortality from ischaemic heart disease will also require specific strategies to treat and prevent heart failure.

(111) MODERATED POSTER

LEFT VENTRICULAR DYSFUNCTION IN THE NORTH GLASGOW MONICA POPULATION

TA McDonagh, *CE Morrison, JJ McMurray, +1 Ford, +H Tunstall-Pedoe and HJ Dargie. Cardiology Department, Western Infirmary, +Biostatistics, Glasgow University, *Scottish Monica Project, Glasgow.

Chronic heart failure is mainly attributable to left ventricular (LV) systolic dysfunction (LVD). Previous epidemiological studies have documented its prevalence using clinical criteria for its diagnosis. Very little work has been based on the objective measurement of LV function by echocardiography. We have carried out an echocardiographic survey on 2000 individuals, randomly sampled from a geographically population in North Glasgow (300 men and 200 women in each 10 year age band from 26-75). 1653 finally attended (response rate 83%). These subjects have all previously attended the Third Glasgow Monics Risk Factor Survey and are therefore characterised for standard cardiovascular risk factors. LV systolic function was assessed using biplane Simpson's Rule function and a LV EF ≤ 35% was taken to indicate LV dysfunction. Exercise capacity was measured by maximal exercise testing and ST segment depression of ≥ 1mm classified as ischaemia. The following results are on the first 1000 echocardiograms to be analysed.

Results

Prevalence of LVD = 8% (n = 82).
This rose with age from 4% in those <35yrs to >10% in those >65 yrs.
Prevalence of asymptomatic LVD = 3.6% (n = 34).
A LVEF ≤ 35% was associated with a reduction in functional capacity; mean exercise duration of 4 ± 14 minutes compared to 667 seconds in those with a LVEF ≥ 35% (p < 0.01).
Of those with LVD, 42% had ST segment depression ≥ 1mm, compared to only 21% of those without LVD (p < 0.01).
Of subjects with symptomatic LVD, 36% were receiving treatment with an ACE inhibitor and/or a diuretic, whereas only 17% of those with asymptomatic LVD were on such therapy (p < 0.01).
Both symptomatic and asymptomatic LVD have a high prevalence within this population in keeping with its inflated rate of coronary heart disease. This common and fatal condition is underdiagnosed and undertreated.
In-Hospital Audit Underestimates Early Postoperative Morbidity After Cardiac Surgery

I Birdi, M B Izzat, G D Angelini, A J Bryans
Department of Cardiac Surgery, University of Bristol, Bristol, BS2 8HW

Current cardiothoracic practice aims at early post-operative discharge but to the extent to which this transfer post-operative mortality to other healthcare services is not known. Two hundred and ninety-five consecutive patients (mean age 61 years, range 19 to 80, with 16% over the age of 70) who underwent the cardiac surgery team were investigated prospectively by in-hospital audit, and retrospectively by questionnaire, telephone interview, and review of hospital notes to assess the incidence of early morbidity and re-admission rate within 6 weeks of discharge. Information was obtained from 281 patients (95%) of which 3 had died after discharge. Operations performed included coronary bypass grafting (222), valve repair or replacement (75) and other procedures (11). Urgent operations were undertaken in 93 cases (30%), and as a result of complications in 25 (9%) cases 52% of patients into Parsonnet score 0 to 4 while 28% had scores of 5 or more. The hospital mortality was 4% (13) and the median post-operative hospital stay was 7 days. Two hundred and sixteen patients (7%) were discharged home directly while 65 (23%) were transferred to another hospital. This required a total of 744 additional hospital days (median 10 days). Thirty five patients (13%) required re-admission to hospital (33 to 13 other hospitals) within 6 weeks, adding a further 219 additional hospital days (median 7 days). Re-admission was required for the management of arrhythmia's (6), respiratory complications (6), chest pain (5), wound complications (5), suspected deep venous thrombosis or pulmonary embolus (4), gastrointestinal bleeding (1), MI failure (1) and other (9). There was no association between re-admission and age, Parsonnet score or length of primary hospital stay. In-hospital major sternal wound problems occurred in 3 patients requiring further surgery. After discharge, 3 further patients with major sternal wound complications presented late and required debridement or plastic surgical reconstruction. A further 83 simple sternal wound problems, of whom 49 received antibiotic therapy. Early morbidity after cardiac surgery is underestimated by prospective in-hospital audit and results in utilisation of a significant number of additional hospital in-patient bed days outside the primary cardiac surgical centre. While inter-hospital transfer of cardiac surgical patients maximises throughput, it may not minimise total hospital stay.

Age Differences in Use of Atrial and Dual Chamber Pacemakers: Differing Indications or Agism?

R K Aggarwal, D T Connelly, S G Ray, J Ball, R G Charles,
The Cardiothoracic Centre, Liverpool

The British Pacing and Electrophysiology Group's guidelines for pacemaker mode prescription recommend pacing or sensing of the atrium unless contraindicated. To assess age differences in indications for permanent pacing and in use of atrial (AAI) and dual chamber (DDD) pacemakers, we prospectively studied 1088 (559 male) consecutive patients undergoing new pacemaker implantation at our institution. The median age was 77 years (range 16-99); 654 patients (60%) were aged 75 or older at implant. Symptomatic indication for pacing was syncope or pre-syncope in 70% of all patients. Patients aged >75 were less likely to be paced in the absence of symptoms (4.1%) than patients aged <75 (8.1%, P=0.007). Electrocardiographic (ECG) diagnosis was dominant atrioventricular block (AVB) in 45% of all patients, sinus node disease (SND) in 29% and atrial fibrillation (AF) with bradycardia in 23% AF was the main ECG diagnosis in significantly more patients aged >75 (27%) compared to those under 75 (17%, P=0.001). The greater prevalence of diabetes mellitus, heart failure or peripheral vascular disease in patients aged >75 (31%) compared to those aged <75 (26.5%) was not statistically significant. Pacing mode was analysed according to ECG diagnosis. Results:

Conclusion: Even in a centre implanting considerably more physiological pacemakers than is the case nationally and allowing for the greater prevalence of AF in patients aged >75, atrial or dual chamber pacemakers are significantly less likely to be implanted in this age group compared to younger patients. Careful pre-implant assessment of this increasingly large group of patients is essential to ensure that they are not denied the benefits of physiological pacing.

Open Access Echocardiography Improves the Primary Care Management of Heart Failure

C M Francis, L Caruana, P Kearney, M Love, G R Sutherland, J R Starkey, T R D Shaw and J J M McMurray
Department of Cardiology, Western General Hospital, Edinburgh

It is difficult to make an accurate diagnosis of heart failure due to left ventricular (LV) systolic dysfunction in general practice. As a result, incorrect diagnosis may lead to inappropriate treatment. Echocardiography provides the best way to identify LV systolic dysfunction but this investigation is not directly available to General Practitioners (GPs). We assessed the value of an open access echocardiography service in the primary care management of patients with suspected heart failure. Following an educational meeting, GPs were encouraged to refer either patients with suspected heart failure treated with diuretics (Group 1) or patients with possible heart failure but not yet on treatment (Group 2). 119 patients in Group 1 and 99 patients in Group 2 were assessed. Patients were referred appropriately. Only 26% of patients in Group 1 and 8% of patients in Group 2 were found to have significant LV systolic dysfunction. In those patients with normal LV systolic function, important valvular disease was found in 4% of Group 1 and 6% of Group 2. As a result of the echocardiogram, changes in management (either stopping diuretic therapy or starting treatment with Angiotensin Converting Enzyme inhibitor and diuretic) were recommended in 65% of patients in Group 1 and 14% of Group 2. This study confirms how difficult it is to make a diagnosis of heart failure due to LV systolic dysfunction on the basis of symptoms and signs alone. Consequently, to ensure appropriate treatment, all patients being treated for heart failure should have an echocardiogram. Open access echocardiography helps to make this possible.

Open Access to Echocardiography for Suspected Heart Failure: Does it Work?

JJ Murphy, JPJ Frain, CM Bousham. Department of Medicine Memorial Hospital, Slingh

Echocardiography is widely regarded as the key investigation in patients with heart failure. Assessment of left ventricular function and the exclusion of valvular heart disease should result in improved management. An 'open access' service could be of value if General Practitioners were to refer appropriate patients and act on the results. This paper addresses both questions. A pilot 'open access' service is now available to 5 GP practices (one fundholding); 24 GPs serving 48,000 patients. Before starting, each practice was visited to discuss the uses of the service and written guidelines were produced. Full echocardiograms are performed, including two dimensional and Doppler studies. Ejection fraction is calculated from the cube of the fractional shortening. The first 150 referrals have now been studied, all but 3 of whom have had suspected heart failure. There were 63 men and 87 women whose ages ranged from 16 to 90 years (mean of 71). 70 had ischaemic heart disease (previous infarction in 33), 44 had hypertension, 3 had known valvular heart disease and 4 a cardiomyopathy. 44 (30%) had none of these. 128 (85%) were taking a diuretic when referred. Results: Left ventricular ejection fraction (EF) was less than 60% in 96 (64%) and below 40% in 33 (22%). Valvular disease was present in 45 (30%) and was considered haemodynamically significant in 9 (mitral regurgitation in 5, aortic regurgitation in 3 and mitral stenosis in 1). Two patients had unexplained hypertrophy and two had pericardial effusions (both small). Outcome: Two months after referral, GPs notes were reviewed to assess the impact of the echo result on management. In 33 cases the GP had started an investigation converting enzyme inhibitor (ACEI), 5 had been referred to hospital for initiation of ACEI and 8 had been referred for further assessment, including 7 of the 9 with a 'significant' valve disease. 22/33 with an EF < 40% have started an ACEI. Of the 24 GPs, 20 have used the service and 18 of these responded to a postal questionnaire. In reply to the question "How easy is it to interpret the results?", the following responses were received; very easy =4, easy =11, difficult =3, very difficult =0. All GPs found the service useful for clinical management and all wished it to continue. Guidelines: the number of 'inappropriate' referrals to the service has been small. GPs have been able to use the information to improve management.
Acquired Aortic Stenosis is the most common valvular disease presenting in adults. Valve replacement is the treatment of choice; favorable outcome is achieved by simultaneous CABG if appropriate. Chest pain is not a good predictor of coronary artery disease (CAD) and pre-operative coronary angiography (CA) is therefore undertaken. A prospective study was undertaken from December 1993 to determine if Tc-99m Tetrofosmin (Myoview) myocardial perfusion scintigraphy (SPECT) was as effective as SPECT (MPS) using a 2 day protocol with symptom limited supine bicycle exercise (SLEEP protocol) could replace CA in the investigation of these patients. 18 patients, mean age 63 (42-77) years were studied. Mean valve gradient assessed by Doppler was 85 (57-140) mmHg. The workload achieved was 77 (25-200) watts; there were no complications. 3 patients had angiographically significant CAD (>70% in ⩾1 artery), 3 had non-significant stenoses (<70%) and 12 had normal vessels. MPS correctly identified the territory of abnormal perfusion in the 3 patients with significant CAD and was reported as normal in the remainder. There were no false positive studies. MPS sensitivity for all CAD is 82% and for significant CAD 100%. Initial results indicate that pre-operative Tc-99m Tetrofosmin MPS will predict significant CAD in patients with aortic stenosis and is a sensitive, safe method of excluding patients with normal coronary arteries from coronary angiography.

Tc-99m Tetrofosmin Imaging Improves Diagnostic Accuracy in the Detection of Coronary Artery Disease Compared to TI-201

R S Khatar, J C W Crawley, U Raval, B S Sridhara, and A Lahiri. Northwick Park Hospital, Harrow.

Tc-99m Tetrofosmin is a new perfusion imaging agent which has advantages over TI-201 including superior image quality and dosimetry. The results of stress studies using planar tetrofosmin were compared with TI-201 by a blinded observer, in 38 patients with suspected coronary artery disease. Defects were allocated to the left anterior descending (LAD), right coronary (RCA) or left circumflex (LCx) arteries using a polar map with 3 levels of severity. Receiver operating characteristic (ROC) curves were plotted using angiographic data and the area under the ROC curve was used as a measure of diagnostic accuracy. ROC curves were created for the presence of coronary artery disease, multivessel (MV) and single vessel (SV) disease as well as for the three main arteries.

Area under ROC curve

<table>
<thead>
<tr>
<th>CAD</th>
<th>MV</th>
<th>SV</th>
<th>LAD</th>
<th>RCA</th>
<th>LCX</th>
</tr>
</thead>
<tbody>
<tr>
<td>50% stenosis</td>
<td>0.80</td>
<td>0.55</td>
<td>0.50</td>
<td>0.69</td>
<td>0.77</td>
</tr>
<tr>
<td>Tetrofosmin</td>
<td>0.67</td>
<td>0.55</td>
<td>0.58</td>
<td>0.70</td>
<td>0.66</td>
</tr>
<tr>
<td>TI-201</td>
<td>0.85</td>
<td>0.55</td>
<td>0.55</td>
<td>0.75</td>
<td>0.57</td>
</tr>
<tr>
<td>70% stenosis</td>
<td>0.58</td>
<td>0.55</td>
<td>0.55</td>
<td>0.75</td>
<td>0.55</td>
</tr>
</tbody>
</table>

This data suggests that there is an overall improvement for the detection of coronary artery disease by tetrofosmin compared to TI-201. However there is no difference in the localization of disease.
Ten patients with resting left ventricular regional function abnormality in at least two consecutive segments on cineangiography and referred for a revascularization procedure were studied. All patients underwent tagged cine magnetic resonance imaging (MRI) combined with dobutamine infusion before and within three months after intervention. Tagged cine MRI was performed at rest and during low-dose dobutamine infusion at a rate of 5-10 mcg/kg/min for 5 minutes. MR images were obtained on a 1.0 Tesla (Magnetom SP, Siemens system) with the use of a FISP sequence. Two tagging 1.33:1 binomial pulses were applied at end-diastole resulting in superposition of an orthogonal grid pattern. Imaging was performed in both long-axis and two short-axis directions. For image analysis, the left ventricle was divided into five segments in long axis, and six segments in short-axis slices. Images were assessed both qualitatively and quantitatively. An in-house image analysis was used for quantification, assessing endocardial and epicardial layers separately whenever it was possible. The distance in between selected grid points in each myocardial region was measured. Regional contractility was expressed as the % segmental shortening (%S) which is percentage change in intergrid distance from diastole to systole. Improvement in %S during dobutamine infusion indicated presence of contractile reserve.

All patients underwent successful revascularization procedure (6 CABG, 4 PTCA). Post-interventional images showed improved regional left ventricular function in regions with contractile reserve. %S values were 9.7 +/- 6.0 at baseline and 14.7 +/- 8.2 (p<0.05) during isotropic stimulation. During follow-up unstimulated %S was 12.8 +/-7.3 (p<0.05, vs baseline). We concluded that contractile reserve is a method for detecting hibernating myocardium and could be identified by tagged cine MRI.

The heart contains a variety of morphologically distinct nerve terminals that are known to influence cardiac function. Little is known about the distribution, morphology and neurochemistry of these terminals in the human heart. We used the technique of endocardial and epicardial surfaces of infant and adult postmortem and transplanted hearts using immunohistochemistry of whole mount preparations in conjunction with confocal and fluorescence microscopy. Terminals arising from nerve fibres (range 6-10 µm), innervating for myelin basic protein, were identified in the atrial endocardium, epicardium and coronary sinus and four types were distinguished by differences in neurochemistry, immunostained nerve area (range 358-797 µm²) and dispersion (range 620-684 µm²). These terminals displayed immunoreactivity for the neuronal marker protein gene product 9.5 as well as tyrosine hydroxylase and neuropeptide Y. Acetylcholinesterase (AChE) activity was detected in less than 5% of endocardial terminals arising from myelinated fibres. Epicardial terminals were observed in close proximity to myothesial cells and nerve fibres supplying some of these terminals were found associated with local ganglia. A distinct population of endocardial terminals (mean stained area 35 µm², 18.5-53 95% CI; mean dispersion 59 µm², 38.80 95% CI) was demonstrated arising from non-myelinated fibres (mean dia. 2.5 µm; 2.2-2.8 95% CI) in the endocardial pleura of the atria and left ventricle and were predominantly AChE positive. Specialized nerve terminals are more widely distributed in the human heart than has been described in experimental animals. These terminals express AChE activity and tyrosine hydroxylase and neuropeptide Y-immunoreactivity, suggesting that acetylcholine, catecholamines and neuropeptide Y in the heart may be present in sensory, as well as autonomic nerves.

Cardiac autoantibodies in dilated cardiomyopathy are early markers associated with better prognosis

Cardiac antibodies (Abs) are common in patients (pts) with dilated cardiomyopathy (DCM) (30-40%) at diagnosis, but become undetectable with disease progression. To determine the relation of antibody appearance to disease severity, we studied 136 DCM pts (pts; mean age 44±13 yrs) undergoing immunological assessment at diagnosis and follow-up. Cardiac autoantibodies (Abs) were found in 46 pts (28, 25% of the “organ specific” and 18, 16% of the “cross-reactive”-l type); at follow-up the frequencies of these antibodies were significantly lower (11, 10% and 11, 10% respectively p<0.002). Of the 47 pts, who were antibody positive at diagnosis, 22 (48%) lost these Abs at follow-up. Abs were found in 22 of the 64 pts, who were negative at diagnosis (0%) became positive at follow-up (p=0.0001). Positive antibody status at diagnosis was associated with greater exercise capacity (VE/PW: 66 ± 23 vs 51 ± 25 respectively p<0.01). Persistence of positive antibody status at follow-up was associated with male sex (p<0.01), NYHA I/II (p=0.06) absence of clinical deterioration (p=0.02), Cardiac Ab+ in DCM are found at an early stage, but become undetectable in advanced disease. Antibody persistence at follow-up may be non-invasive marker for identifying patients with delayed disease progression and better prognosis.
EVIDENCE FROM FAMILY STUDIES OF AUTOIMMUNITY TO α MYOSIN IN IDIOPATHIC DILATED CARDIOMYOPATHY

JH Goldman, PJ Keeling, R Warrach, S Redwood, MK Baig, L Dallas Libera, JE Sanderson, ALP Cafaro, WJ McKenna
Cardiological Sciences, St. Georges’ Hospital Medical School, London.

Autoimmune features in idiopathic dilated cardiomyopathy (DCM) include the presence of disease and cardiac specific autoantibodies in 30% of patients and 25% of their relatives. Western blotting has established that α myosin is an important autoantigen recognised by these antibodies, but is not a practical screening test. To assess the frequency and disease specificity of the anti-α myosin antibodies we developed an ELISA and evaluated a large cohort of DCM patients and their relatives. Serological assessment was performed on 123 consecutive DCM patients (WHO criteria) (age 42 ±14 years), 203 normals (age 45 ±16 years), 92 IHD (age 65 ±11 years), and 252 relatives (age 51 ±17 yrs). These were from 53 of the 123 DCM index cases. Abnormally raised anti-α myosin antibody levels were found in 25 (20%) of DCM patients, 4 (2%) normal and 4 (4%) IHD (p=0.001). Anti-α myosin antibody levels (~SEM) were greater in DCM than IHD patients or in the normals (0.27 ±0.02, 0.20 ±0.01, and 0.17 ±0.01, p=0.001). 41 (16%) of the relatives had an abnormal result compared to 4 (2%) normal (p=0.001). In 20/53 (38%) pedigrees anti-α myosin antibodies were detected in proband or ≥1 relative. The proportion of antibody positive relatives was higher in nonfamilial (35, 21%) than familial pedigrees (8, 8%; p=0.005). Anti-α myosin antibody levels in relatives were greater than in normals (0.26 ±0.01 vs. 0.17 ±0.01; p=0.001). Higher antibody levels were identified in relatives for whom the index case had a positive antibody result compared to those for whom the index case did not (0.37 ±0.02 vs. 0.22 ±0.01; p<0.001).

In conclusion, Organ and disease specific anti-α myosin antibodies were detected by ELISA in 20% of DCM patients, in 16% of their asymptomatic relatives and in 38% of their families. Anti-α myosin antibodies may identify asymptomatic relatives at risk of developing dilated cardiomyopathy.

MODULATION OF SKELETAL MUSCLE SODIUM CHANNELS BY THE HUMAN MYOTONIC MUSCULAR DYSTROPHY KINASE

JP Mounesy, Puting Xu, JE John, H Taylor, J Gilbert, AD Roses, JR Moorman. John Radcliffe Hospital, Oxford, Duke University, Durham NC and University of Virginia, Charlottesville VA USA

Myotonic muscular dystrophy (DM) is characterized by abnormal membrane Na currents, and the product of the DM gene (HMPK) has structural homology to protein kinases. To test the idea that faulty regulation of Na channels is a mechanism of DM, we measured Na currents (INa) through N-type oocyte-expressed skeletal muscle Na channels, and in the presence of normal HMPK. Coexpression of normal HMPK reduced whole cell INa by 48% (7-9 frogs, 64-81 oocytes; p<0.001). The effect of normal HMPK was not present in oocytes expressing mutated Na channels in which a phosphorylation site in the inactivation mechanism was disabled (S1321A, 7 frogs, 53-64 oocytes). In cell-attached patches, the charge across patches of oocytes expressing Na channels alone was 15-fold larger than in oocytes coexpressing normal HMPK (13-16 patches; p<0.005).

These findings are consistent with T cell activation in DCM, as seen in other autoimmune diseases.

**Table:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mean absorbance at 450 nm (sem)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-IVE</td>
<td>0.179 (0.018)</td>
</tr>
<tr>
<td>HIV N</td>
<td>0.241 (0.023)</td>
</tr>
<tr>
<td>HIV HMD</td>
<td>0.279 (0.023)</td>
</tr>
</tbody>
</table>

Pairwise comparison using Fisher’s LSD test confirmed a significant difference between HIV IVE and normal controls (p<0.001), and between HIV N patients and controls (p=0.028). The antibody level was higher in the HIV HMD group compared with HIV N, but this was not significant (p=0.261).

Conclusion: This study demonstrates an increased level of organ specific anti-α myosin antibody in HIV positive individuals and suggests that cardiac autoimmunty may be important in the pathogenesis of HIV related heart muscle disease. Cardiac autoantibodies may be present several years before the onset of ventricular dysfunction.
GLIBENCLAMIDE AND MAGNESIUM HAVE SIMILAR EFFECTS ON REPolarisation OF THE MONOPHASIC ACTION POTENTIAL DURING LOW-FLOW ISCHAEMIA.

H W L Bethell*, SR Redwood†, JI Vanderberg*, ND Carter*, AJ Camm‡ and AA Grace‡*

*Department of Biochemistry, University of Cambridge, Cambridge and †Department of Cardiological Sciences, St George's Hospital Medical School, London.

KATP channel activation during myocardial ischaemia is thought to contribute to K+ efflux and action potential (AP) shortening. Inhibition of the channel by glubenclamide variably inhibits K+ efflux and AP shortening in multicellular tissue, and is potentially arrhythmogenic. Simultaneous measurement of the relevant parameters during ischaemia in the whole heart has not been performed. Mg2+, which underlies rectification of the KATP channel, can modify the potential for ischaemic arrhythmogenesis. We investigated the effects of glubenclamide (10μM) and Mg2+ (10mM), measured with suction electrodes, during low-flow ischaemia (7.5% control) in ferret heart. Simultaneous 86Rb efflux was measured in the glubenclamide group. Hearts were perfused at femi g⁻¹ min⁻¹ with 25mM HCO3⁻; 1mM Mg2+ buffer at 30°C. Some hearts were loaded with 86Rb for 2 hours before 30 minutes ischaemia. After 5.5 minutes of ischaemia the APD90 shortened from 203±2ms to 169±1ms (p<0.05; n=4), with a 4.6 fold increase in the 86Rb efflux rate constant (τ = 1: 1.8±0.41 x 10⁻⁵ min⁻¹; τ = 5.5: 8.25±1.59 x 10⁻⁴ min⁻¹; p<0.05; n=4) assessed on-line β activity counting. Addition of glubenclamide caused an increase in APD90 from 226±6ms to 251±8ms (p<0.05; n=4) at 5.5 minutes, with a reduction in the increased 86Rb efflux rate (τ = 5.5: 2.71±0.55 x 10⁻⁴ min⁻¹; p<0.05; n=4 compared with t=5.5 above). After 5.5 mins of ischaemia Mg2+ caused an increase in APD90 from 226±6ms to 251±8ms (p<0.05; n=8). These results show that glubenclamide abolishes initial AP shortening and causes late AP lengthening during ischaemia with partial inhibition of 86Rb efflux, consistent with KATP channel inhibition. Increased block of the KATP channel by Mg2+ during ischaemia is consistent with published cellular effects, and may underlie an arrhythmogenic action. Its effect on K+ flux is being investigated.

MAGNesium abolishes epicardial action potential prolongation in early Ischaemia in the human heart.


Studies investigating epicardial monophasic action potential (MAP) duration during ischaemia have noted an initial prolongation which has been thought, at least in part, to be due to temperature fall. Magnesium (Mg²⁺) is known to modulate potassium channels and is therefore likely to be involved in repolarization. Patients undergoing elective coronary artery bypass surgery were randomized double blind to Mg²⁺ (n = 8) or placebo (n = 8). Mg²⁺ was given intravenously (0.2 mmol/kg bolus followed by 0.1 mmol/kg/hr) after induction of anaesthesia, 4 mmol Mg²⁺ (or placebo) was added to the 2 litres of pump prime solution. Patients were placed on cardiopulmonary bypass; paced at 600 msec; stable epicardial MAP recordings obtained. Global ischaemia was achieved by aortic cross clamping for 2 mins, maintaining near normothermia. Serum Mg²⁺ rose from 0.60 ± 0.03 to 1.68 ± 0.07 mmol/l in the Mg²⁺ group (p < 0.0001). Epicardial temperature was identical in the two groups and did not alter during ischaemia (35.7 ± 1.2 at 30 secs; 35.1 ± 0.7 at 60 secs). At 70% repolarization (mean ± SEM), MAP duration increased from 254 ± 5.3 msec at 0 secs to 265 ± 4.5 msec at 60 secs in the placebo group (p < 0.05) and did not change in the Mg²⁺ group (249.5 ± 5.7 to 247.5 ± 5.4 respectively). Thus raising external Mg²⁺ abolishes the MAP prolongation in early ischemia. These results suggest that MAP prolongation is not due to fall in epicardial temperature.
MAGNESIUM HAS CONCENTRATION AND TIME-DEPENDENT EFFECT ON ACTION POTENTIAL DURATION DURING MYOCARDIAL ISCHAEMIA

S Redwood*, HWL Bethell†, JI Vandenberg†, AJ Camm* †, A Grace†
*Dept. of Biochemistry, University of Cambridge, †Dept. of Cardiovascular Sciences, St George’s Hospital, London.

Magnesium has multiple effects on the function of sarcoplasmic reticulum, ion channels, pumps and carriers. Magnesium also has modulatory effects on cardiac function and rhythm during acute myocardial ischaemia and it has been suggested that Mg\(^{2+}\) may modify K\(_{ATP}\) channel activity. We have studied the effects of varying perfusate Mg\(^{2+}\) concentrations ([Mg\(^{2+}\)]\(e\)) (1.25, 5 and 10 mM) on the action potential duration (APD) measured with suction electrodes in isolated Langendorff-perfused ferret hearts (n = 6 in each group) at 37°C paced at 10 Hz subjected to 10 mins global low-flow (7.5% control) ischaemia. Raising external [Mg\(^{2+}\)] resulted in APD prolongation during early ischaemia. At 70% repolarization, APD at 3 mins ischaemia was 122.6 ± 3.7 msec ([Mg\(^{2+}\)]\(e\) = 1 mM); 140.0 ± 4.5 msec ([Mg\(^{2+}\)]\(e\) = 2.5 mM) and 162.0 ± 4.8 msec ([Mg\(^{2+}\)]\(e\) = 10 mM). After 10 mins ischaemia, there was no significant difference in APD. These results indicate significant effects of Mg\(^{2+}\) on repolarization during early myocardial ischaemia and effects on the concentration and time-dependency of these effects would be consistent with an influence on several modulators of repolarization. Significant differences observed during ischaemia with no significant effects at the concentrations tested during steady state is consistent with mediation via the K\(_{ATP}\) channel.

THE CARDIAC ELECTROPHYSIOLOGICAL EFFECTS ASSOCIATED WITH PLATELET ACTIVATION DURING MYOCARDIAL ISCHAEMIA ARE INFLUENCED BY NITRIC OXIDE AND PROSTACYCLIN.

N V Goulieou, Z E Esayat, D J Sheridan, H C Cohen, N A Flores
Academic Cardiology Unit and *Department of Haematology, St. Mary’s Hospital Medical School, London W2 1NY

Myocardial ischaemia induces platelet activation which is associated with adverse cardiac electrophysiological and arrhythmogenic effects. Nitric oxide (NO) and prostacyclin (PGI) are produced by the endothelium to inhibit platelet aggregation. Since endothelial dysfunction occurs during ischaemia and reperfusion, some of the effects may be due to reduced release of these compounds. To investigate this we studied the cellular electrophysiological and arrhythmogenic effects of platelet activation, during normal perfusion, myocardial ischaemia (10% control) and reperfusion, in isolated, buffer perfused guinea-pig hearts. Washed human platelets were infused into the hearts in groups which received 100 μM L-NAMe (n=12), 100 μM sodium nitroprusside (SNP, n=12), or 2.3 mM iloprost (n=10).

Platelets were also infused into a group of hearts (n=7) obtained from guinea-pigs which had been treated with Aspasil (Bayer, a soluble aspirin analogue, 50 mg/kg i.p.) 12 hours served as controls. Infusion of platelets with L-NAMe reduced action potential duration (APD) during ischaemia (95 ± 6 ms vs 115 ± 5 ms at 25 min, P < 0.05) and tended to increase the incidence of arrhythmias, which occurred earlier compared to hearts receiving untreated platelets (12.9 ± 2.1 min v 19.4 ± 2.0 min, P = 0.04). Infusion of platelets with SNP attenuated the ischaemia induced reduction in APD (114 ± 6 ms vs 115 ± 4 ms at 20 min, P < 0.05) and tended to reduce the incidence of arrhythmias during ischaemia. Infusion of platelets with iloprost reduced the arrhythmogenic effects of the platelets during ischaemia (VF was reduced from 75% to 25%, P < 0.01) and attenuating the reduction in APD during ischaemia (115 ± 4 ms vs 94 ± 4 ms at 20 min, P < 0.05). Aspasil pretreatment had no effect on arrhythmias, but accentuated the reduction in APD observed during ischaemia (96 ± 6 ms vs 115 ± 5 ms at 25 min, P < 0.05). SNP and iloprost also abated the arrhythmogenic response to the washed platelets to 5 μM ADP and reduced the responses to 4 μM collagen. Thus, NO and PGI, are capable of influencing the deleterious cardiac electrophysiological effects associated with platelet activation during myocardial ischaemia. Reactions in circulating levels of these compounds during ischaemia may therefore contribute to the arrhythmogenic effects of platelet activation.
DOES ISCHAEMIC PRECONDITIONING REDUCE THE INCIDENCE OF VENTRICULAR ARRHYTHMIA IN ACUTE MYOCARDIAL INFARCTION? A W. Haider, F Andreotti, D Hackett, D Tousoulis, R Narang, G J Davies, Cardiology Division, Hammersmith Hospital London

We investigated the influence of early intermittent closure and reopening of the infarct artery (IRA) on the incidence of ventricular arrhythmia during acute myocardial infarction (AMI). Continuous ST segment Holter monitoring was performed in 55 patients with AMI receiving I.V. +PA (0.30-0.60 MUI/kg) and heparin, within 6 hours of onset of symptoms. Intermittency was defined as ±2 episodes of resolution of ST segment elevation lasting ≥1 min, seen before the start of lytic therapy. The incidence of arrhythmias was calculated by dividing the 24h Holter recordings in two phases: 0-6 hours (early phase) and 18-24 hours (late phase). Intermittency was documented in 49% (Group 1) and was absent in 51% (Group 2) of patients. The two groups were comparable regarding age, delay in treatment from the onset of symptoms, re-vascularisation time and 90 minute patency of the IRA. The results (mean ±SD) were:

<table>
<thead>
<tr>
<th>Incidence of arrhythmia during the Early Phase</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated PVCs</td>
<td>476±164</td>
<td>98±38</td>
<td>0.014</td>
</tr>
<tr>
<td>Couples</td>
<td>2±0.2</td>
<td>10±6.1</td>
<td>0.003</td>
</tr>
<tr>
<td>Ventricular Tachycardia</td>
<td>16±3</td>
<td>8±1</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Thus, spontaneous intermittent recanalisation represents an unstable state during early AMI with an increased incidence of ventricular arrhythmia. Ischaemic preconditioning may be a mechanism by which it reduces the incidence of subsequent arrhythmias.

HUMAN INDUCIBLE NITRIC OXIDE SYNTHASE IS EXPRESSED IN DILATED CARDIOMYOPATHY, VALVULAR AND ISCHAEMIC HEART DISEASE

GA Haywood, PJ Keeling, P Tao, NP Lewis, H von der Leyen, CD Byrne, P Trindade, FP Cooke, WD McKenna, MB Fowler. Department of Cardiological Sciences, St George's Hospital, London UK and Division of Cardiovascular Medicine, Stanford University, Stanford, CA.

Nitric oxide is known to exert negative inotropic effects on myocytes. Initial reports using activity assays have suggested increased generation of nitric oxide in myocardium from patients with dilated cardiomyopathy and acute myocarditis. However, myocardial detection of mRNA encoding the cytokine-inducible form of nitric oxide synthase (iNOS) has not been reported in patients with heart failure. We extracted total RNA from right ventricular myocardium obtained from 48 human hearts: explanted hearts - dilated cardiomyopathy (DCM: n = 17), ischaemic heart disease (IH; n = 11); intra-operative biopsies in patients with compensated heart failure - valvular heart disease (n = 9) / ischaemic heart disease (n = 1); and donor hearts and necropsy specimens from subjects who had suffered sudden death from a non-cardiac cause (n = 10). Reverse transcription - polymerase chain reaction (RT-PCR) was used to detect iNOS, aminonitric acid peptide (ANP) and beta actin gene expression.

Expression: Controls Valvular DCM IH
iNOS 1/10 9/9 11/17 8/12
ANP 9/9 9/9 10/10 12/12
Beta actin expression was present in all samples.

Conclusions: The frequency of iNOS gene expression was increased (p < 0.05) in right ventricular tissue from patients with heart failure irrespective of aetiology. Although this phenomenon might result from the effects of drug therapy and/or cardiac surgical procedures, it may be that expression of iNOS, like ANP, is part of the molecular phenotype of the failing heart. Further experiments are in progress to determine whether iNOS gene expression results in synthesis of iNOS protein in the myocardium. If local generation of the iNOS enzyme occurs in heart failure, nitric oxide production may contribute to contractile impairment in patients with valvular and ischemic heart disease as well as in patients with dilated cardiomyopathy.

DETECTION AND PATHOLOGICAL ROLE OF INDUCIBLE NITRIC OXIDE SYNTHASE IN MAN

NMM Robinson1, REA Smith2, JR Mcepeake1, SA Bayliss1, IG Charles1, ND Heaton1, RW Martin1, SF Moncada1

King's College School of Medicine1, London and Wellcome Research Laboratories, Beckenham, Kent2.

Nitric Oxide (NO) synthesised in large quantities by inducible NO Synthase (iNOS) may be an important cause of pathological vasodilatation seen in high output cardiac states such as endotoxaemia and hepatic failure. This contrasts with the normal control of physiological vascular tone by a low output of NO from endothelial NO synthase (eNOS). Human hepatic artery was obtained from donor (n=7) and recipient (n=10) patients at the time of liver transplantation for hepatic failure associated with a low systemic vascular resistance.

Arterial rings were removed for organ bath pharmacology or frozen at -70°C for molecular analysis. We detected mRNA iNOS and mRNA eNOS using the Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) using novel oligonucleotide primers based on the published sequence of human iNOS and eNOS. DNA products from the RT-PCR were sequenced to confirm their identity and to exclude contamination. Assay of citrulline production was used to assess NOS enzyme activity. Histology revealed the presence of scattered inflammatory cells by day 3, minor focal myocarditis by day 5 and severe myocarditis by day 6. Messenger RNA iNOS was present in infected samples from day 6 onwards while mRNA eNOS was present in all samples. Calcium-independent NOS activity was detected in infected mice by day 6 and peaked by day 8, while calcium-dependent activity was present in all samples. Control mice showed no myocarditis, calcium-independent NOS activity or mRNA iNOS, while mRNA eNOS was detected in all samples. In conclusion, iNOS induces NO gene transcription and active enzyme within the myocardium. This supports the hypothesis that induction of NOS occurs in inflammatory myocardial conditions. The functional significance of this iNOS expression within the myocardium remains to be established.
(140) POSTER

CONSTITUTIVE NITRIC OXIDE SYNTHASE GENE EXPRESSION IS NORMALIZED WITH ENDOTHELIAL REGROWTH FOLLOWING BALLOON ANGIOPLASTY

PH Groves, AP Banning, R Studer, MJ Lewis, H Cheadle, H Just, H Grosser. University of Freiburg, Germany and University of Wales College of Medicine, Cardiff.

Endothelium-dependent vasodilation is chronically impaired after balloon angioplasty despite early endothelial regeneration.

Decreased endothelium-derived nitric oxide (EDNO) production associated with endothelial G protein dysfunction has been proposed as an underlying mechanism. EDNO is generated in response to a number of stimuli through the action of the enzyme constitutive nitric oxide synthase (cNOS).

We therefore investigated cNOS gene expression at early and late time points after balloon injury of the pig carotid artery. Angioplasty was performed using an over-sized balloon (6 atms; 5 inflations; 30 secs each) and arteries were retrieved 48 hours (n=4) and 21 days (n=8) after injury. Samples were taken from the area of injury and from distal uninjured control vessel in all arteries. Total RNA was isolated and cNOS mRNA levels were quantified by a competitive RNA polymerase chain reaction incorporating human sequence specific primers to cNOS and internal standard. At 48 hours after angioplasty, cNOS mRNA levels were reduced more than 8 fold in injured as compared with uninjured artery - mean±SEM - (0.80±0.31x10^6 vs. 6.51±2.14x10^6) RNA transcripts/100ng total RNA, p<0.05.

However, at 21 days after angioplasty when endothelial regeneration was complete (DBA lectin staining), cNOS mRNA levels were similar to uninjured samples (8.03±2.16x10^6 vs. 10.42±3.81x10^6) RNA transcripts/100ng total RNA, p=NS. Thus, cNOS gene expression is reduced but not abolished early after angioplasty and normalizes with endothelial regeneration. Residual endothelial dysfunction and reduced EDNO production that is present despite endothelial regeneration is not attributable to a defect in cNOS gene expression.

(141) POSTER

VASULAR EXPRESSION OF ENDOTHELIN-1 (ET-1) mRNA INCREASES IN SEPSIS

NP Curzen, S Kaddoura, PH Sugden, PA Poole-Wilson and TW Evans

National Heart and Lung Institute, London.

The characteristic systemic vasodilatation seen in severe sepsis is often accompanied by increased pulmonary vascular tone. ET-1 is a constrictor peptide whose plasma levels are elevated in patients with sepsis. ET-1, however, appears to act primarily as a local, rather than as a circulating factor. We assessed whether expression of ET-1 mRNA in aorta and pulmonary artery (PA) is elevated in sepsis.

Methods: 18 male Wistar rats (300g) were divided into 3 groups:
1) Control (C) - saline (1ml intraperitoneal injection (ip)), 2) Endothelin (E) - (20mg/kg ip), 3) Dexamethasone (D) - (3mg/kg 30 mins prior to endothelin). Rats were sacrificed at 1 or 6 hours. The aorta and PA were removed and total RNA was extracted. A ribonuclease protection assay was performed using one probe protecting 154 bases of ET-1 mRNA and another protecting 134 bases of constitutive glyceraldehyde 3-phosphate dehydrogenase (GAPDH) mRNA. Protected bands were quantified by laser densitometry.

Results: In both vessels there was increased ET-1 mRNA expression. Results (mean±SEM of n=3) are expressed as ET-1 mRNA/GAPDH mRNA ratio.

(142) POSTER

INHIBITION OF BASAL ENDOTHELIN ACTIVITY ENHANCES VENTRICULAR RELAXATION IN THE ISOLATED HEART

BD Prendergast, PB Anning, MJ Lewis, AM Shah*

Cardiovascular Sciences Group, Departments of Pathology and Pharmacology, University of Wales College of Medicine, Cardiff.

The vasoactive peptide endothelin-1 exerts positive inotropic and chronotropic effects on myocytes. Thus, it can induce myocardial hypertrophy, but whether endogenous endothelin has a physiological role in cardiac regulation is still uncertain. Recent studies in isolated ferret papillary muscles have demonstrated the release of endothelin by endocardial endothelium with consequent delay in isometric twitch relaxation. In the present study we examined the effects of the specific ETA receptor antagonist, BQ123, on left ventricular (LV) performance in isolated ejecting guinea-pig hearts (n=6) perfused with Krebs buffer (1μM indomethacin) at 37°C, constant loading and heart rate. High fidelity LV pressure was measured by an apical 2F Millar catheter and an end-systolic dye-filled balloon (Am J Physiol 1994, 266; H1699). BQ123 (1μM) induced a progressive acceleration of early LV pressure decline (ie. decreased Tw) and significantly reduced left ventricular end diastolic pressure (LVEDP), but had no effect on peak LV pressure (LVP), dP/dt, stroke volume (SV) or coronary flow (CF). All these parameters remained stable in control (ungrafted) hearts (n=15).

% change (mean±SEM) at 16 mins; *p<0.05 cf. control group

Conclusions: Reversal of basal endothelin activity by the ETA antagonist, BQ123, enhances LV relaxation without altering 'systolic' performance or coronary flow. Thus, the tonic toxic effect of endocardial cardiac release of endothelin may exert physiologically significant effects on basal ventricular function. The lack of effect of BQ123 on coronary flow may reflect the site of endothelin release in the isolated heart.

(143) POSTER

UP REGULATION OF MATRIX Degrading GELATINASES IN PIG SAPHENOUS VEIN GRAFTS

KM Southgate, MB Izzat, D Knight and GD Angelini. University Academic Department of Cardiac Surgery, Bristol, BS2 8BW, UK.

Smooth muscle cell (SMC) migration and proliferation is the principal cause of late saphenous vein (SV) bypass graft failure in man. Both these processes have been shown to require extracellular matrix remodelling by matrix-degrading metalloproteinases (gelatinases). To investigate if these enzymes are activated in vein grafts, gelatinase activity was studied in organ cultures of ungrafted SV, graft SV, and carotid artery (removed four weeks after implantation) and carotid artery from the same animal (n=6). Vessel segments were cultured for 72 hours in serum-free media. The secretion of gelatinase activity into conditioned media was measured by gelatin zymography and densitometry. Induction of 95 kDa gelatinases were observed only in conditioned media of vein grafts; the activity of active 68 kDa gelatinases were also significantly increased in these vein grafts compared with ungrafted SVs (fig 1). The 72 kDa gelatinases were constitutionally secreted in all cultures (fig 1). The data demonstrate that the 95 kDa and 68 kDa gelatinases are strongly up regulated in saphenous vein following arterial grafting. These enzymes may therefore play an important role in vein graft failure by initiating intimal SMC migration and proliferation and be potential targets for therapy.

Fig 1: Densitometry of zymograms of conditioned media from 2 day cultures. Values are mean±SEM (n=6).

*p<0.005 vs ungrafted vein, **p<0.005 vs carotid artery.
**PROSTACYCLIN SYNTHESIS IS MARKEDLY DIMINISHED IN PROCEDED VEIN GRFTS**

JY Jeremy, MB Izzat, D Wright, S Berkitt, AJ Bryan, GD Angelini
Department of Cardiac surgery, Bristol Royal Infirmary, Bristol BS2 8HW.

Prostacyclin (PGI₂) inhibits myointimal hyperplasia, leucocyte and platelet adhesion (release of mitogens), and cholesterol accumulation, all of which are components of vein graft failure. Since PGF₂α status may play a role in vein graft failure, the synthesis of this prostanooids by saphenous vein to carotid artery graft (SVG) as well as control saphenous vein (CSV) and control carotid artery (CCA) in the pig was investigated. One month after surgery SVGs, CSVs and CCA were excised, cut into 2mm square segments and incubated for 4hr in minimum essential medium (MEM). Segments were saponified into test tubes and PGI₂ synthesis stimulated with various concentrations of noradrenaline, arachidonic acid and calcium ionophore A23187 and incubated at 37°C for 30 min. PGI₂ synthesis was assessed by radioimmunoassay of 6-oxo-PGF₁α. In response to all stimulators, PGI₂ release was markedly diminished in SVG compared to CSV and CCA (table 1).

<table>
<thead>
<tr>
<th>Table 1. Maximal release of PGI₂ (pg 6-oxo-PGF₂α/mg tissue / min [mean ± SEM; n = 4]) in response to different stimulators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arachidonic acid</td>
</tr>
<tr>
<td>SVG</td>
</tr>
<tr>
<td>CSV</td>
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<tr>
<td>CCA</td>
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</tbody>
</table>

This data indicates that there is a profound down-regulation of cyclooxygenase and/or PGI₂ synthase in porcine vein grafts. Intimal hyperplasia is characterised by a change of medial cells from a contractile to a migratory/proliferative phenotype. Since PGI₂ possesses properties which counter this transformation, down-regulation of PGI₂ synthesis may constitute a further phenotypic change which would augment the hyperplastic process.

**ENHANCER STIMULATION AUGMENTS GENE EXPRESSION AFTER ADENOVIRUS MEDITATED GENE TRANSFER INTO HUMAN VASCULAR SMOOTH MUSCLE CELLS**

GJ Clesham, H Browne, PJ Adam, S Elstathou, PL Weissberg
Department of Medicine and Division of Virology, University of Cambridge, Addenbrooke's Hospital, Cambridge.

A replication deficient, recombinant adenoviral vector (RA265) expressing β-galactosidase and driven by the cytomegalovirus immediate early promoter (CMV-IEP) was used to transduce human vascular smooth muscle cells (VSMC) in culture. The CMV-IEP permits constitutive expression in VSMC's and possesses enhancer elements able to bind the transcription factors cyclic AMP responsive binding protein (CREB) and NF-κB. The aim of this study was to examine the effect of stimulation of cAMP using 10μM forskolin and NF-κB using 50ng/ml phorbol-12-myristate-13-acetate (PMA) and 4mg/ml phytohemagglutinin (PHA) on gene expression in human VSMC's after exposure to RA265. Cultured human VSMC's were maintained in 0.5% serum for 48 hours then exposed to 50 or 100 plaque forming units (pfu) per cell of RA265. β-galactosidase activity, measured as absorbance units per mcg protein (AU/mcg/hr), was assessed on cell extracts 48 hours later using a standard ONPG assay.

<table>
<thead>
<tr>
<th>Table 2. Control</th>
<th>RA265 only</th>
<th>RA265 + Forskolin</th>
<th>RA265 + PMA/PHA</th>
<th>RA265 + Forsk + PHA/PHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.012 ± 0.004</td>
<td>0.15 ± 0.009</td>
<td>0.25 ± 0.005</td>
<td>0.17 ± 0.02</td>
</tr>
<tr>
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<td>0.25 ± 0.005</td>
<td>0.17 ± 0.02</td>
</tr>
</tbody>
</table>

Conclusion: Expression of a transfected gene linked to the CMV-IEP in human VSMC's may be considerably increased by chemical stimulation of enhancer binding agents. This approach may allow increased gene expression using lower adenoviral titres.

**LIPOSOMAL TRANSFECTION ENHANCES UPTAKE AND EFFICACY OF ANTISENSE OLIGODEOXYNUCLEOTIDES IN CULTURED CARDIAC MYOCYTES**

P E Glennon, S J Fuller, E A Sale, G J Sale, P H Sugden
Department of Cardiac Medicine, National Heart & Lung Institute, Dovehouse Street, London, UK

An antisense oligodeoxyribonucleotide (ODN) is a short (1-20 bases), single-stranded DNA molecule which binds to a complementary mRNA sequence, preventing translation and thus inhibiting the synthesis of a particular protein in a powerful and specific manner. Structural alterations (such as phosphorothioate modification) confer resistance to nucleosome degradation, but poor entry of ODNs into many cell types, including cardiac myocytes, remains a problem. Our initial experiments showed that uptake of fluorescently-labelled phosphorothioate-modified ODNs by cultured cardiac myocytes was markedly increased in the presence of a liposomal transfection reagent. The ODNs predominantly localised to the nucleus. We subsequently carried out liposomal transfection of cultured cardiac myocytes with a phosphorothioate-modified antisense ODN directed against mitogen-activated protein (MAP) kinase, an intracellular signalling protein which regulates cell growth and proliferation. Immunoblotting showed marked down-regulation of the 42 kDa isoform of MAP kinase. Down-regulation was significant by 24 hours and maximal (>90% depletion) at 48 hours after transfection with 0.2 μM ODN. Sense and random ODN sequences had no effect. We studied the effects of antisense treatment on two markers of hypertrophy; anti-MAP kinase ODN inhibited the increase in cell surface area seen in response to serum, and also inhibited induction of a transfected ANF promoter/luciferase reporter gene construct by phenylephrine. Liposomal transfection greatly enhances uptake, and therefore efficacy, of antisense ODNs in cardiac myocytes. Down-regulation of MAP kinase using this technique inhibits two well recognised markers of the hypertrophic response. We now have the opportunity to investigate the function of other specific cardiac myocyte proteins using appropriately designed antisense ODNs.

**DETERMINANTS OF PAI-1 ACTIVITY IN ACUTE MYOCARDIAL INFARCTION**

R Gray, V Mohamed-All, DLH Patterson, JS Yudkin
Department of Medicine, University College London Medical School, Whittington Hospital, London

The determinants of plasminogen activator inhibitor (PAI-1) activity levels, which may be an important determinant of the outcome of thrombolytic therapy, in acute myocardial infarction are unknown. We have previously reported a significant relationship between PAI-1 in patients with acute myocardial infarction (AMI) and plasma insulin measured by radioimmunoassay. However, these assays have been shown to overestimate plasma insulin levels due to cross reaction with proinsulin-like molecules, and the latter molecules may be more important determinants of PAI-1 activity. In this study we examined the relationship between PAI-1 activity in 150 non-diabetic and 42 diabetic subjects with acute myocardial infarction and plasma insulin, intact proinsulin and des-31,32-proinsulin measured by specific two site immunoenzymometric assays. In univariate analysis there were significant correlations between admission levels of PAI-1 activity and fasting intact proinsulin (r = -0.20; p = 0.004) and fasting des-31,32-proinsulin (r = -0.25; p = 0.011) but not fasting plasma specific insulin (r = 0.07; ns) or insulin sensitivity (HOMA) (r = -0.11; ns). Levels of PAI-1 activity on day 1 following AMI also correlated with fasting intact proinsulin (r = -0.26; p = 0.008) and fasting des-31,32-proinsulin (r = -0.35; p = 0.001). In multiple regression analysis, only intact proinsulin remained as a significant determinant of admission PAI-1 activity levels and des-31,32-proinsulin as a significant determinant of day 1 PAI-1 activity levels accounting for 8.9% (p = 0.016) and 7.8% (p = 0.003) of the variation respectively. These results indicate that while proinsulin-like molecules may be more important than plasma insulin in determining levels of PAI-1 activity in AMI, other factors must also be involved.
POSTER

CORRELATION OF POOR OUTCOME AND ANGIOGRAPHY FEATURES IN PATIENTS WITH ECG "TOMBSTONING" OF THE ST-SEGMENT IN ACUTE MYOCARDIAL INFARCTION
X Guo, L Chen, J Camm. Department of Cardiological Sciences, St. George's Hospital Medical School, London.

The prognostic and diagnostic values of elevation of the ST segment in AMI have not been fully evaluated. It is suggested that "Tombstoning" ("T"), a characteristic transient upward convex ST-segment elevation, is associated with poor outcome. Patients with ECG-T have significantly severe autonomic dysfunction, worse left ventricular function and a higher mortality. To understand more about the reasons for poor prognosis in patients with ECG-T, we have undertaken a retrospective, but blind, study of angiography data from 124 consecutive patients with AMI, whose ECG was taken within 1 day of the AMI and who underwent angiography either within 17 days (n=64) or 2 years (n=124) of AMI. In two time group, 13 (20%) and 24 (19%), respectively, showed T ECG and the remainder were defined as normal (N) elevation of the ST-segment ECG. T was strongly associated with anterior, rather than inferior, infarction (77% vs. 31%; 83% vs. 31%; p = 0.003; p < 0.0001, respectively). All the patients with T had total or partial occlusion of the left anterior descending (LAD) artery (100% vs. 45%; 100% vs. 44%; p = 0.0004, p < 0.0001). LAD occlusion in N patients was less frequent and less severe, (total occlusion p = 0.078; 0.02 and <50% occlusion, p=0.073;0.39). T patients had highly significantly greater incidence of total or partial occlusion of all 3 coronary arteries (62% vs. 18%; 54 vs. 17%; p = 0.001, 0.0002); Whilst of the few T patients with inferior infarction, all had all 3 arteries affected (T 100% (n=6) vs. 17% (n=5); T 100% (n=4) vs. 19% (n=3); p = 0.0002), and all had suffered a previous infarct. Thus, T seems to be associated with damage to the LAD artery (usually with 1 or more other arteries) and anterior infarction. The severe and extensive pathological change cause presumably the poorer outcome of patients whose ECG shows T. T may have potential prognostic and diagnostic value.

POSTER

MORTALITY FROM ACUTE MYOCARDIAL INFARCTION OUTSIDE AND INSIDE CLINICAL TRIALS
Gaynor Dixon, Royal Sussex County Hospital, Brighton on behalf of the UK Heart Attack Study Group.

Results from an overview of thrombolytic trials suggest that 35 day mortality with optimum hospital treatment for acute myocardial infarction (MI) should be about 10%. However the relationship between trial results and patient mortality in routine clinical practice remains unclear. We have examined the delivery and outcome of care in all hospitalised MIs in Brighton since 1.1.93 and in York and Cardiff since 1.1.94. Thirty-day mortality was 21% (n = 1006) but was only 11% in the subset of 150 patients enrolled in trials during our study. The main reasons for this discrepancy were (i) a high mortality in patients for whom thrombolysis was contraindicated. For example, mortality for patients presenting with ST elevation treated with thrombolysis in the trials was 10% (n = about 16,000); in our experience (n = 555) mortality was 10% for the 75% of patients who received thrombolysis but 34% for the 25% who were unsuitable. (ii) a higher proportion of younger patients within age group >75 years in the trials than in clinical practice. For example, patients aged 65-74 years comprised 32% of the under 75 age group in the trials but 52% in our series. We conclude that mortality from hospitalised myocardial infarction is about double that found by meta-analysis of thrombolytic trials.

POSTER

TEMPORARY CARDIAC PACING FOLLOWING ACUTE MYOCARDIAL INFARCTION
JJ Murphy, Department of Medicine, Memorial Hospital, Darlington.

Information on the practice and complications of temporary cardiac pacing is surprisingly limited. This abstract includes results from the first study of temporary pacing in district general hospitals. 18 of the 20 acute hospitals in the Northern Region participated in a 6 month prospective study. 104 temporary pacings were reported of which 102 were to treat the complications of acute myocardial infarction (AMI). The sites of infarction were as follows: Inferior (including inferior-posterolateral). Anteroseptal (including anterior septal and lateral) = 19, Anteroseptal + Inferior c 2; Unknown = 13 (bundle branch block present); not stated = 2. The indication for temporary pacing was complete heart block (CHB) in 84, 10 had sinus nodal bradycardia / arrest, 4 had atrial flutter / fibrillation + CHB, 2 had paroxysmal atrial fibrillation with pause and two had alternating left and right bundle branch block. 24 were performed within 24 hours of thrombolysis and routes of access were as follows: right internal jugular in 14, subclavian in 6, femoral in 3, and external jugular vein in 1. Immediate bleeding problems were reported in only one, following an internal jugular approach.

Mortality in the group was high. 57/102 (56%) died, 29 (28%) recovered and 16 (16%) required permanent pacing, 38/66 (58%) of patients with inferior infarction died as did 11/19 (58%) of those with anterior infarction. The timing of infarction was known for 58 of those with inferior infarction, 30 underwent pacing within the first 24 hours of AMI of whom 31 (82%) died. 20 were paced beyond the first 24 hours and mortality in this group was much lower (6/20 = 30%, p =< 0.001 between the groups).

Conclusions: (a) Temporary pacing following AMI is associated with a high mortality, whether the infarction is inferior or anterior. (b) Temporary pacing within the first 24 hours of acute inferior infarction is associated with a very high mortality. The mortality of those who require pacing after this time is significantly lower. (c) For those undergoing pacing within 24 hours of thrombolysis, the femoral and external jugular routes were used in only 4/24 cases. This practice is at odds with recent recommendations of the British Cardiac Society.

POSTER

CAN THE PRESSURE TO ACHIEVE SHORT DOOR TO NEEDLE TIME LEAD TO INAPPROPRIATE THROMBOLYSIS?
A Al-Mohammad, F Fath-Ordoubadi, A Amadi, K J Beatt. Academic Unit of Cardiovascular Medicine, Charing Cross and Westminster Medical School, London, UK

Current management of acute myocardial infarction emphasises the importance of early treatment. Thrombolysed patients during a six month period in two institutions were studied. The final confirmed diagnosis was used to assess the appropriateness of thrombolysis. The resulting two groups were compared according to whether or not thrombolysis was commenced within the first sixty minutes of the patient’s arrival to the accident and emergency department. Data on consecutive patients was recorded on the Coronary Care unit databases. During the study period, 184 patients were thrombolysed, data regarding the door to needle time and final diagnosis was available in 127 patients. Of those on whom data was recorded, 103 patients had myocardial infarction( MI), and 24 patients were inappropriately thrombolysed. 24% of the patients whose door to needle time was ≤ 60 minutes were inappropriately thrombolysed whereas, of those with a door to needle time > 60 minutes, only 18% were thrombolysed inappropriately. Therefore, the pressure to achieve low "door to needle" time may be compromising the diagnostic accuracy, with patients being inappropriately exposed to the hazards of thrombolytic treatment. Hence, more emphasis should be put on the accuracy of diagnosis and not only on the speed of management.
LOGISTIC REGRESSION (LR) AND NEURAL NETWORK (NN) MODELS FOR EARLY DIAGNOSIS OF AMI
R L Kennedy, A Burton, H S Fraser, L McCoy, R Harrison K Fox
Departments of Medicine, The University of Edinburgh and Control Engineering, The University of Sheffield

A NN model for the early diagnosis of AMI was developed and tested using data 1470 patients with acute chest pain. The model used 39 clinical and ECG data items available at presentation. Performance was tested on data from two centres - Edinburgh and Sheffield, and compared with that of a LR model and with the diagnosis of A & E Doctors. The LR and NN models were derived from a subset of the Edinburgh patients. The optimal diagnostic thresholds for the LR and NN models and for the Doctors were determined using receiver operating characteristic (ROC) curves. Sensitivity, Specificity, Positive Predictive Value (PPV) and Accuracy for LR on a test set of Edinburgh data were 87.8%, 87.2%, 66.0% and 87.3% respectively compared with 88.7%, 89.4%, 70.3% and 89.2% for the NN. Areas under the respective ROC curves were 92.8 ± 1.5 and 94.1 ± 1.4 (NS). When tested on data from Sheffield patients, the Sensitivity, Specificity, PPV and Accuracy for LR were 83.1%, 82.7%, 68.1% and 82.8% respectively compared with 87.7%, 85.3%, 73.8% and 86.1% for the NN. Areas under the ROC curves were 87.8 ± 1.8 and 90.3 ± 1.1 (p < 0.05). On these patients, the NN was better at diagnosing Q wave MI (p < 0.02) and excluding MI in patients with non-cardiac diagnoses (p < 0.05). The Doctors had Sensitivity, Specificity, PPV and Accuracy of 71%, 91.1%, 83.3%, 75.7% and 83% respectively. Combining their opinion with the output of the NN produced figures of 92.0%, 91.2%, 74.2% and 91.4%. Areas under the ROC curves for NN and for the NN/Doctor combination were significantly greater than that for the Doctors alone (p < 0.05 and p < 0.001 respectively).

In conclusion, neural networks appear to be a useful tool for analysis of clinical data from chest pain patients. The model described performed better than either admitting doctors or a standard statistical technique and operated well on data from two centres.

THE INCIDENCE AND PRESENTATION OF ISCHAEMIC HEART DISEASE: A POPULATION SURVEY
R H Roberts, C McEvoy, K Stock, S S Lo, R Egdoll, A Rochatelle, C C Sutton, D A Wood
Department of Clinical Epidemiology, National Heart and Lung Institute, London, and Department of Cardiology, The Millingdon Hospital, Ubridge, London.

The incidence of the major presentations of ischaemic heart disease (IHD), stable and unstable angina, myocardial infarction (MI) and sudden cardiac death, was measured in a population survey.

In June 1993, an acute referral chest pain clinic (CPC) was opened at a district hospital which serves a population of 231600 people, comprising 87700 cases, 6186 south asians and 642 other races. 80 general practitioners, covering 69% (15600) of the population, referred all new cases of suspected angina under the age of 71 years, to the CPC. New cases of unstable angina and MI were identified by monitoring hospital admissions, and sudden cardiac deaths were recorded through the district pathologist. In one year 256 patients were seen in the CPC, oF whom 71 (28.1%) had newly diagnosed IHD on clinical grounds, including an exercise ECG, 65 with stable angina (25.4%), 2 with unstable angina (0.78%) and 5 with recent MI (2.0%). The remaining 184 (71.9%) had non-cardiac pain. 376 patients attended the emergency department of the hospital with chest pain, of whom 76 (20.2%) had a new IHD. There were 18 cases of unstable angina, 4 (2.8%) and 12 cases of MI (15.4%). Sudden cardiac deaths was diagnosed at autopsy in 44 individuals. Of the 192 cases of new IHD, 142 (74.3%) were male and 50 (25.7%) were female. The overall incidence of IHD per 1000 patients per year is thus 1.20, comprising stable angina 0.41, unstable angina 0.13, MI 0.39 and sudden cardiac death 0.27.

In patients presenting for the first time with symptomatic IHD in a defined population, 34% have stable angina, 45% acute ischaemia or infarction and 23% died suddenly.

DEATH FROM ISCHAEMIC HEART DISEASE IN NOTTINGHAM 1973-1992
KW Clarke, D Gray, JR Hampton
Cardiovascular Medicine, University Hospital, Nottingham.

Ischaemic heart disease is the leading cause of death in England and Wales. The Health of the Nation proposes a strategy for health based on selected "key areas" one of which is coronary artery disease. The aim is to reduce the death rate for under 65s by 40% (to 35/100,000) and for those aged 65-74 by at least 30% (to 629/100,000).

To determine the efforts which may be required to achieve this in our District a decline in coronary artery disease and the trends in deaths over a 20 year period. Official mortality statistics obtained as part of the normal data collection of the Nottingham Heart Attack Register were reviewed.

In Nottingham, age-standardised mortality from ischaemic heart disease declined steadily in men from 5.17/1000 in 1973 to 4.10/1000 in 1992. In the same period, mortality declined similarly in the Trent region from 5.44/1000 to 4.24/1000 and in England and Wales from 5.39/1000 to 3.97/1000. Mortality rates in Nottingham tracked those in the Trent region and in England and Wales closely.

In Nottingham, age-standardised mortality in women changed very little in the same period: 2.82/1000 in 1973 to 2.63/1000 in 1992. Mortality in women outside Nottingham showed no evidence of a decline.

If the present rate of decline continues, mortality from ischaemic heart disease in men will be similar to that in women by the year 2015. By the year 2000, the predicted mortality from ischaemic heart disease for the under 65s in Nottingham is 60/100,000 and for those aged 65-74 850/100,000. If the trend derived from those data continues, further investment must be made in cardiological services in Nottingham to achieve the Health of the Nation targets.

Routine assessment of left ventricular function following myocardial infarction has a positive impact on patient management
J Byrne, MJ Metcalfe, S Reid, E Rooney, J Christie and HJ Dargie
Department of Cardiology, Western Infirmary, Glasgow.

It is now established that the use of ACE-inhibitors (ACE-I) following myocardial infarction (MI) is of major benefit to those patients who manifest signs of heart failure, while in comparison the benefits in an unselected population are relatively small. There are concerns however that a policy of assigning patients to an ACE-I on clinical grounds alone may miss a considerable proportion of patients with significant left ventricular (LV) dysfunction (LVD) who would also benefit. In order to investigate this matter we routinely measured LV Ejection Fraction (LVEF) between 3 and 7 days following MI using radionuclide ventriculography (RNVG).

Out of a consecutive series of 183 patients admitted to our CCU within a 6 month period, 129 survived and consented to (RNVG). 63% of this cohort had received thrombolytic therapy (TT). The stratification of LVEF was as follows (Normal Range >40%);

<table>
<thead>
<tr>
<th>LVEF%</th>
<th>Total(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20%</td>
<td>29 (23)</td>
</tr>
<tr>
<td>20-39</td>
<td>77 (60)</td>
</tr>
<tr>
<td>40-49</td>
<td>40 (31)</td>
</tr>
<tr>
<td>&gt;50</td>
<td>22 (17)</td>
</tr>
</tbody>
</table>

Significant systolic LVD was prospectively defined as an LVEF less than 25% of normal (ie LVEF <30%) and this was the suggested threshold for the use of ACE-I. By these conservative criteria, 62 patients (48%) were eligible for treatment. In approximately 20 (32%) of these there was no clinical evidence of heart failure during hospitalisation. 68 out of 129 (53%) surviving patients actually commenced treatment for heart failure, and 70 (54%) of the 129 ACE-I prior to discharge from hospital during this 6 month period. This compares with a figure of only 19% in the preceding year.

CONCLUSION: Appropriate measurement of LVEF using RNVG facilitates the identification of patients most likely to benefit from an ACE-I following MI, including a significant number of patients with clinically "silent" LVD who would otherwise be missed. The introduction of this policy on our Unit has been associated with a dramatic increase in the use of ACE-I post-MI.
MORTALITY FROM ISCHAEMIC HEART DISEASE OUTSIDE HOSPITAL: MORE BAD NEWS FROM THE UK HEART ATTACK STUDY (UKHAS)

R M Norris, Royal Sussex County Hospital, Brighton. On behalf of the UKHAS group.

We previously showed that in Brighton during 1993, more than 3% of all 263 deaths from acute coronary syndromes (sudden death and fatal myocardial infarction) occurred outside hospital, making the emergency intervention difficult or impossible. Extension of our Study to Health Districts South Glamorgan (population 407,100) and York (population 276,000) has enabled geographical comparisons. Standardised methods are used to identify out of hospital deaths from transcripts of death certificates and to verify and check details with coroners pathologists and general practitioners. Hospital cases of myocardial infarction (MI) are identified from multiple sources. Results for the first half of 1994:

**Number of events** Brighton S Glamorgan York

<table>
<thead>
<tr>
<th>Age</th>
<th>Age</th>
<th>Case Fatality</th>
<th>Case Fatality</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65</td>
<td>116</td>
<td>183</td>
<td>134</td>
</tr>
<tr>
<td>65 - 74</td>
<td>130</td>
<td>190</td>
<td>156</td>
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</table>

**Fetal events outside hospital**

<table>
<thead>
<tr>
<th>Age</th>
<th>Age</th>
<th>Fetal</th>
<th>Fetal</th>
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<tr>
<td>&lt;65</td>
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<td>65 - 74</td>
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<td>56</td>
<td>62</td>
</tr>
</tbody>
</table>

* = Fetal and non fatal MI + sudden death.

What can be done to reduce out of hospital mortality? Evidence will be presented that (i) patients with known ischaemic heart disease (IHD) are undertreated and insufficiently counselled to stop smoking; and (ii) a majority of sudden death victims do have premonitory symptoms making ambulance or hospital treatment feasible. Although reduction in IHD mortality depends largely on primary prevention, better medical management and public education on heart attack also have an important role.

PRESENTATION AND MANAGEMENT OF ACUTE MYOCARDIAL INFARCTION (AMI) IN IRISH HOSPITALS: A NATIONAL CENSUS

H M McGee, C Browne, J H Horgan and the Council on Acute Coronary Osculation of the Irish Heart Foundation Department of Cardiology, Beaumont Hospital, Dublin, Ireland

Early presentation for AMI is associated with reduced morbidity and mortality. Irish data from ISISS-2 indicate longer delays to treatment for AMI than in other countries. This study examines factors associated with presentation of AMI in Irish hospitals. Details on 25 consecutive admissions for suspected AMI to 30 (of 40) Irish intensive care coronary care units (ICCU) dealing with AMI were recorded. The two excluded centres had referral rates of <23 patients annually. Of 950 cases, 67% were male; mean age was 65 years (SD 12); 24% had experienced a previous MI with a further 15% having unstable angina, 36% were current smokers. A majority (68%) were admitted via general practitioner (GP) referral. 7% of patients drove themselves to hospital; median distance from hospital was 9 miles. Over one-third (38%) of patients received thrombolysis. Of those who did not, the main reasons given were ECG unclear (52%) and ‘arriving too late’ (22%). Thrombolysis was administered to 2% of patients in Accident and Emergency Departments. Overall time to treatment was 4 hours 55 minutes (median); patient delay (onset of symptoms to hospital arrival) was 3 hours 30 minutes; hospital delay (arrival to ICCU transfer) was 55 minutes and thrombolysis delay (arrival at ICCU to administration of thrombolysis where given) was 25 minutes. Some 69% of referrals were confirmed as AMI with an 8% in-hospital mortality for confirmed AMI patients. Patients with a previous MI were admitted more rapidly to hospital than those without (3 hours 17 minutes vs 4 hours 00 minutes, ns). Those attending hospital following GP referral arrived significantly later than self-referrals (2 hours vs 2 hours 07 minutes, p<0.01). Delay times are similar to comparable components in recent studies by the Irish Heart Foundation and a British Cardiac Society Audit Committee. The study provides evidence from which to target improved management of AMI in Ireland.

REDUCTION IN TREATMENT DELAY BY PARAMEDIC ECG DIAGNOSIS OF MYOCARDIAL INFARCTION WITH DIRECT CCU ADMISSION

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Benefit from thrombolysis has been shown to be increased if delay between symptom onset and treatment after myocardial infarction (MI) is reduced. In a prospective study, paramedics were trained to record and interpret a standard 12-lead ECG when called to suspected myocardial infarction patients. During the initial training phase (Ph I), ECGs were recorded and patients were taken to the hospital Emergency Department (ED) with subsequent transfer to the Coronary Care Unit (CCU) for thrombolytic therapy, where appropriate, after assessment by casualty and admitting medical staff. Phase II (Ph II) commenced when satisfactory ECG recording and interpretation skills had been achieved by paramedics. During Ph II, patients with ECG evidence of acute MI or ischemia were admitted directly to CCU by paramedics using a radio link with CCU. All other patients were taken to the ED in the usual way. MI was subsequently confirmed in 61 of 121 (50%) of Ph I patients admitted to CCU, and in 67 of 116 (57.5%) Ph II patients admitted directly to CCU, but in none of the 35 Ph II patients who were not admitted to CCU but taken to the ED.

**Number of cases**

<table>
<thead>
<tr>
<th>Phase</th>
<th>CCU</th>
<th>MI</th>
<th>Thrombolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I</td>
<td>366</td>
<td>121</td>
<td>61</td>
</tr>
<tr>
<td>Phase II</td>
<td>151</td>
<td>116</td>
<td>67</td>
</tr>
</tbody>
</table>

Mean delay times (minutes) for patients who received thrombolytic therapy are shown below:

<table>
<thead>
<tr>
<th>Call-site</th>
<th>On site</th>
<th>Site-loop</th>
<th>Door-needle</th>
<th>Total time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I</td>
<td>10</td>
<td>30</td>
<td>17</td>
<td>97</td>
</tr>
<tr>
<td>Phase II</td>
<td>8 (NS)</td>
<td>31 (NS)</td>
<td>16 (NS)</td>
<td>38*</td>
</tr>
</tbody>
</table>

Phase I v Phase II *p<0.001

Accurate and early diagnosis of MI can be achieved with a trained paramedic service with a substantial reduction in thrombolysis delay times.

MANAGEMENT AND OUTCOME OF PAEDIATRIC INFECTIOUS ENDOCARDITIS


To assess the effect of current management on outcome, a case-note review of all patients (pts) with pediatric infectious endocarditis (PIE) over a 10 year period to 1994 was performed. 36 episodes of PIE in 31 children (18M, 13F; 8 < 2 years old) were identified. 28 pts had congenital heart defects - CHD; PIE was related to recent (<4 months) interval from event cardiac surgery (N=10), cardiac catheterization (N=3), dental procedure (N=2), or in-situ central venous line (N=2). Blood cultures (BC) were positive in 32/36 PIE episodes (Strep. viridans N=12, Staph. N=11, others N=9). Prior empirical treatment with antibiotic + AB (in 16 PIE episodes) led to a significant (p<0.01) delay in diagnosis (mean ± SD, 70±164 days) compared with 20 PIEs which did not receive Ab (12±13 days). There was no difference between the 2 subgroups for serious sequelae (defined as embolic phenomena, renal failure, cardiac compromise from a new intracardiac shunt or death; 28% vs 17%; p=NS) or requirement for cardiac surgery acutely (33% vs 33%; p=NS). Conversely, blood culture positivity was not significantly different between the sequelae/ surgery group and patients without serious complications (94% and 85% positivity respectively; p=NS). At 2-D echo (2DE), vegetation complications (abcess, fistula, acquired shunts) were seen in 10 pts with CHD, and in all 3 pts without CHD. Positive 2DE was predictive of serious sequelae (sensitivity 70%, specificity 50%) and requirement for surgery (sensitivity 57%, specificity 66%). Staphylococcal pathogens also correlated with positive 2DE findings. Surgery was required by 12 pts (4/8 < 2 years old vs 8/23 > 2 years old; p=NS) with no surgical deaths. Overall mortality from PIE was 9% (3/31 pts; 2 acute deaths, 1 late death). Poor outcome was unrelated to age, presence of complex CHD, delayed diagnosis or requirement for surgery.

(156) POSTER

(157) POSTER

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POSTER

ASSESSMENT OF CONGENTIALLY CORRECTED TRANSPPOSITION OF THE GREAT ARTERIES BY 3-DIMENSIONAL ECHOCARDIOGRAPHY.
M Vogel, S Y Ho, R H Anderson
Dep. Pediatrics, National Heart and Lung Institute London

This study was undertaken to evaluate utility of 3-dimensional (3D) echocardiography in assessing anatomy of congenitally corrected transposition. 12 patients aged 0.1-12 (mean 4) years were examined with the tomographic ultrasound probe steered by a stepper motor, which acquires perpendicular parallel images of the heart with ECG and respiration gating. 60-100 parallel slices of the heart were thus obtained, which form the 3D dataset. Associated lesions included Ebstein's anomaly of the left side tricuspid valve in 5, ventricular septal defect in 7 associated with subpulmonary obstruction in 3. Ventricular morphology was identified by the ability of 3D echo to visualize the moderator band and coarse trabeculations of the RV in contrast to the smooth septum of LV. Additional information over 2D echo was obtained on morphology of the tricuspid valve in Ebsteins anomaly, which could be imaged en face. The degree of subpulmonary obstruction and its morphological mechanism could be best judged from a view looking upwards from the LV apex towards the RV outflow. VSD morphology and location could be evaluated by turning the 3D data set of the heart around the right atrial axis enabling right and left ventricular views onto the VSD. 3D echo offers information superior to 2D echo on tricuspid valve morphology and LV outflow obstruction, which aid in planning surgical therapy.

POSTER

INTRAPULMONARY RECONSTRUCTION OF PULMONARY ARTERIES USING A HETEROLOGOUS PERICARDIAL ROLL.
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Reconstruction of obstructive or non-confluent pulmonary arteries are important step in the quest to achieve definitive repairs for patients with complex cardiac malformations associated with pulmonary atresia or stenosis. Surgical resection of the anomalous branches of the pulmonary arteries are occasionally difficult to repair through a median sternotomy, and agenesis of the intrapulmonary pulmonary arteries is well recognized as a hazard for successful definitive repair. Pulmonary arterial reconstruction using a handmade heterologous pericardial roll was achieved in 5 patients with severe hypoplasia or agenesis of the intrapulmonary pulmonary arteries, and in 9 with critical hilar pulmonary stenosis occurring subsequent to previous construction of a systemic-to-pulmonary shunt. Age at operation ranged from 1.8 to 13.7 years, and body weight from 8.2 to 24.6 kg. The pericardial roll was of 12 to 16 mm diameter, and was anastomosed to the hilar pulmonary arteries through divided interlobar fissures. At the opposite end, it was fixed anteriorly to the chest wall and connected to a prosthetic tube so as to obtain blood supply from systemic arteries. The quantity of flow through the roll measured intraoperatively was 95 ± 23 ml/kg/min. Postoperative catheterization showed that the mean pressure in the roll was 31 ± 18 mmHg. Eleven patients have subsequently undergone anatomic (10) or functional (1) biventricular repair with external conduit after a period of 8 ± 4 months. It proved an easy matter to create a confluence for the reconstructed pulmonary arteries at the time of completion of the repair without affecting the operative mortality but one patient died later after the intracardiac repair due to esophageal bleeding. We conclude that this technique can provide a feasible surgical option for patients with apparently unsuitable pulmonary arteries, as a part of staged operations leading to biventricular repair.

POSTER

3-DIMENSIONAL ECHOCARDIOGRAPHY PROVIDES NEW INFORMATION ON AV SEPTAL DEFECT ANATOMY
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Dep. Pediatrics, National Heart and Lung Institute London

We evaluated, whether 3-dimensional (3D) echocardiography can provide additional information over 2D echo on anatomy of AV septal defect (AVSD) in 32 patients aged 0.2-6 (mean 0.8) years and 3 autopsy specimens. The tomographic ultrasound probe acquires parallel images of the heart steered by a stepper motor, which moves the probe in 5 mm steps with ECG and respiration gating. 60-100 parallel slices of the heart were thus obtained, which form the 3D dataset. The AVSD could be displayed as seen through a right atriotomy simulating a surgical view, the AV valves could be displayed as if seen en face and the ventricular septal defect component of the AVSD was displayed as if viewed from either ventricle. Additional information was obtained on AV valve morphology especially on the distance between anterior (superior) and posterior (inferior) common bridging leaflet, which determines the size of the "fiolet". In 2 patients with small LV the en face view demonstrated the small component of the common AV valve commited to the LV cavity. 3D echo proved useful in delineating the mechanism of partial dynamic or complete closure of ventricular component of AVSD by AV valve leaflets and their respective chordae. We conclude that 3D echo offers diagnostic information superior to 2D echo on AVSD anatomy and can thus aid in better planning surgical therapy.

POSTER

THE OUTLET SEPTUM IN HEARTS WITH INTERRUPTED AORTIC ARCH (MALALIGNMENT VS. DEVIATION)
S Y Ho, A Redington, R H Anderson
Department of Paediatrics, National Heart & Lung Institute, London, UK

The outlet septum (infundibular septum) is commonly implicated as an anatomical obstruction to aortic flow but its relationship to adjacent structures and need for close morphological assessment when planning surgical management. The terms "malalignment" and "deviation" are often used, sometimes interchangeably, to describe the abnormal arrangement of the outlet septum. We examined 11 heart specimens with concordant atrioventricular and ventriculo-arterial connections in order to establish the morphology of the outflow tracts. All hearts had interruption of the aortic arch together with a ventricular septal defect and a detectable outlet septum. Malalignment of the outlet septum was judged by viewing the specimen along the cardiac short axis. It was deemed to be present when the outlet septum makes an angle with the muscular ventricular septum. Deviation was described when the outlet septum, viewed in the cardiac long axis, protruded into the outflow tract. Using these definitions, 4 hearts had sepal malalignment together with deviation, 6 hearts had sepal malalignment without deviation and 1 heart had only septal deviation. In 1 heart with septal malalignment, the anterior component of the outlet septum was attached to the anterolateral wall of the left ventricle or to an anomalous muscle band adherent to the wall. Although the length of the subpulmonary infundibulum (4-4.5mm), the left ventricular length of the outlet septum was considerably shorter (0.5-3mm, median 1mm). None of the hearts had overriding of the pulmonary or aortic valve. This postmortem series shows the worst end of the spectrum but also demonstrates the variability in the arrangement of the outlet septum. The features of malalignment, deviation and orientation of the outlet septum are independent variables. Precise definitions will aid in understanding the morphology of the outflow tract.
FETAL CARDIAC MASSES - PREVALENCE, FOLLOW UP AND DIFFERENTIATION

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Cardiac masses were identified in 44 of 1354 fetal scans performed in a paediatric cardiac unit over a 4 year period. Such masses fell into one of three groups. In the first group of 59 fetuses they appeared as discrete, single (36 cases) or multiple (3 cases), highly echogenic masses 1-5mm in diameter within the ventricular cavities and associated with the MV apparatus (38), a LV band (1), TV apparatus (1) or RV moderator band (1). 13 cases were followed with serial ultrasound scans through the pregnancy and into infancy. All the lesions became smaller and although 10 were detectable at 4 weeks of age none were seen after 4 months. Histology of these lesions in 4 pregnancies terminated for other reasons showed small areas of fibrosis in 2 cases. The second group comprised of 4 fetuses who had larger masses of variable echogenicity; 2 involved the RV myocardium and extended into the cavity and 2 were contained within the ventricular septum. These lesions all had the appearance of rhombomylomas, suggesting a high risk for tuberous sclerosis. The 2 pregnancies with septal masses were terminated. At autopsy large fibrotic scars alone were found with dystrophic calcification, consistent with ischaemic injury although there was no other evidence of ischaemic damage in the fetuses. In the other 2 cases tuberous sclerosis was confirmed postnatally. In the third group, a single fetus had a 3cm mediastinal mass attached to the pericardium and a diagnosis of a teratoma was confirmed on autopsy following termination. In conclusion, benign masses in the fetal heart are common and recognisable by their echogenicity and their position. Rhombomylomas appear within the myocardium and are likely to be related to tuberous sclerosis, but masses of similar appearance may be of a more benign nature, possibly related to fetal ischaemia. This finding has major importance when counselling parents on the risk of a fetus having tuberous sclerosis.

CARDIOVASCULAR DRUGS IN EARLY PREGNANCY

GYH Lipt, D Churchill, J Zantis, M Beeveros, L Shaffer, DG Beavereos
University Department of Medicine, City Hospital, Birmingham

There remains concern about the use of cardiovascular drugs in early pregnancy. To investigate the effects of early drug therapy and pregnancy outcome we reviewed antenatal records of 344 pregnancies (112 white, 85 black, 147 Asian women; mean age 29.7 years ± 6.6) referred to our Antenatal Hypertension Clinic between 1985 and 1994. 213 women were not on any therapy in the first 20 weeks of pregnancy whilst atenolol was taken by 66 women, labetolol in 6, other beta-blockers in 34, calcium antagonists in 10, dietetics in 11, and ACE inhibitors in 2 women (with 33 women taking multiple drug therapy). There were no significant differences in mean birth weights (one way ANOVA, p=NS) and intrauterine death rates when women on various drugs were compared with untreated cases (12% vs 14%, X^2=7.5, p=0.09). Mean birth weights and median placental weights are summarised as follows:

- **atenolol**
  - Birth weight (kg) 2.25±0.24
  - Placental weight (grams) 460±29.7

- **labetolol**
  - Birth weight (kg) 2.54±0.25
  - Placental weight (grams) 500±480

- **other beta blockers**
  - Birth weight (kg) 2.72±0.26
  - Placental weight (grams) 460±460

- **methyl dopa**
  - Birth weight (kg) 2.69±0.27
  - Placental weight (grams) 540±540

In each drug group there were significant differences in birth weight and placental weight compared with the untreated group (ANOVA, p<0.01). There was a trend for a similar placental weight in untreated and labetolol treatment groups (p=0.08).

Babies born to women taking atenolol were significantly lighter (one way ANOVA F=2.75, *p=0.009) and had lower mean placental weights (Kruskal-Wallis test H=17.4, d.f=5, *p=0.004) when compared to women taking other drugs or no therapy. Stepwise multiple regression analysis demonstrated that only placental weight, gestation and ethnic origin predicted birth weight (F=26.9, p<0.0001). This preliminary study suggests that atenolol may be detrimental in early pregnancy. This drug should therefore be used with caution in women who are trying to conceive or who are pregnant.
Prediction of Atrioventricular Block during Radiofrequency Ablation of the Atrioventricular Node

St. George's Hospital and St Mary's Hospital, London

Selective radiofrequency (RF) ablation of the slow pathway (SP) is an effective curative treatment of AV nodal reentrant tachycardia but the procedure carries a small risk of creating AV block. A previous report has shown that when RF energy application produces an accelerated junctional tachycardia (JT) associated with loss of ventriculo-atrial (VA) conduction, there is an increased risk for AV block. The aim of our study was to determine whether measurements made from electrophysograms could be used to predict the risk of AV block before onset of RF delivery. 38 patients (pts) underwent selective RF ablation of the SP in 46 (26.9%) of 171 JTs caused by RF VA block was observed and in 11 this was followed by AV block of various degrees. Electrophograms before each application showed the A(H)-A(Md) interval for the interval between the atrial signal in the proximal His bundle catheter and in the distal mapping catheter (A(H)-A(Md)), the interval between the atrial signal in the proximal His bundle catheter and in the proximal coronary sinus catheter (A(H)-A(CS)), A-H interval, AV ratio and presence of a potential generated by the SP of the AV node or a fractionated atrial signal in the distal mapping catheter. Mean cycle length (CL) of JT, identified by low to high right atrium activation and irregularity, was calculated if it consisted of at least 10 beats. These parameters were compared in pts with JT who developed VA block and subsequent AV block (group 1) to pts with JT and VA block but without subsequent AV block (group 2) and to pts with JT without VA block (group 3). The A(H)-A(Md) interval was significantly shorter in group 1 (17.9±7.7 ms) compared to group 2 (23.7±10.1 ms) and when it was similar in group 2 (33±7 ms) and 3 (32±10 ms). There was no correlation between either CL of JT, A(H)-A(CS) interval, AV ratio, presence of a potential or a fractionated atrial electrogram and ocurrence of AV block. The A(H)-A(Md) interval provides an electrophysiological marker for the probability of the ablation catheter to the compact AV node that can be used in addition to the radiological catheter position to assess the risk for AV block before onset of RF delivery. CL of JT caused by RF and occurrence of VA block are not related to the risk of AV block.

PATTERN SATISFACTION AND RESIDUAL SYMPTOMS FOLLOWING RADIOFREQUENCY ABLATION FOR SUPRAVENTRICULAR TACHYCARDIA

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

Symptoms of palpitations can occur following radiofrequency ablation (RFA) and may be present despite a successful procedure confirmed by electrophysiological testing. We conducted a retrospective survey by postal questionnaire in a consecutive series of patients who had undergone successful RFA. 119 patients (mean age: 37±13.8 58 male [52%]) constituted the study population in which the response rate was 93.2% (n=111). 91 patients (82%) had RFA of an accessory pathway (AP), 18 (16.2%) slow pathway RFA for atrioventricular nodal re-entrant tachycardia (AVNRT) and 2 nodal ventricular pathways (Mahaim: 1.8%). The questionnaire was completed a mean 3.7 months following the procedure. In regard to overall progress 85 (76.5%) patients felt symptomatically improved and the remainder (n=26, 23.5%) said they felt no different or possibly worse. Patients reported symptoms more frequently than men, 38.7% vs 22.5% (p=0.002). It was found that 41 (37%) patients noted frequent (daily or weekly) missed beats and 27 (24.3%) patients reported the sensation of palpitations about to occur. Patients having had slow pathway ablation were more likely to have a higher number of missed beats (p=0.004) than those having AVNRT ablation. Dissatisfied patients were more likely to have symptoms of missed beats (p<0.0005). 31.7% of those who experienced present-sentimental palpitations would have preferred a warning about residual symptoms. In conclusion, residual symptoms of palpitations and missed beats are common following radiofrequency ablation even with a good technical result. Symptoms were more likely to occur in women and in those following slow pathway ablation. Overall, patient satisfaction was high (85%). Patients with residual symptoms were more likely to be dissatisfied. Pre-procedure counselling may help to increase patient satisfaction.

CORONARY SINUS MORPHOLOGY IN PATIENTS WITH ATRIOVENTRICULAR JUNCTIONAL RETRY

TACHYCARDIAS AND OTHER SUPRAVENTRICULAR TACHYCARDIAS

J C Doug, J Sains, L Harris, E Downar
Flemish Hospital, Newcastle upon Tyne, and Toronto General Hospital, Toronto, Canada

Canulation of the coronary sinus from the femoral vein is simpler in patients with atrio-ventricular junctional reentrant tachycardia (AVJRT) than in patients with other supraventricular tachycardias (SVTs). This study examined the size and shape of the coronary sinus in 29 consecutive patients (15 with AVJRT and 14 controls with other SVTs). Direct angiography was performed in each of four patients and echocardiography for the remaining 25 patients. The mean diameter of the proximal coronary sinus was measured. The mean maximal diameters recorded in any projection were larger - os: 14.3±2.6 mm vs 10.4±1.7 mm, p=0.0001; 15 mm: 12.2±2.1 mm vs 9.5±2.2 mm, p=0.0023; 10 mm: 10.4±2.1 mm vs 8.8±2.5 mm, p=0.03. The range of maximal os measurements for the patients with AVJRT was 10.4-21.6 mm compared to 7-14 mm in the control group. 73% AVJRT patients had marked windsocking of the proximal coronary sinus. This pattern was seen in only 7% controls, 93% of whom demonstrated a tubular vessel with gradual tapering. Patients with AVJRT have markedly larger, more proximal coronary sinus dimensions than a control population with other SVTs. In addition, the coronary sinus has a pronounced windsock appearance. These findings explain the simpler canulation of the coronary sinus, and may explain why some patients develop junctional reentry tachycardia.

THE NEED FOR IMPLANTABLE CARDIOVERTER DEFIBRILLATORS AFTER RESUSCITATION FROM PRE-HOSPITAL VENTRICULAR FIBRILLATION

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Several studies have shown that ventricular fibrillation (VF) in patients surviving an out-of-hospital cardiac arrest without acute myocardial infarction (AMI) has a high recurrence rate, implying the need for a high frequency of implantable cardioverter defibrillators (ICDs). Many such patients do not receive an ICD. We studied the need for ICDs in patients discharged after resuscitation from pre-hospital VF in West Yorkshire. There has been an active ICD programme in this region since July 1989, all implants being performed at a single centre. Twenty-nine patients from the West Yorkshire Metropolitan Ambulance Service (WYMAS) operational area have received an ICD from the start of the programme until September 1994. During the same time period 121 patients were discharged after resuscitation from pre-hospital VF by WYMAS staff. Twenty-four of these 121 patients (mean age 64, range 29-81) were diagnosed not to have had an AMI by their attending physician, 7 (29%) of whom were seen by a cardiologist. Three (2 no AMI, 1 AMI) patients received an ICD. The indications for ICDs were VF in all 3 patients. Antiarrhythmic drug therapy at discharge were patients with ICDs - none=2, amiodarone n=1; patients with no MI and no ICD (n=23) - none n=17, amiodarone n=6, Class 1 agents n=1. In the first year after discharge all ICDs in patients with pre-hospital VF arrests fired appropriately. Only 1 of the 23 patients with VF but without an AMI or ICD died in the first year. None had a further out-of-hospital resuscitation. We conclude that the incidence of recurrent VF in this population of pre-hospital VF without an AMI is lower than reported, but those at risk appear to have been fairly well selected. The infrequent cardiological assessment of these patients makes it difficult to conclude that the relatively low use of ICDs is appropriate for this population.
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(172) POSTER

ISO:LATED HUMAN HEARTS AND MULTIPoINT NAPPING OF VENTRICULAR TACHYCARDIA - DESCRIPTION OF A TECHNIQUE

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Treatment of ventricular tachycardia by surgical and ablative means is an area of intense interest. To successfully deliver therapy, more complete understanding of the mechanisms and circuits involved is required. We report on the use of a perfused heart preparation, combined with endocardial and epicardial multielectrode arrays in the investigation of ventricular tachycardia. Six hearts were retrieved at the time of cardiac transplantation. They were carried in cold Ringer's Lactate solution, rewarmed and established on a Langerdorff perfusion system with Tyrode perfusate. Cardiac mapping was performed using 224 electrodes and systolic and diastolic activation maps were constructed. Four cases had previous myocardial infarction, three with previous coronary bypass grafting, and one with a history of ventricular tachycardia. One explanted heart had valvular disease, and one had a dilated cardiomyopathy. The mean age of the explanted hearts was 51.4 years, and the mean ischaemic time to re-warming and establishment of perfusion was 43 minutes. One heart was not pacaee with re-warming because of technical problems.

In all hearts from patients with ischaemic heart disease, at least one ventricular tachycardia could be induced. In the patient with an arrhythmia history, four ventricular arrhythmias were induced. These all used separate reentry circuits. Earliest systolic activation was always endocardial, but in only one arrhythmia was the entire reentry circuit, including the diastolic return pathway, accessible from the endocardium. Unipolar recordings added little to bipolar data. This model is a useful tool for the understanding of the reentry circuits involved in ventricular tachycardia, especially in the post-infarct setting. All hearts from patients with ischaemic heart disease had inducible ventricular tachycardia. Patients presenting with an arrhythmia history may have other "non-clinical" forms to be considered. These findings have considerable implication for catheter ablation techniques.

(174) COIL OCCLUSION OF SMALL ARTERIAL DUCTS

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Transcatheter occlusion of the arterial duct with the Rashkind double umbrella is widely used and has become the method of choice in many centres. The sizes of the catheter delivery system and of the device limit its use. Implantation into small ducts (< 2 mm) can be difficult. A persistent leak is present in 10% - 20% of patients after umbrella closure and implantation of a second device is then performed. We attempted coil occlusion of the arterial duct in 14 patients aged 1.5 to 14.5 years (median 4.1) years (range 2.4 - 12.1) (median 15) kg. In 11 patients - 1 of whom duct ligation had been performed - the narrowest duct diameter was < 2 mm. In 2 a leak persisted after previous umbrella implantation. In 1, the smallest patient, the duct measured 3 mm. Standard radiological coils of 4 different types were chosen according to the duct morphology: Gianturco (Cook) 0.038" coils, platinum 0.018" coils (Cook or Target), Jackson controlled release 0.038" coils (Cook) or interlocking detachable 0.018" coils (Target). Coils were placed inside the duct in long tubular ducts or straddling short ducts. All coils were implanted using SF catheters placed in a femoral artery.

In those with a duct < 2 mm, the duct was occluded at the end of the procedure in 2 patients, by the following day in a further 6 patients (including the patient with a residual duct after ligation), and by 3 months in 1. In 1 patient the duct was patient 1 day after the procedure. In 1 patient it was not possible to position a coil successfully. The coil was embolised and was retrieved. The duct was ligated at the time of surgical repair for recoarctation. In the patients with a leak following umbrella implantation, colour flow Doppler the following day showed the duct was occluded in 1 and flow was reduced in 1. In the patient with a 3 mm duct, a 5 mm diameter coil was implanted initially. This embolised to the pulmonary artery, was retrieved and replaced with an 8 mm coil. Persistent flow across this coil caused haemolysis. The coil was removed 2 days later and a Rashkind umbrella implanted with resolution of the haemolysis.

Conclusions: Occlusion of small ducts is readily accomplished using coils selected according to the duct anatomy. This has both clinical and practical benefit. It has a role in leaks following implantation of a Rashkind umbrella or after duct ligation. Standard coils, however, may not be suitable for larger ducts.

(173) VENo-ATRIAL CONNECTIONS IN HEARTS WITH ISOMERIC ATRIAL APPENDAGES

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National Heart & Lung Institute, London

When attempting to improve surgical outcomes in patients with isomeri atrial appendages, it is undoubtedly crucial to know the patterns of systemic and pulmonary venous drainages. Aiming to provide information regarding veno-atrial connections as well as to determine precise criteria for arrangement of atrial appendages, we investigated 124 autopsied specimens with isomerism of the morphologically right appendages, and 58 with left isomerism. From both external and internal appearances of the atrial chambers, it was the presence or absence of pectinate muscles at the crux of the heart which proved to be the pathoanatomic feature for distinguishing morphologically right and left appendages. Thus, in spite of some equivocal or intermediate external features of the appendages in some specimens, the posterior extension of pectinate muscles to the crux was the rule in hearts with right isomerism, while those with left isomerism exhibited a smooth-walled vestibule along the posterior atrioventricular junctions. Bilateral superior caval veins were common in both groups (51% and 66%) of each group. The inferior caval vein was either right-sided or left-sided with close to equal frequency in both groups, but the inferior caval vein was interrupted with azygous continuation only in hearts with left isomerism (75%). The pulmonary veins drained to an extra-tracheal sump in 48% of cases with right isomerism, while bilateral connections of the pulmonary veins to the sinuses were the commonest pattern in left isomerism (60%). When all pulmonary veins drained directly into the atrial chamber in hearts with right isomerism, abnormal pulmonary venous confluence was recognised in most cases (90%) with lack of patellar musculature between right and left pulmonary venous connections, while such musculature within the atrial wall was the rule in the normal heart and in hearts with left isomerism. Additionally, independent pulmonary venous drainage which does not join the confluence formed by other pulmonary veins was seen in 13 hearts with right isomerism (10%). The drainage of all the systemic veins into one atrium, with the pulmonary veins connected to the other atrium was relatively rare, being seen in 13 hearts with right isomerism (10%) and in 8 of the group of left isomerism (14%). These findings are of importance in establishing precise diagnoses and in determining surgical strategies.

(175) TOTAL UK MULTI-CENTRE EXPERIENCE WITH A NOVEL ARTERIAL OCCLUSION DEVICE

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Thirty-two patients aged 4 months - 14 years (median 4 years), mean weight of 19.5 kg, underwent attempted occlusion of aorto-pulmonary connections under general anaesthesia with a new detachable coil device (Duct Occl, Paris). The device is a detachable balloon delivery catheter. Each device has a known length and number of windings and when deployed assumes a diabolo configuration with a central diameter of less than 3 mm. Once in position a number of windings can be deployed beyond the delivery catheter, the device is withdrawn into the lesion and further windings released. Importantly the device remains fully retrievable until complete deployment. There were 28 persistent arterial duct (PDA) lesions, of which 4 had a previously implanted Rashkind umbrella device and 1 which remained patent following surgical ligation. Three patients had a modified Blalock-Taussig shunt (mBTS) which was superfluous. Lastly one case of a native aorto-pulmonary collateral (APC). A transvenous approach was employed in 27 cases. Five required transarterial placement (3 mBTS, 1 APC and 1 native PDA). Five patients were found to have a PDA too large to close with the device and the procedure was abandoned. Complete occlusion within 24 hours was accomplished in 19/23 (82%) PDA cases Four patients have trivial leaks on colour flow mapping but do not have a continuous murmur. Emboiliation to left pulmonary artery occurred in 2 cases with uncomplicated retrieval. One device was unretreived in the distal right pulmonary artery and another a small am较强 retained in the chamber of the tricuspid valve. All 3 mBTS cases had complete occlusion and the sole case of native APC had a trivial leak at 48 hours. Difficulties with the release mechanism occurred on 3 occasions but did not complicate the procedure. One patient had a transient pulse deficit and another a moderate groin haematoma. These early results compare favourably to currently available devices. The delivery system allows its use in small children.
COMPLEX PULMONARY ATRESIA: SUCCESSFUL PALLIATION BY STENTING OF AORTOPULMONARY COLLATERALS

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Since 1990, 9 selected patients (aged 4-32, median 24 years) with disabling hypoxia have had attempted stenting of stenosed major aortopulmonary collaterals (APCs). Three patients had previous surgical palliation (shunts to other collaterals) and three had pulmonary vascular disease in the contralateral lung. All underwent initial balloon dilatation of 'elastic' lesions. The stent could not be deployed in one patient because of failure to cross the stenosed collateral. A self-expanding stent (Wallstent, Schneider) was deployed in the remainder, diameter 5-8mm, length 15-48mm. The longer stents were used for long, tortuous or multiple stenoses. There were no procedural complications, with adequate stent position in all. Stent placement in a proximal stenosis in our first patient was unsuccessful because of coexistent peripheral stenoses. Excellent palliation was achieved in the remainder, mean SAO2 pre=66 post=81% (P<0.001). Mean distal pressure 11mmHg pre, 17mmHg post (P<0.01). In one patient a side branch supplying the upper lobe was almost completely occluded after stent placement. A surgical shunt to this vessel led to a further increase in SAO2. Follow up ranges from 1 to 38 months (median 10).

The first patient underwent heart-lung transplantation. All patients reported improvement in exercise tolerance and exercise SAO2 improved in the 5 oldest patients (exercise time pre=2.7 ± 1.6, post=4.9 ± 3.4 minutes, p<0.01). In the only patient not requiring anticoagulation there was late (3 months) desaturatation and at recatheterisation there was severe stenosis within the stent requiring a surgical shunt to the distal vessel. The improved SAO2 has persisted in the remainder, 4 of whom have satisfactory appearances documented at follow up catheterisation.

Self-expanding stents can provide good palliation in selected patients with complex pulmonary atresia and may be an alternative to surgery.

OUTCOME OF ISOLATED CONGENITAL COMPLETE HEART BLOCK DIAGNOSED IN UTERO

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Complete heart block is now reliably diagnosed in utero. The prognosis is better in the absence of structural heart disease. Little is known, however, about the prognostic value of the presenting fetal heart rate.

We have observed the outcome of a consecutive series of 36 fetuses with complete heart block and structurally normal hearts diagnosed in utero between 1980 - 1993. Presenting fetal heart rate, change in fetal heart rate and development of fetal hydrops were documented. The maternal anti-Ro antibody status was determined in 34/36 pregnancies and was positive in 2.

Significant and progressive hydrops developed in 12 fetuses. Pregnancy was terminated in 2 of these and a further 6 died in utero. Two fetuses were delivered prematurely because of worsening hydrops before death in the neonatal period from cardiac and renal failure - a self-despite effective pacing in 1. 2 fetuses with hydrops recovered - after a course of maternal sympathomimetic treatment. One non-hydropic fetus died suddenly in utero (mother anti-Ro negative).

Heart rate at presentation ranged between 45 - 80 beats per minute (bpm). A fall in heart rate with advancing gestation was detected in 9/25 fetuses who had more than one examination: of these 5 died in utero. The presenting heart rate was related to the outcome as follows:

<table>
<thead>
<tr>
<th>no.</th>
<th>Died</th>
<th>Pacemaker</th>
<th>Alive - no pacemaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 50 bpm</td>
<td>7</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>51 - 60 bpm</td>
<td>19</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>&gt; 60 bpm</td>
<td>10</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>

One non-paced infant died from pertussis. Of the 24 survivors, 11 patients (46%) have required pacing with follow up ranging from 1 - 13 years. One patient whose mother was anti-Ro negative developed a cardiomyopathy despite pacing and underwent heart transplantation.

Conclusions: Isolated complete heart block does not always have a good prognosis. Hydrops carries a poor prognosis. A heart rate ≤ 50 bpm at presentation, or a falling heart rate, dictate the need for careful evaluation of cardiac function to guide possible prenatal intervention and carries a guarded prognosis.

GASTROINTESTINAL PROTEIN LOSS IN LONG TERM SURVIVORS OF THE FONTAN OPERATION

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Protein losing enteropathy (PLE) is an important cause of morbidity and mortality following the Fontan operation, occurring in up to 10% of long term survivors. It presents with heart failure, ascites, peripheral oedema and hypoalbuminaemia. High pre-operative pulmonary artery pressure (PAP) and post operative conduct obstruction predispose to its development. Laboratory measurement of fecal s-1-antitrypsin (S-1AT) is a well established and reliable diagnostic test for PLE. However, the incidence and clinical significance of subclinical PLE following the Fontan operation is not known. The aim of this study was therefore to detect patients with subclinical PLE by quantifying S-1AT, and to correlate results with clinical findings. Methods: Random stool samples were taken from patients 3-14 years post Fontan operation (n=10, 7 male, age range 16-37), and from age and sex matched controls without right-sided heart lesions. S-1AT was quantified by immunonephelometry. All patients had normal serum proteins. Results: 44% of the Fontan subjects had S-1AT levels above the normal range (<0.5mg/g faeces). Concentrations were between 0.4-0.8, mean 0.55 mg/g faeces. Control values were significantly lower than those for the Fontan subjects, range 0.2-0.4, mean 0.28 mg/g faeces, p=0.001 (unpaired t-test). Elevated venous pressure and hepatomegaly were associated with elevated S-1AT. Conclusions: Increased protein loss from the gastrointestinal tract is common in this group of long term survivors of the Fontan operation without overt PLE. High S-1AT correlated with elevated venous pressure and hepatomegaly. Whether such patients are at risk of developing further complications is the subject of continuing study. Increased S-1AT may be a useful marker reflecting elevated PAP or conduit obstruction and its routine measurement may pre-empt the development of clinical PLE, coagulopathy or atrial arrhythmias.

ASSESSMENT OF STEADY-STATE MYOFILAMENT RESPONSE TO CALCIUM IN INTACT CARDIAC MYOCYTES

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Inotropic agents modulate cardiac contraction either by altering cytosolic Ca++ and/or the myofilament response to Ca++. The latter is conventionally studied in skinned fibres, but this technique is unsuitable for agents that act via membrane receptors or second messenger pathways. We studied the steady-state relationship between intracellular Ca++ (indo-1/ura-2 fluorescence-R) and cell length (video edge detection) in intact rat ventricular myocytes. Following inhibition of the sarcoplasmic reticulum (SR)-ATPase by thapsigargin (0.2μM, 10 mins), reproducible tetani (10Hz) could be obtained. A novel endothelium factor, MDF, reduced tetanic shortening (S) (-28.2±4.7%; n=9, p=0.01), increased resting cell length (Ld) (+3±0.4%; p=0.02), R remaining unchanged (eg peak R -0.1±2.0%, p=ns), suggesting reduction in myofilament responses to Ca++ (fig). Similarly, 8-bromo-cGMP (50μM) which activates cGMP-dependent protein kinase reduced S (-19.5±4.8%; n=5, p<0.05), and increased Ld (0.6±0.1%, p<0.05) while intracellular R was unchanged (peak R +4.±0.2%, p=ns). By contrast, the direct acting Ca++ sensitiser, EMD57033 (1μM) and the cardioactive peptide, endothelin, which acts via sarcolemmal receptors, caused a reduction in Ld and increase in S, with little change in R, suggesting an increase in myofilament response to Ca++. Thus, tetanisation of SR-disabled, intact myocytes allows assessment of steady-state myofilament Ca++ responses mediated both by cell surface receptors and subcellular signalling pathways.
**ANGIOPLASTY INDUCES DOWNSTREAM ENDOTHELIAL INJURY**

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Endothelium is denuded at the site of balloon dilatation. We studied the effect of angioplasty upon endothelium at uninstrumented sites distal to the injury. After pre-injection of 111In labelled plts, pigs underwent unilateral carotid artery angioplasty from the femoral artery using a standard inflation protocol (5 x 30 sec inflations, 6 atmospheres). At sacrifice (90 mins later) the arteries were serially sectioned. Gamma counting assessed platelet (plt) deposition. Endothelial integrity was assessed by NADPH diaphorase staining (which co-localises with nitric oxide synthase (NOS) and scanning electron microscopy. In the contralateral uninjured artery, endothelial staining for NOS was confluent and plt deposition minimal (<8 x 10⁶plts/cm², mean). At inflation sites, de-endothelialisation was complete and plt deposition maximal (>8 x 10⁶plts/cm²). Sections 1 cm distal to balloon inflation showed extensive de-endothelialisation and increased plt deposition relative to the normal vessel (16 x 10⁶plts/cm², p<0.05). Sections 2-3 cm distal to the inflation site showed confluent endothelium and some plt deposition (<8 x 10⁶plts/cm²). Sections 4 cm distal showed extensive de-endothelialisation and marked plt deposition (27 x 10⁶plts/cm²). Balloon inflation thus caused endothelial denudation and loss of NOS activity in uninstrumented artery 4 cm distal to the site of balloon inflation. The data suggest that balloon inflation has a previously unrecognised deleterious effect on downstream endothelium. This effect may be caused by collateral flow and downstream shear stress.

**DIFFERENTIAL DISTRIBUTION OF ANGIOTENSIN II (AT₁ AND AT₂) RECEPTORS IN FAILING HUMAN HEART**

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Local production of angiotensin II (ANG II) has been implicated in cardiac hypertrophy and myocardial fibrosis, the actions of ANG II being mediated by two distinct receptors, designated AT₁ and AT₂. Quantitative autoradiography and Picrosiris red staining were used to determine the distribution of AT₁ and AT₂ receptors and demonstrate collagen deposition respectively. Transmural samples of atria and ventricle were obtained at cardiac transplantation from patients with ischaemic heart disease (IHD, n=9), dilated cardiomyopathy (DCM, n=7), cystic fibrosis (n=2), valvular disease (n=3) or pulmonary hypertension (n=1). Binding sites were identified in unfixed tissue sections by radioligand binding with [3H]-[Sar₁, Ile₈]ANG II (250 PM, 90 min, 20°C). AT₁ and AT₂ sites were distinguished by their sensitivity to dihydrothreitol (10⁻⁴ M DTT) and non-peptide AT₁ (10⁻⁴ M losartan) and AT₂ antagonists (10⁻³ M PD123319). Specific [3H]-[Sar₁, Ile₈]ANG II binding was localized to the interstitium, endocardium, myocardium, nerves and coronary arteries. Binding to AT₁ sites was inhibited by both losartan and DTT and was localized to nerves, myocardium and vascular smooth muscle. A relatively high density of AT₁ binding sites was associated with regions of collagen deposition and fibrosis, in the ventricular interstitium, endocardium and perivascular adventitia, of patients with IHD and DCM. Specific binding (anmol mm⁻², mean±SEM, n=6 IHD/DCM) was inhibited by PD123319 (P<0.01) and enhanced in the presence of DTT:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Total Activity (fmol/mg tissue)</th>
<th>AT₁ Activity (fmol/mg tissue)</th>
<th>AT₂ Activity (fmol/mg tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>45.5±12.6</td>
<td>1.2±0.4</td>
<td>37.3±13.1</td>
</tr>
<tr>
<td>PD123319</td>
<td>77.5±20.2</td>
<td>37.4±13.1</td>
<td>40.1±10.2</td>
</tr>
</tbody>
</table>

The differential distribution of AT₁ and AT₂ binding sites suggests that, in contrast to the infarcted rat heart, the AT₂ receptor subtype is selectively associated with collagen deposition and fibrosis in human cardiac tissues.

**SAFETY AND ACCURACY OF MAGNETIC RESONANCE IMAGING IN ACUTE THORACIC AORTIC DISSECTION: A PROSPECTIVE STUDY OF 50 PATIENTS**


Magnetic resonance imaging (MRI) is an accurate, non-invasive method of defining thoracic aortic dissection. This is a prospective study designed to examine the safety of an emergency on call service for MRI in 50 patients (mean age 67yrs, range 36-79, 33 males) with a clinical diagnosis of acute thoracic aortic dissection. There are concerns regarding clinical monitoring and consequent delays in the initiation of cardiopulmonary resuscitation (CPR). Therefore before offering this service, trial runs were performed until the delay in moving the patient into the resuscitation area was less than 40 seconds. T1 weighted axial and left anterior oblique scans were performed. 7 patients also had additional cine imaging.

**RESULTS:** Diagnosis of acute dissection was made by MRI in 26 out of 50 patients (14 Type A and 12 Type B dissections). 1 patient with Type A dissection involving the root with periadventitial effusion had his scan terminated with 20 seconds to go because of a deterioration in his condition. He suffered cardiac arrest in the resuscitation area and despite immediate resuscitation, died. In the remaining 24 patients, 6 had aortic aneurysms of which 2 had leaked, 1 had a right sided aortic arch, 1 had a dilated aortic root and 15 were normal. The remaining patient had a circumferential tear in the aortic root which was misdiagnosed as aortic root thickening. The patient died 24 hours after MRI and the diagnosis of dissection was made at post-mortem. Maximum time in the scanner was 13 minutes.

**CONCLUSION:** MRI is a rapid and safe method for diagnosis of acute dissection. A nurse and doctor are able to closely monitor patients during scanning and moving the patient from the scanner to a resuscitation area is rapid and does not delay the institution of CPR. Out of 50 scans performed in 26 dissections only one death occurred in the scanner building and resuscitation was not delayed. MRI is accurate and may be used safely in the diagnosis of acute dissection.
TRANSTHORACIC DETECTION OF REGIONAL MYOCARDIAL PERFUSION ABNORMALITIES USING A PERVENOUS CONTRAST AGENT: A COMPARATIVE STUDY OF DOPPLER ENERGY AND GREY SCALE IMAGING

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Prior successful studies on pervenous myocardial echo contrast agents have either used epicardial imaging or have demonstrated perfusion using only non-physiologic doses. To determine 1) whether transthoracic imaging (TTE) of myocardial perfusion is consistently possible and 2) the potential role of a new technique, Doppler Energy Mapping (DE) in data acquisition, a series of closed-chest pigs were studied during a) normal perfusion, b) following diprydamole induced coronary dilatation and c) during and post temporary anterior descending or circumflex artery occlusion. A galactose air bubble transport (SHU 805A) was injected in constant physiologic doses into the venous circulation. TTE data was obtained in the following 4 modes using sequential spaced injections - Grey scale 2-D and M-mode; and DE 2D and M-mode. Off-line comparative videodensiometric signal intensity analysis was performed with results expressed in arbitrary SI units (0-255). Findings - TTE 2-D grey scale imaging consistently detected myotral echographic enhancement in normally perfused myocardium (Mean intensity = 20 SI units (range 15-40). DE data was, however, more sensitive in detecting the presence of contrast than grey scale imaging. Mean intensity = 31 SI units vs 20). DE TTE consistently detected absent perfusion and immediate re-perfusion (immediate mean SI = 19 SI units (range 4-38). In addition, DE TTE consistently demonstrated the normal non-heterogenous pattern of trans-mural flow and was more sensitive in detecting flow changes induced by diprydamole.

Conclusions - DE data acquisition combined with an effective myocardial echo contrast agent is superior to standard grey scale imaging in evaluating perfusion. This combination can potentially identify regional and intramural changes in myocardial perfusion in the clinical setting.

THE ACE I/D POLYMORPHISM IDENTIFIES CORONARY ARTERY DISEASE

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We analysed an insertion/deletion (I/D) polymorphism of the angiotensin I converting enzyme (ACE) gene in 1226 subjects from the Caerphilly Prospective Heart Disease Study. Amplification of genomic DNA using the polymerase chain reaction, yielded the genotypes II, ID and DD. Distribution of the polymorphism was analysed amongst the whole group and within subgroups (specified following multiple risk factor analysis) for coronary artery disease (CAD) and against multiple risk factors. Allele frequencies were I=0.413, D=0.587. No association was observed between the polymorphism and CAD amongst the whole group. Amongst subjects defined at lower risk of CAD by total cholesterol/HDL-cholesterol (TC/HDL) ratios, we found significant associations of the DD genotype with CAD, p<0.0053, n=856, for TC/HDL <5.654 (median) and p<0.009, n=385, for TC/HDL <5.0 (clinical threshold). On further excluding subjects >14900 or on hypotensive medications, the DD genotype still associated with CAD, p<0.07, n=210, TC/HDL <5.654 and p<0.016, n=135, TC/HDL <5.0. Further stratification of risk incorporating other risk factors, except BMI, did not alter or enhance this association. The DD genotype is a linkage marker for an as yet unknown locus, at or near the ACE gene, which confers risk of CAD detectable in subjects previously undefinable using "classical" risk factors. However, this risk may be quantitatively small amongst the general male population.
SERUM ACTIVITY AND GENE POLYMORPHISM OF ANGIOTENSIN-CONVERTING ENZYME IN RELATION TO RESTENOSIS FOLLOWING CORONARY ANGIOPLASTY.

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Angiotensin-converting enzyme (ACE) has recently been implicated in the pathogenesis of cardiovascular disease. To investigate the possible association with coronary heart disease (CHD) and restenosis (RS) following percutaneous transluminal coronary angioplasty (PTCA) we measured serum ACE activity and insertion/deletion (ID) ACE genotypes in 141 PTCA patients (103 men), 41 of whom showed RS on clinical and angiographic grounds over a mean 15 months follow-up period. 126 age-matched subjects (63 men) with normal coronary angiograms served as controls. ID/ACE genotypes were determined by PCR. PTCA patients had significantly higher serum ACE activity when compared to controls (mean (SEM): 49.4 (2.86) vs 40.2 (1.59) IUL, respectively, p=0.005).

However, ID/ACE genotype frequencies showed no significant difference (PTCA-I 0.24, ID 0.51, DD 0.25, vs Controls- I 0.20, ID 0.54, DD 0.26, p=0.8). PTCA patients with RS did not differ from nonRS with respect to serum ACE activity (49.0 (4.15) vs 49.6 (3.67) IUL, p=0.9) or ID/ACE genotype (II-0.24, ID 0.49, DD 0.27, vs nonRS- II 0.24, ID 0.52, DD 0.24, p=0.9).

These data suggest an association between serum ACE activity and risk of CHD which is independent of ID/ACE genotype. Serum ACE activity and ID/ACE genotype do not predict RS following PTCA.

THE ANGIOTENSIN CONVERTING ENZYME GENE INSERTION / DELETION POLYMORPHISM AND THE RISK OF RESTENOSIS AFTER CORONARY ANGIOPLASTY

Departments of Cardiology and Medicine, University of Leicester, Leicester; Regional Cardiac Unit, Papworth Hospital, Cambridge; and the Cardiothoracic Centre, Liverpool.

Clinical prediction of risk of restenosis after percutaneous transluminal coronary angioplasty (PTCA) remains poor. Much experimental evidence points to an involvement of the renin-angiotensin system in intimal hyperplasia. Recently, an insertion/deletion (D) polymorphism in the angiotensin converting enzyme (ACE) gene, which influences plasma and tissue ACE levels, has been associated with the risk of myocardial infarction. To investigate whether this polymorphism also influences the risk of restenosis after PTCA, 233 subjects who underwent single vessel angioplasty in the SHARP study (Subcutaneous Heparin and Angioplasty Restenosis Prevention) were genotyped for the ID polymorphism and pre–PTCA, post–PTCA and 4 month clinical and quantitative angiographic data were compared in the three genotype groups. The groups (n= 53, 117 and 63 for II, ID and DD genotypes respectively), were well matched for baseline clinical and both pre and post–PTCA angiographic features. At 4 month follow–up there was no significant difference between the genotype groups with respect to either any of the angiographic features of restenosis (minimal luminal diameter at the site of the angioplasty, the number of subjects with > 50% loss of the acute diameter gain following the PTCA, or the number of subjects with > 50% diameter stenosis), or the number of patients with clinical angina or a positive exercise stress test. There was no interaction between heparin treatment and ACE genotype with respect to any of the parameters. We conclude that, in patients undergoing elective coronary angioplasty, the ID polymorphism in the ACE gene does not significantly influence the risk of restenosis and will not serve as a useful predictor of such risk.
As well as converting angiotensin I to angiotensin II, angiotensin-converting enzyme (ACE) catalyses the breakdown of bradykinin (BK). BK activates B2 receptors on endothelial cells to cause the release of nitric oxide (NO), prostaglandins and other factors, and may be involved in the mechanism of action of ACE inhibitors (ACEI). We have previously shown that exogenous BK (20 nM) modulates left ventricular (LV) relaxation via an NO-dependent mechanism. In this study we examined the effects of the ACEI, captopril (CAP, 1 μM) and lisinopril (LIS, 1 μM), both alone and with a sub-threshold concentration of exogenous BK (0.1 nM), on LV function in isolated ejecting guinea-pig hearts (constant loading & heart rate; Kreb’s buffer; 37°C; 1 μM indomethacin). LV pressure (P) and dP/dt were measured using a 2F Millar catheter inserted into the LV cavity. LV relaxation was assessed by an exponential time constant (TE), (Am. J. Physiol. 1984, 266: H1698). BK (0.1 nM) had no significant effect on LV function. CAP caused an enhancement of LV relaxation (TE decreased by 15.0 ± 2.1%, n=6, p<0.01; 16min), but had no effect on peak LV dP/dt. By contrast, LIS had no effect on LV relaxation (TE, 2.5 ± 4.2%, n=5, p=NS; 16min). Reduction in TE by CAP was blocked by haemoglobin (Hb, 1 μM), which inactivates NO (TE, 1.7 ± 1.2%, n=5, p=0.01, c.f. CAP alone; 16min). In the presence of BK (0.1 nM), the CAP induced fall in TE was enhanced (21 ± 1.5%, n=6, p<0.01, c.f. CAP alone; 16min). The presence of LIS and BK together did not alter LV performance.

These data show that the LV relaxant effect of CAP, either alone or in the presence of exogenous BK, is not mimicked by LIS, suggesting the involvement of the sulphhydril group of CAP in this response consistent with its previously reported anti-oxidant (ie, NO-protective) effect. Inhibition of this effect of CAP by haemoglobin implicates an NO-dependent mechanism.
**ABNORMAL ANTI-OXIDANT STATUS IN HYPERTENSION: THE BENEFICIAL EFFECTS OF LISISOPRIL TREATMENT**

HWP Whyl, ABNORMAL ANTI-OXIDANT STATUS

PREEDY2.

The relationship between hypertension and antioxidant status is poorly understood, however, as are the subsequent effects of antihypertensive therapy. These issues were addressed in 15 week old spontaneously hypertensive rats (SHR) and 15 week old normotensive Wistar Kyoto rats (WKY). Rats were treated with lisinopril in water (5 mg/kg body wt/day) for 8 weeks. Control rats were given plain tap water. At the end of the study period plasma was collected and assayed for levels of the antioxidant alpha-tocopherol by reverse phase HPLC. Blood pressure (BP) in SHR was significantly lowered by lisinopril whilst BP in WKY was unaltered. Plasma alpha-tocopherol levels were markedly reduced in untreated SHR compared with normotensive WKY (1.3 ± 0.2 mg/ml vs 2.9 ± 0.3 mg/ml, p<0.001). Treatment with Lisinopril, however, ameliorated this adverse finding (SHR + Lisinopril 2.2 ± 0.3 mg/ml; p = NS vs WKY control; p = 0.01 vs untreated SHR). Lisinopril had no effect on the plasma alpha-tocopherol level of WKY (WKY + Lisinopril 2.4 ± 0.4 mg/ml; p = NS vs WKY control). In conclusion, hypertension in the spontaneously hypertensive rat is accompanied by highly significant reductions in the plasma anti-oxidant, alpha-tocopherol. Treatment with Lisinopril restores the levels of alpha-tocopherol to normal. This may have profound implications for a reduction in the cardiovascular complications of hypertension.

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**THE NEED FOR PERMANENT PACING IN PATIENTS WITH TRICUSPID VALVE REPLACEMENTS**

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There is no ideal solution to permanent pacing if a patient has a mechanical tricuspid valve replacement (TVR). An epicardial permanent pacemaker (PPM) is frequently used but its insertion is a major operation in a patient who are often prone to previous heart surgery. Furthermore, pacing problems and physical complications are often worse than with endocardial systems. To determine if patients may benefit from placement of an endocardial lead at the time of initial TVR we identified the proportion of patients undergoing TVR who required a PPM. Forty five patients (11 male, 34 female) who underwent TVR (34 Starr Edwards valves (SEV) and 11 Bioprosthetic valves (BPV)) at the Middlesex hospital between 1978-1993 were followed up for a total follow up time after initial valve replacement of 104.2 patient years (mean ± 27.8 months range 0-180). Ten patients (22.2%) required permanent pacing in a mean 10.1±4.0 (μ±SE) months following TVR. One PPM was therefore inserted for every 10.4 years of patient follow up.

Five epicardial and 5 endocardial systems were inserted. Of the endocardial systems 1 was inserted at the time of TVR through the tricuspid annulus, 2 later through SEVs and 2 later through BPVs. Epicardial leads had higher initial thresholds (1.64±0.42V) than endocardial leads (0.66±0.12V) (P<0.05) paired t-test), and epicardial systems had more pacing problems subsequently; 2 required further surgery for their correction. Significant tricuspid regurgitation occurred in the 2 patients with endocardial leads across their SEVs.

The need for pacing was independent of the age at the time of initial TVR (PPM 62±1.8 yrs, No PPM 59±1.8 yrs), type of associated valve surgery (MVR vs TVR replacement; PPM 9/10 (90%) vs No PPM 3/10 (30%) (88%) Acute valve replacement; PPM 1/10 (10%) No PPM 5/35 (14%) the mean number of open heart operations (PPM 1.7±0.2, No PPM 1.2±0.1) and type of tricuspid valve replacement (SEV; PPM 8/10 (80%), No PPM 26/35 (74%), BPV, PPM 2/10 (20%), No PPM 9/35 (26%) a high proportion of patients with tricuspid valve replacements will go on to require permanent pacing. As endocardial pacing is preferable to epicardial, particular care should be taken to try and identify patients who may need a PPM prior to TVR so that an endocardial system may be inserted at the time of operation.

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**EARLY & LATE ANTHRACYCLINE CARDIOTOXICITY: THE PROBLEM WITH 'SUCCESS'**

FA Bu'Lock, MG Mott, A Oakhill, RP Martin

Bristol Royal Hospital for Sick Children

Anthracycline cardiomyopathy may present soon after treatment or many years later. Improvements in long-term survival rates might have significant cardiopathological implications. Clinical & echocardiographic data from 125 children with malignant disease and subsequent anthracycline treatment were reviewed. The finding of anthracycline therapy were therefore compared with similar data from 226 patients surviving >6 months from treatment. Total cumulative anthracycline doses received were between 45 & 1150 (median 270mg/m²) in the on-treatment group & 50-750(300)mg/m² in the follow-up patients (p = 0.8). Four patients studied during treatment & 11 long-term survivors received cardiac irradiation. Median (range) time from first treatment was 5.3 (0.5-17) years for the follow-up studies. Six patients (5%) developed symptomatic cardiac failure during or soon after treatment from which 3 died, the other 3 dying from recurrent malignancy. Eleven (5%) of the long-term survivors also had symptomatic left ventricular (LV) dysfunction. LV shortening fraction (SF) was inversely related to cumulative anthracycline dose in both groups, with a reduction in SF = of 1% per 100mg/m² of anthracycline (R = -0.29 and -0.47). Twenty-four patients (19%) had abnormal SF (-30%) by the end of treatment, as did 51 (22%) of the long-term survivors. However, 11 of the 24 (46%) patients with end-of-treatment SF <30% died within 6 months of last anthracycline treatment, mostly from recurrent malignancy. Thus the follow-up group probably consists of patients finishing treatment with both lesser degrees of anthracycline cardiomyopathy. Even so, SF was lower overall in the follow-up group, at 31.5 (28-35)% compared to 34 (31-38)% at end of treatment (p = 0.02). Differences between the groups increased with prior anthracyline dose and also with time from treatment. LV wall thickness was not reduced during treatment. However, in the follow-up group, wall thickness was marked (p <0.01), and the degree of thinning increased with both dose and time from treatment. Anthracyline induced changes in LV function evolve with time from treatment. Long-term survivors are currently being highly selected, both for relative resistance to anthracycline cardiotoxicity and by the nature of their malignant disease. The LV wall thinning seen late after treatment suggests that anthracycline-treated myocardium cannot grow normally. Improvements in tumour-free survival will result in the nature of late cardiac sequelae unless additional measures to protect the myocardium during treatment can be employed.

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**INCREASING EVIDENCE FOR THE FAMILIAL NATURE OF DILATED CARDIOMYOPATHY**

AS Coonar, PJ Keeling, HJ Goldman, MK Baig, K Prasad, PM Elliott, SE Bent, ALF Caforio, WJ McKenna

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

Background - Recent population studies suggest a familial contribution to dilated cardiomyopathy (DCM); estimates varying from 6-20% of total disease.

Method - To assess the prevalence and mode of inheritance of familial DCM we evaluated 69 relatives (± 16 years old; mean age 35 +/-17 years; 180 males; 97 consecutive DCM patients (WHO criteria) Screening involved clinical examination, 12 lead ECG and 2-D echocardiography. Relatives with systemic hypertension (n=21) were excluded. Echocardiograms were performed by a dedicated echocardiographer blinded to the clinical information. 340 Relatives were classified as having DCM, left ventricular enlargement (LVE) (left ventricular diastolic diameter > 4.12 cm), other cardiac abnormality or as being normal. Relatives with abnormal investigations underwent invasive evaluation where appropriate.

Results - 32 relatives from 14 families were found to have DCM indicating a familial prevalence of at least 18.2%. Pedigree analysis was most consistent with autosomal dominant inheritance with incomplete penetrance. Of the remaining apparently healthy relatives 49 (14.4%) had LVE; and 12 (3.5%) had DCM. The frequency of LVE and DCM was higher in these relatives than in a healthy control population screened using the same methodology (LVE 24/238, 10%; DCM 13/238, 5.4%). 48% and 0.1% respectively). In total, 131 relatives from 41 families (53%) had structural cardiac abnormalities.

Conclusions - Our survey confirms that familial DCM is common. Also that the frequency of cardiac abnormalities (DCM or LVE or DCM) in relatives of patients with DCM is high. This represents further evidence of a familial contribution to this condition itself may represent only the extreme form of a larger disease spectrum. The pattern of autosomal dominant inheritance with incomplete penetrance is also confirmed.
DILATED CARDIOMYOPATHY IN CHILDREN WITH CONGENITAL MEROSIN DEFICIENT MUSCULAR DYSTROPHY

N Syprou, J Philpot, F Mustoni and PG Camici. MRC Clinical Sciences Centre and Department of Paediatrics, Royal Postgraduate Medical School, Hammersmith Hospital, London.

Congenital muscular dystrophy (CMD) is the most common autosomal recessive muscular dystrophy. Affected individuals present with muscle weakness and hypotonia at birth or within the first 6 months of life. The disease tends to be static, but clinical severity and delay in motor development may vary substantially between affected children. It has recently been shown that merosin (laminin M), an extracellular matrix protein linked to the dystrophin-associated glycoproteins, is deficient in a proportion of patients with CMD. Merosin is also expressed in cardiac muscle, peripheral nerve (Schwan cells) and placenta. To determine whether the lack of merosin in the cardiomyocytes affects cardiac function, we studied 8 patients with CMD (4 merosin-positive, age range 5 to 16 years, and 4 merosin-deficient, age range 3 to 8 years) using 2D echocardiography. All patients with merosin-positive CMD had normal cardiac function. In contrast, 2 of the 4 merosin-deficient cases had echocardiographic evidence of dilated cardiomyopathy. The first case (male age 7 years) had a dilated left ventricle and an ejection fraction of 28% (using Teichoritz formula). The second case (male aged 3 years) also had a dilated left ventricular cavity with an ejection fraction of 33%. These preliminary data would suggest that a proportion of merosin-deficient CMD cases suffer from a form of dilated cardiomyopathy. Merosin, dystrophin and 50-dystrophin associated glycoprotein (DAG) all colocalize to the sarcolemma and transverse tubules of cardiac muscle. The deficiency of dystrophin has been shown to give rise to dilated cardiomyopathy in the human, while the 50-DAG deficient hamster is a recognised animal model from dilated cardiomyopathy. Our data seem to indicate that merosin deficiency can also be a cause of dilated cardiomyopathy in children.

Abnormal blood pressure response during exercise predicts unstable hemodynamic status during daily activity in patients with hypertrophic cardiomyopathy


Hypotension on exercise occurs in a third of young patients with hypertrophic cardiomyopathy (HCM) and is often associated with symptoms of syncope or pre-syncope. Occurrence of such hypotension during normal daily activity is not documented. We studied 18 patients (mean age 29±6 yrs) with HCM (8 with abnormal blood pressure (BP) response on exercise (Group-1; age=26±6 yrs) and 10 with normal BP (Group-2; age=32±4 yrs)) using 24 hour ambulatory BP monitoring. A finapress system using finger plethysmography recorded beat to beat BP, heart rate (HR) and stroke volume (SV) during normal daily activities. 5 normal healthy controls also participated in the study. The beat to beat data were analysed in hourly aliquots and number of episodes of sudden, spontaneous drop of >30 mm Hg Systolic BP (SBP) or >20 mm Hg mean arterial pressure (MAP) were coded. The mean values of BP (systolic and mean) , heart rate and stroke volume are presented below.

N= SBP MAP HR SV
Group1 8 123±17 89±18 74±5 61±6
Group2 10 120±10 94±12 70±10 66±7
Controls 5 106±20 86±10 82±12 70±9
19 episodes of sudden drops in both SBP and MAP were noted in 3 patients in group-1 (age 16, 23 & 35 [37%]; 6 episodes in the first, 8 episodes in the second and 5 episodes in the last patient respectively. 50% of these episodes were associated with symptoms of pre-syncope and syncope. Patient-1 (with 6 episodes) had one episode of frank syncope with SBP of 45 but steady HR (56) for 2 mins during the episode. No such episodes of drop in BP were seen in the other two groups.

In conclusion young patients with abnormal BP response during exercise have unexplained hypertensive episodes during daily life unrelated to severe exertion. The exact stimulus or mediator for this fluctuation in blood pressure is unknown and needs further study.

CLINICAL IMPLICATIONS OF CARDIAC TROPONIN T AND ALPHA TROPOMYOSIN MUTATIONS IN HYPERTROPIC CARDIOMYOPATHY

H Watkins, L Thierfelder, C MacRae, H J Sok, R Anan, JG Seidman, CE Seidman and WJ McKenna. Harvard Medical School, Boston, USA, and St George's Hospital Medical School, London.

Familial hypertrophic cardiomyopathy (FHC) can be caused by mutations in three cardiac contractile protein genes. In addition to mutations in the b cardiac myosin heavy chain gene, we have recently identified FHC-causing mutations in the a tropomyosin and cardiac troponin T genes. Neither the proportion of FHC caused by mutations in these two genes nor the associated clinical phenotypes are known. Linkage analyses were therefore performed in families unlinked to the b cardiac myosin heavy chain gene; these were informative in 24 families. In addition, direct screening for mutations was performed in a series of unrelated probands. Together these analyses identified only one, previously described, a tropomyosin mutation. Five novel cardiac troponin T mutations, and one previously described, were identified. Sufficient numbers were available to assess the clinical phenotype produced by four troponin T mutations (101 affected individuals in 7 unrelated families). With each mutation the phenotype was similar and characterized by poor prognosis (life expectancy approximately 35 years) and a very high incidence of sudden death. Survival was similar to that seen with "malignant" myosin mutations, e.g. Arg403Gln. However, mean maximum left ventricular wall thickness in individuals with cardiac troponin T mutations (16.7 ± 5.5) was significantly less than in individuals with b cardiac myosin heavy chain mutations (23.7 ± 7.7, p < 0.0001).

Conclusions: a Tropomyosin mutations are a rare cause of FHC and account for approximately 3% of cases. Cardiac troponin T mutations account for approximately 15% of FHC and are characterized by relatively mild and sometimes sub-clinical hypertrophy. Despite the mild hypertrophy, cardiac troponin T mutations are associated with a particularly high incidence of sudden death. Genetic diagnosis may therefore be especially important in this group.
THURSDAY 25 MAY 1995

08.00 Conference Centre, Entrance Foyer
Registration

08.30 – 10.00 Auditorium
Plenary session
RF ablation of cardiac arrhythmias in clinical practice
Chairmen: Prof Ronnie Campbell and Prof John Camm
1. Is catheter ablation now first line treatment for "SVT"?
Speaker: Dr Anthony Nathan
2. What role does RF ablation have for atrial tachycardias, atrial flutter and atrial fibrillation?
Speaker: Dr Wyn Davies
3. Should RF ablation be considered for ventricular arrhythmias?
Speaker: Dr Stephen Furniss
4. Are the UK provisions for arrhythmia care adequate?
Speaker: Dr Edward Rowland

King’s Suite
Moderated posters
Challenging the myocardium
Chairmen: Prof Derek Yellon and Dr Roger Hall
Papers 203–214

Harewood Suite
British Association for Cardiac Rehabilitation
Introduction to BACR
Dr Hugh Bethell
Current provision of rehabilitation in the UK
Dr David Thompson
Practical models of rehabilitation (15 minutes each)
In hospital: Ms Helen Stokes
In the community: Dr Douglas Watts
At home: Dr Bob Lewin
Evidence for the effectiveness of cardiac rehabilitation
Dr Andrew McLeod

Ripley Suite
Free communications
Myocardial perfusion
Chairman: Prof Jennifer Adgey
Papers 215–220

10.00 Royal Hall
Nurses’ Day
For programme see p. 63

10.00 – 11.00 Exhibition Halls B, C & D
Coffee (B & C)
Poster viewing (B & C) – Posters 221–269
Exhibition viewing (B, C & D)

11.00 – 12.30 King’s Suite
Moderated posters
Lysis and clotting
Chairman: Prof David de Bono
Papers 270–281

Harewood Suite
Free communications
Vascular biology
Chairman: Prof David Crossman
Papers 282–287

Ripley Suite
Free communications
Echocardiography
Chairman: Dr Petros Nihoyannopoulos
Papers 288–293

Royal Hall
Nurses’ Day

12.30 – 14.00 Exhibition Halls B, C & D
Lunch (B & C)
Poster viewing (B & C) – Posters 221–269
Exhibition viewing (B, C & D)

14.00 Exhibition closes

14.00 – 16.00 Auditorium
Practical cardiology
Chairman: Dr Andrew McLeod
Co-chairman: Dr Roger Boyle
The investigation and management of mitral regurgitation
Dr Roger Hall
Recent advances in cardiopulmonary resuscitation
Dr Douglas Chamberlain
The investigation and management of 'vasovagal' syncope
Dr Richard Sutton

Ripley Suite
Free communications
Coronary stents
Chairman: Dr Chris White
Papers 294–299

Royal Hall
Nurses’ Day

16.00 Close of meeting
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<th>Time</th>
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<tr>
<td>10.00</td>
<td>Welcome</td>
<td>13.30</td>
<td>Chairman: Ms Ann Townsend and Ms Ann Townsend</td>
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<td>10.10</td>
<td>Mobile catheter laboratories</td>
<td>13.35</td>
<td>Update on prosthetic heart valves</td>
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<td></td>
<td>Chairman: Ms Julie Burgess, London and Mr Tom Quinn, York</td>
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<td>Mr Tim Hooper, consultant cardiothoracic surgeon Wythenshawe Hospital, Manchester</td>
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<td>For: Dr Phillip Thomas, Singleton Hospital, Swansea</td>
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<td>Advanced nurse practitioner and the law</td>
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<td>Against: Dr Duncan Dymond, St Bartholomew's Hospital, London</td>
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<td>Miss Ghislaine Watson-Hopkinson, London</td>
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<td></td>
<td>Discussion and vote</td>
<td>15.15</td>
<td>Tea and posters</td>
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<td>11.10</td>
<td>Coffee and posters</td>
<td>15.35</td>
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<td>Update on the treatment of heart failure and the use of ACE inhibitors</td>
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<td>Mr Ian Phipps, British Heart Foundation</td>
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<td>Chairman: Dr John McMurray, consultant cardiologist Western General Hospital, Edinburgh</td>
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<tr>
<td>12.30</td>
<td>Lunch and posters</td>
<td>16.15</td>
<td>Conclusion and comments</td>
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<td>16.30</td>
<td>Annual General Meeting of ABCN</td>
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THE VENTILATORY RESPONSES TO EXERCISE IN ADULTS AFTER RIGHT PULMONARY TETOlogy OF FALLOT.
AL Clark, M Gatzoulis, AN Redington
Department of Cardiac Medicine and Department of Paediatric Cardiology
National Heart & Lung Institute, London SW3 6LY

Adult patients with total correction of tetralogy of Fallot may have poor exercise capacity associated with impaired right heart function and in particular pulmonary regurgitation. We wished to study the ventilatory responses to exercise in a group of such patients to assess the relationship between ventilation, exercise capacity, and right ventricular function.

30 patients (7 female), aged 27.8 ±6.0 years and 30 (7 female) age matched controls were studied prospectively. All subjects underwent exercise testing with metabolic gas exchange to determine peak oxygen consumption (peak VO2), and as indices of the ventilatory response, the slope of the relationship between both respiratory rate (RR) and ventilation (V̇E) against carbon dioxide production (VCO2). Patients were studied with pulsed wave Doppler echocardiography to determine pulmonary arterial systolic and diastolic flow characteristics. Patients were defined as having restrictive right ventricular function where diastolic pulmonary forward flow was seen coincident with atrial systole.

In the Fallot group, average peak VO2 was 35.3 ± 7.5 ml/kg/min (93.6 ± 15.3% of expected for age, weight height sex). The RR/V̇E slope was steeper in the Fallot group (6.8 ± 2.6 vs. 9.6 ± 4.7; P < 0.05). Those with restrictive right ventricles achieved a higher peak VO2 than those without (82.5 ± 10.1 vs 100.9 ± 13.8; P < 0.001). There was an inverse relationship between ventilatory response and peak VO2 (RR/V̇E vs. peak VO2; r=-0.63; P=0.005. V̇E/VCO2 vs. peak VO2; r=-0.62; P=0.001).

Many patients of Fallot had near normal exercise capacity, but as exercise capacity decreased, the ventilatory response to exercise was increased. This was not due to alterations in pulmonary function tests or due to the effects of cardiac size causing decreased lung volume. It may be that the increased ventilatory rate at a given level of carbon dioxide production acts as a respiratory pump aiding right ventricular function.

Intramyocardial Steal Mechanisms Contribute To Post-Prandial Angina.
RR Baliga, SD Rosen, PG Camici, CM Oakley, JS Kooner.
Royal Postgraduate Medical School and MRC Clinical Sciences Centre, Hammersmith Hospitals NHS Trust, London.

Food ingestion commonly precipitates chest pain and ischaemic ECG changes in patients with coronary artery disease (CAD). To investigate the role of myocardial oxygen consumption 'steal' mechanisms we measured blood pressure (BP), heart rate (HR), rate-pressure product (RPP), regional myocardial blood flow (MBF, mg/ml/min), with positron emission tomography (PET and H215O), before and after a mixed meal (MM), in 9 males (age 63±7 years). All patients had a history of repeated and reproducible post-prandial angina, a positive treadmill exercise test for ischaemia and angiographic CAD. Patients were studied after an overnight fast and were off drugs (except GTN) for 48 hrs. Symptoms and 12 lead ECG were recorded before and 30 min after a liquid MM (1500 calories).

At baseline MBF was similar in the territories supplied by stenotic (STEN) and normal (NOR) arteries (1.01±0.35 and 0.89±0.16, p<0.05). Four out of 9 patients experienced angina and had ischaemic ECG changes after the MM. Total MBF at baseline (0.96±0.14) and after MM (1.14±0.25) were not statistically different. However, the coefficient of variation (SD/mean) for MBF increased from 19.29±10.36% at baseline to 34.07±8.28%, p<0.05) after the MM. Following MM, MBF decreased to 0.76±0.27 (p<0.05 vs baseline) in STEN, but increased to 1.16±0.23 in NOR (p<0.05 vs baseline and p < 0.01 vs STEN). HR rose (60±11 to 66±12 min-1, p<0.02), but there was no significant changes in BP or rate pressure product (RPP).

There was no change in RPP after the meal. Although overall MBF did not change there was a significant increase in the coefficient of variation indicating regional redistribution of MBF. MBF diminished in the territories supplied by the most stenotic coronary arteries and increased in those supplied by normal arteries suggesting that intramyocardial steal mechanisms contribute to post-prandial angina.

FLOW INHOMOGENEITY PRODUCED BY INTRAVENOUS DIPYRIDAMOLE DOCUMENTED BY CORONARY FLOW VELOCITY CHANGES.

Dipyridamole (D) is believed to cause a defect in the T1212χ scintigram by producing flow inhomogeneity due to coronary vasodilatation. We assessed the changes of coronary flow velocity measured at a segment distal to a significant stenosis (>70%) and at an adjacent normal coronary artery, produced by intravenous (IV) administration of D, in patients undergoing coronary angioplasty (PTCA) who had a documented reversible defect with D at T212CH scintigraphy in 5 days of the hemodynamic study, in 13 pts (aged 57.3 ± 11.4 years, 11 men and 2 women) with stable or unstable angina pectoris. We studied the changes of time-averaged peak flow velocity (APV) at the segment distal to a stenosis and at the proximal (prox) segment of the adjacent normal (norm) coronary artery. Measurements were performed simultaneously by two Doppler guide wires (Flow-wire, 0.014") at baseline and after 4 min of IV infusion of D at a dose of 0.56 mg/kg. Heart rate (HR) and mean aortic blood pressure (MABP) were continuously recorded.

The changes in coronary flow velocity were measured in both arteries every 2 min for a total time period of 10 min. Statistical analysis was performed using t-test and ANOVA.

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<th>APV (cm/sec)</th>
<th>D0</th>
<th>D90</th>
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<tr>
<td>distal</td>
<td>12.2</td>
<td>15.4</td>
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<td>prox</td>
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*p<0.001

The HR increased from 72±14 to 97±614 (p<0.05) while the MABP did not change significantly.

In conclusion the coronary flow velocity at the segment distal to the stenosis does not change significantly following IV infusion of D. On the contrary a more than twofold increase of flow velocity is observed at an adjacent normal coronary artery. These findings may be the first direct proof that flow inhomogeneity is the cause of a defect in T212CH scintigraphy with D infusion.

ENHANCED DETECTION OF MYOCARDIAL ISCHEMIA IN PATIENTS WITH WALL MOTION ABNORMALITY BY UTILISING THE "BIPhasic" RESPONSE OF STRESS DOBUTAMINE DURING SERIAL ECHOCARDIOGRAPHY
R Senior, A Lahiri
Northwick Park Hospital, Harrow, UK.

Stress echocardiography is known to have reduced sensitivity for the detection of myocardial ischaemia in patients with coronary artery disease with rest wall motion abnormality. We have evaluated the "biphasic" echocardiographic response of initial improved wall thickening with low dose dobutamine (5-10 mcg/kg/min) with subsequent reduction of wall thickening with peak/high dose of dobutamine (15-40 mcg/kg/min) in 54 patients with coronary artery disease and wall motion abnormality, and correlated this with simultaneous dobutamine radionuclide imaging with either Tc-99m sestamibi or Tc-99m tetrofosmin. Separate day rest perfusion imaging was performed in all. The left ventricle was divided into 3 regions and a total of 68 regions were identified as having wall motion abnormality. Fifty seven (84%) regions were shown to be ischaemic by perfusion imaging. The "biphasic" response detected 56(98%) regions as ischaemic, whereas when only the basal and the peak/high dose echocardiographic images were analysed only 31(54%) regions were found to be ischaemic (p<0.001). The concordance for detection of ischaemia between perfusion imaging and the "biphasic" echocardiographic response was 88% (kappa=0.54), but the agreement between perfusion imaging and the peak/high dose dobutamine echocardiographic images was only 31(54%) regions were found to be ischaemic (p<0.001). The concordance between perfusion imaging and the echocardiographic "biphasic" response. Utilisation of the "biphasic" echocardiographic response during dobutamine stress substantially enhances the diagnosis of ischaemia in regions with wall motion abnormality.
**IMPROVED DETECTION OF CORONARY ARTERY DISEASE IN HYPERTENSIVE PATIENTS BY DOBUTAMINE STRESS ECHOCARDIOGRAPHY**

R Senior, S Basu, C E Handler, E B Raferty, A Lahiri
Northwick Park Hospital, Harrow, UK

From a cohort of 43 hypertensive patients (BP>160/95 mmHg) who had undergone coronary angiography for the diagnosis of chest pain, the results of exercise testing (EXT) and dobutamine stress echocardiography (Echo) were compared to assess their relative roles for the detection of coronary artery disease. These selected patients had no electrocardiographic evidence of left ventricular hypertrophy or basal ST-T changes. Graded stress dobutamine (5-40mcg/kg/min) Echo was carried out until end-points were achieved. Graded treadmill EXT was performed using the Bruce protocol. A coronary artery lesion >50% was considered significant. Left ventricular mass index was calculated by Echo and 28 out of the 43 patients had increased left ventricular mass index. Coronary artery disease was present in 29, of whom, 21 had multi-vessel disease, and 14 patients had normal coronary anatomy. Sensitivity and specificity for the detection of coronary artery disease by dobutamine Echo were 93% and 100%, and for the EXT these were 72% and 29%, respectively. Similarly, for detection of multi-vessel disease the values were 82% and 95%, for dobutamine Echo and 77% and 33% for EXT, respectively. Logistic regression analysis revealed that EXT was a poor predictor of coronary artery disease (p=0.09) while dobutamine Echo was significantly better (p<0.001). When patients with increased left ventricular mass index were excluded, prediction of coronary anatomy by EXT improved only marginally (p=0.4) while dobutamine Echo remained unchanged (p>0.001). One patient developed self-terminating supra-ventricular tachycardia. Stress dobutamine Echo is safe in hypertensive patients and is probably the method of choice for evaluating underlying coronary artery disease.

**LOW DOSE DOBUTAMINE ECHOCARDIOGRAPHY PREDICTS IMPROVEMENT IN LEFT VENTRICULAR FUNCTION FOLLOWING REVASCULARISATION IN PATIENTS WITH SEVERE ISCHAEMIC HEART FAILURE**

R Senior, B Glenville, S Kaul, U Raval, S Basu, C E Handler, E B Raferty, A Lahiri. Northwick Park Hospital, Harrow

The purpose of this study was to assess the role of low dose dobutamine (0.2mcg/kg/min) echocardiography (DE) for predicting improvement in regional and global left ventricle (LV) function after revascularisation in patients with severe chronic LV dysfunction due to coronary artery disease (CAD). Accordingly, 22 patients with symptomatic chronic LV dysfunction associated with CAD (mean ± SD LV ejection fraction 0.26±0.08) were studied. Wall thickening was assessed (Grade 1 = normal, Grade 5 = dyskinetic) at baseline and at 5, 10 and 15mcg/kg/min of dobutamine. Echocardiography was repeated without dobutamine 9±1 weeks after revascularisation to assess change in wall thickening compared to baseline. Improvement in wall thickening in at least two segments (1 segment model) was considered as evidence of contractile reserve assessed by 2 observers blinded to all other clinical information. Of the 22 patients, 18 showed improved contractile reserve after revascularisation; DE predicted improvement in all 18 patients. Out of the 4 patients who did not show improvement, DE identified 2 patients on the basis of lack of contractile reserve. LV ejection fraction improved from 0.27±0.08 to 0.38±0.09 (p<0.001) in the 20 pts who showed contractile reserve with DE. DE predicted contractile reserve in 103/87% of the 118 segments that improved after revascularisation and correctly predicted lack of improvement in 41/82% of the 50 segments that did not improve after revascularisation. It is concluded that DE accurately predicts improvement in both regional and global LV function following revascularisation in patients with chronic LV dysfunction and congestive heart failure due to CAD. These findings have important therapeutic implications in the management of patients with severe ischaemic heart failure.

**PERSISTENCE OF REGIONAL LEFT VENTRICULAR DYSFUNCTION AFTER MYOCARDIAL ISCHEMIA INDUCED BY INTRAVENTRICAL DOBUTAMINE. A STRESS ECHOCARDIOGRAPHY STUDY.**

A Tsoukas, E Iliomindis, N Kouri, A Kassimatis, P Nihoyianopoulos
RPMs, Clinical Cardiology, Hammersmith Hospital, London

The purpose of this study was to evaluate the significance of persisting regional wall motion abnormalities (RWMA) of left ventricle during recovery. Fifty-eight patients with known coronary artery disease (CAD) underwent dobutamine stress echocardiography (DSE) and in 30 (24 male and 6 female, mean age 64±10 years) DSE was positive with new or worsening RWMA. Eight patients had one-vessel (1-VD), 11 had two-vessel (2-VD) and 11 had three-vessel (3-VD) disease while 16 did and 14 did not have visible collaterals during coronary angiography. Incremental intravenous dobutamine (from 5 to 40mcg/kg/min) in 3 min intervals was given. Cross sectional echocardiographic images (parasternal long and short axis, apical four and two chamber views) as well as ECG-blood pressure monitoring at rest, infusion period and recovery (30 min) were obtained. An 11-segment protocol for assessing RWMA was used. Each segment was scored as follows: Normal-1, hypokinetic-2, akinetic-3, dyskinetic-4. B-blockers or calcium channel blockers were withdrawn at least 48 hours prior to DSE. A positive ECG response (with ST depression greater than 1mm 60sec after J point) was found in 14/30 (46%) while 4/30 (13%) had resting LBBB. Chest pain was observed in 16/30 (53%) and breathlessness in 11/30 (36%) patients. The duration of ST depression and RWMA in to recovery were 8.9±6 min and 11.8±6 min respectively (p<0.01). RWMA persisted for 5.3±4.6 min after 2-VD normalisation. However in 1 patient with 3-VD and without collaterals, RWMA normalised 4 min before the ECG. RWMA during recovery persisted longer in patients with multivessel CAD: 6.4±5.5 min in 1-VD, 11.2±5.4 in 2-VD and 17.9±5.2 min in 3-VD. These were also longer in the absence of collaterals (15.5±6.5 vs 9.1±4.8 min). There was a significant difference in recovery duration of RWMA between patients with 1-VD vs 2-VD (p<0.05), 1-VD vs 3-VD (p<0.001), 2-VD vs 3-VD (p<0.001) as well as in the presence or absence of collaterals (p<0.01). Conclusions: DSE in patients with CAD is associated with persistent RWMA during recovery at a time when chest pain and ECG changes are usually resolved. Delayed resolution of RWMA might be the result of multivessel CAD while rapid resolution the result of present collaterals.

**IMPORTANCE OF QUANTITATIVE THALLIUM TOMOGRAPHY (SPECT) IN PATIENTS WITH MULTIVESSEL CORONARY ARTERY DISEASE UNDERGOING CORONARY ANGIOPLASTY.**

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Coronary angiography is the reference standard for identifying the culprit lesion in patients with multivessel disease, but does not assess the functional significance of each vessel. We examined whether thallium SPECT could identify the culprit lesion in 12 patients with multivessel disease, who were undergoing single vessel angioplasty (PTCA). 7 patients completed the study with thallium SPECT before and 2 weeks after the PTCA. SPECT identified the culprit vessel in 7 of the patients, the extent of myocardial ischaemia in the culprit vessel was 19.1±4.2% vs 10.3±1.8% in the remote vessel, p=0.04. Following single vessel PTCA, the extent of myocardial ischaemia in the culprit territory improved substantially (19.1±4.2% to 6.4±2.1%, p=0.02). Severity was equally improved, (1.8±0.6 to 0.4±0.1, p=0.03). Ischaemia in the remote territory (pre 10.3±1.8%, post 8.0±1.2%, p=NS) was unaffected. Exercise capacity improved substantially also (360±45 to 475±27 seconds, p=0.05). We believe qualitative thallium SPECT is of value in identifying the culprit lesion in patients with multivessel coronary artery disease in whom single vessel PTCA is considered.
MODERATED POSTER

THE VALUE OF COMBINED RADIONUCLIDE PERFUSION IMAGING USING TEBALMILLUM AND TECHNETIUM TETROFOsin in PATIENTS WITH CORONARY ARTERY DISEASE AND LEFT VENTRICULAR DYSFUNCTION

S Burn, S Howey, S Steel, J L Caplin. Departments of Cardiology and Nuclear Medicine, Hull Royal Infirmary.

Rest and late-restart thallium imaging is useful in assessing myocardial viability in patients with coronary artery disease (CAD) and left ventricular (LV) dysfunction. This protocol does not provide data about stress-induced ischaemia, a known prognostic factor in CAD. This study evaluated the feasibility of using a new technetium-labelled perfusion agent, tetrofosmin, as part of a same-day imaging protocol involving rest and late-restart thalliumand exercise tetrofosmin. Fourteen patients with angiographically demonstrated CAD and a prior Q-wave myocardial infarction were studied. Mean LVEF was 42% (range: 15-60%). A resting injection of 74 MBq of thallium-201 was followed at 15 min. and at 4 hours by single photon emission computed tomography (SPECT) imaging. One hour later a treadmill exercise test was performed. At peak exercise 400 MBq of technetium-99m tetrofosmin was given and then repeat SPECT imaging was performed after 1 hour.

Results: All 14 patients had resting thallium perfusion defects corresponding to the site of Q waves on the surface ECG. In 10 patients there were areas of increased uptake at 4 hours (indicating cellular viability); 6 were within the areas of surface Q waves and 4 in areas separate from Q wave zones. Six patients had stress-induced areas of ischaemia on the tetrofosmin images, separate from the resting thallium defects; these corresponded to areas supplied by known coronary stenoses. Seven patients had evidence of exercise-induced LV dilatation.

Conclusion: A combined imaging protocol utilising rest and late-restart thallium and stress-tetrofosmin SPECT is feasible and demonstrates areas of viable myocardium both within previous Q-wave infarctions and at sites distant; and 2) further areas of exercise-induced ischaemia at sites separate from the rest abnormalities. This imaging protocol will allow better selection of patients likely to benefit from revascularisation, especially to vessels that subend areas of infarction.

MODERATED POSTER

CHANGES IN MYOCARDIAL HEAT SHOCK PROTEINS IN RESPONSE TO CHRONIC ETHANOL EXPOSURE

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Chronic ethanol consumption may produce a specific heart muscle disease characterised by global left ventricular dilatation and dysfunction. The cellular mechanisms involved in the pathogenesis of the disease are unknown. Heat shock proteins (HSP) are polypeptides which are expressed in response to cellular insults and are thought to play a cardioprotective role. The hypothesis that alterations in HSP contribute to the cardiac effects of chronic ethanol consumption was tested in a rat model of alcohol toxicity. Male Wistar rats (at approx. 0.1 kg body weight) were fed a nutritionally complete liquid diet containing 35% total caloric as ethanol (N = 6). Control rats of similar age and weight were fed identical amounts of the same diet in which ethanol was replaced by isocaloric glucose (N = 6). After six weeks the rats were sacrificed and the hearts removed and frozen at -196°C for subsequent analysis by 2 dimensional electrophoresis. Proteins were separated by isoelectric focusing in the first dimension and SDS-PAGE in the second dimension. Gels were stained, scanned and protein patterns analysed using the PDQuest system.

INDUCTION OF HSP 72 BY THE TYROSINE KINASE INHIBITOR HERBIMYCIN-A PROTECTS CARDIOMYOCYTES FROM A SUBSEQUENT STRESSFUL STIMULUS

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Heat shock protein (HSP) induction by stressful stimuli such as heat and ischaemia is known to protect cardiac cells from a subsequent lethal stress. The ability to increase the level of HSPs via a pharmacological means has yet to be demonstrated in the heart, however in non-cardiac cells the tyrosine kinase inhibitor Herbimycin-A has been shown to induce HSP72. Therefore we examined whether Herbimycin-A and another tyrosine kinase inhibitor, Genistein could induce HSP72 in primary cultures of rat neonatal cardiomyocytes, and whether these treatments could have a protective effect on survival following a subsequent stressful stimulus. Primary cardiomyocytes were incubated with Herbimycin-A or Genistein. HSP induction was measured 16-20 hours later by Western blotting. Cell survival following subsequent lethal heat stress (47°C for 1 h) was assessed using trypan blue exclusion. Our preliminary results, using Western blot analysis, indicates that Herbimycin-A induces HSP72, however Genistein has no such effect on HSP72 levels. Moreover HSP induction correlated with the ability of Herbimycin-A to protect cells against a lethal heat stress, whereas Genistein had no protective effect. Cell death in Herbimycin-A treated cells was 45% (+3.5), whereas cell death in control groups was 64% (+4.2), (p<0.005, n=10). Cell death in Genistein treated cells was similar to that in controls, 59% (+5.0), with no significant protection observed and no increase in HSP expression. In conclusion, Herbimycin-A induces HSP72 in primary cardiomyocytes, and this induction has a protective effect against subsequent lethal stress. In view of the lack of effect of Genistein on both HSP72 induction and protection, the action of Herbimycin-A may well be via a tyrosine kinase independent mechanism. For the first time this raises the possibility of a pharmacological approach to HSP72 induction and cardiac protection, which may be of clinical relevance.

MODERATED POSTER

ISCHAEIC PRECONDITIONING ACCELERATES ISCHAEMIC CONTRACTURE AND ATP DEPLETION IN THE BLOOD-PERFUSED RAT HEART

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Using the crystalloid-perfused rat heart, we have previously shown that, despite protecting post-ischaemic contractile function, ischaemic pre-conditioning accelerates ischaemic contracture and depletion of adenosine triphosphate (ATP). In contrast, cardioplegia slows ischaemic contracture and ATP depletion. However, using perfused-perfused preparations, we used the blood-perfused rat heart to compare the effects of preconditioning and cardioplegia on tissue high-energy phosphate metabolism and diastolic state during ischaemia. Isolated rat hearts were aerobically perfused with blood from a support rat for 20min, and subjected to zero flow global ischaemia (37°C) for various periods up to 35min (n=5 hearts/group). The hearts were then freeze-clamped and then submitted to a metabolic analysis. Ischaemic contracture was assessed with an isoluminant intraventricular balloon. Three groups were studied: (i) controls (C) with unprotected ischaemia, (ii) hearts subjected to two cycles of preconditioning (PC: 3min ischaemia + 3min reperfusion) prior to ischaemia, and (iii) hearts infused with St John’s cardioplegic solution (CP) prior to ischaemia. Preconditioning accelerated whilst cardioplegia delayed ischaemic contracture (mean time-to-peak contracture PC=8.150 min, CP=25.190 min whereas in control hearts t=15.610 min, P<0.05). The ischaemia-induced decline in tissue ATP was delayed by cardioplegia but accelerated by preconditioning (e.g. after 9min ischaemia C=8.120.4 min, PC=4.120.6 min and CP=17.281.3 min, P<0.05). Our results were in agreement with our earlier findings in the crystalloid-perfused rat heart, preconditioning in the blood-perfused rat heart accelerates ischaemic contracture and depletion of ATP. In contrast, cardioplegia slows ischaemic contracture and ATP depletion. The possibility remains that species differences (dog vs rat) may explain the ATP results. However, our results do show that cardioplegia protects against contracture and depletion of ATP, which is concordant with findings in the dog.
ADVERSE OUTCOME RATES IN UNSTABLE ANGINA ARE HIGH MAINLY IN THE FIRST SIX WEEKS: PROGNOSTIC VALUE OF EARLY CONTINUOUS ST SEGMENT MONITORING

W. Wicks, W. D. MAINLY Royal In, known of a (Ml) remaining TMI, and in compared age > high angiographic progression of ischemia-related with angina) angiography. George's Hospital non-IRS IRS of occurrence or pts and (Group 2). Following introcoronary PLAQUE VERSUS PLATE versus IRS progression. Multiple ± unstable In Conclusion. plaque proportion risk, D typical vs. non-IRS and 9 of 284 patients. was = 17 (15.1%) patients. within it. It was highly significant predictor for death or MI (p=0.001), or any adverse cardiac event, and age ≥ 65 years was also identified as a significant predictor for CD or MI (p<0.05) Almost half of all adverse events occurring within 4 years, were observed within 6 weeks of admission (see table).

Event 48hrs-6 wks 6wks-3 mths 3-6mths 6mths-4 yrs CD or MI 11 (41%) 3 (11%) 2(7%) 11 (41%) Any event 47 (43%) 10 (10%) 11 (11%) 35 (34%) Conclusion: Early in-hospital risk stratification is important in UA since a high proportion of adverse events occur within 6 weeks of admission, before exercise testing is usually undertaken. MI recorded on admission using continuous ST segment monitoring identifies those at early high risk, with little additional value for the long term.

RAPID ANGIOGRAPHIC PROGRESSION OF INACTIVE UNSTABLE PLAQUE VERSUS STABLE PLAQUE IN PATIENTS WITH STABLE ANGINA

M R Chester, L Chen, J C Kaki St. George's Hospital Medical School, London, U.K.

The angiographic progression of ischemia-related stenoses (IRS) and non-IRS stenoses was assessed in 256 patients (pts) with stable angina (stable symptoms for at least 3 months) using computerized angiography. Pts were categorized as inactive unstable plaque (IRS which was responsible for a previous (>3 months) episode of unstable angina) in 76 pts (Group 1) and stable plaque (IRS which was not associated with a previous acute episode) in the remaining 180 pts (Group 2). Following diagnosis angiography, pts were put on a waiting list for PTCA and restudied (8 ± 3 months after first angiogram) immediately preceding PTCA (230 pts) or soon after occurrence of coronary events (MI in 9 pts, unstable angina in 17 pts). IRS were complex (irregular borders, overhanging edges or intracoronary thrombus) in 40 of 76 (53%) inactive unstable plaques and 38 of 180 (21%) stable plaques (p<0.001). Stenosis progression (>20% diameter reduction or new total occlusion) and coronary events occurred more frequently in Group 1 than in Group 2 (26% vs. 11%, p=0.01 and 17% vs. 7%, p=0.02, respectively). IRS progressed in 14 pts of Group 1 and 9 pts of Group 2 (18% vs. 5%, p=0.001). Progression of non-IRS (15 of 284 (5%)) was similar in Groups 1 and 2 (25% vs. 23% vs. 5%). Group 1 was younger than patients of Group 2 (55 ± 8 vs. 59 ± 10 years, p=0.002). Pts gender, risk factors, multivessel disease, baseline severity of IRS were not associated with IRS progression. Multiple regression analysis showed that inactive unstable plaque, angiographic complex morphology, and coronary events independently predicted IRS progression (p=0.03, p=0.02, and p=0.001, respectively). Conclusion. In pts with stable angina, inactive previously unstable plaques and stenoses with complex morphology are predictors of rapid progression. This data provides further evidence of the role of plaque disruption in coronary stenosis progression.

ISCHAEMIA-RELATED STENOSSES IN "CLINICALLY STABILISED" UNSTABLE ANGINA REMAIN AT HIGH RISK

M R Chester, L Chen, J Huang, E Leatham, D Tousoulis, J C Kaki St. George's Hospital Medical School, London, U.K.

Stenosis progression was prospectively studied in 84 unstable angina patients (pts) with ischaemic ECG changes (new onset: 19, crescendo: 29, at rest: 36), who stabilized on medical therapy. Following diagnostic angiography, pts were put on a waiting list for routine PTCA and restudied (mean ± SD: 8 ± 3 months after first angiogram) immediately preceding PTCA (59 pts) or soon after the occurrence of coronary event (MI: 4 pts, unstable angina: 21 pts). Ischaemia-related stenoses (IRS) were identified in all pts and classified as "complex" (irregular borders, overhanging edges, or intracoronary thrombus) or "smooth". Stenosis progression, assessed by computerized angiography, was defined as >20% diameter reduction or new total occlusion. At initial arteriography, there were 197 stenoses (>50%; 101, <50%; 96). Of 84 IRS, 53 were complex and 31 smooth. At restudy 21 (25%) of 84 IRS had progressed compared with 8 (7%) of 113 non-IRS (p=0.001). Seventeen (81%) of 21 IRS and 3 (38%) of 8 non-IRS that had progressed developed into total occlusion (p=0.02). 8 of 53 complex IRS had progressed, compared with 3 of 31 smooth IRS (34% vs 10%, p=0.02). Changes of percent stenosis (%) and minimal stenosis diameter (mm) in different subgroups were as following: 1st angio 2nd angio Δ (%) Δ (mm)

IR 66.7 ± 6.7 75.2 ± 16.6 8.5 ± 15.4* 0.31 ± 0.65 non-IR 43.7 ± 11.8 48.2 ± 13.1 4.5 ± 9.7* 0.20 ± 0.32 Com IRS 67.0 ± 10.1 77.1 ± 16.0 10.1 ± 16.3* 0.42 ± 0.67 Smo IRS 66.0 ± 5.6 67.9 ± 11.8 1.9 ± 10.1* 0.11 ± 0.41* Data are mean ± SD. *p<0.05 vs 1st angio by paired t-test; §p<0.05 vs IRS & fp<0.05 vs Com IRS by unpaired t-test. Com=complex, Smo=smooth

Conclusion. In pts with clinically stabilised unstable angina, IRS are at greater risk than non-IRS for rapid progression usually to total occlusion. Complex morphology identifies a high risk subgroup.

HIBERNATING MYOCARDIUM: THE INCIDENCE AND PERSISTENCE AFTER ACUTE MYOCARDIAL INFARCTION TREATED WITH THROMBOLYSIS

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Hibernating myocardium arises when myocardial perfusion is reduced below the level required to produce myocardial contraction, but is still adequate to maintain cell integrity and thus tissue viability. The purpose of this study was to establish the incidence and persistence of hibernating myocardium after myocardial infarction. 41 patients (36 male, mean age 60 years), admitted with a first myocardial infarction underwent gated positron emission tomography (PET) at a median of 8 days (range 5-21) post-infarction. All subjects received thrombolysis (Streptokinase) at a median of 3.5 hours (range 1-10.25) after onset of chest pain. N13 ammonia was used as the tracer for myocardial blood flow and 18 fluoro-deoxyglucose (FDG) for myocardial metabolism. All 41 (100%) patients had a matched deficit with reduced contraction in the region of myocardium identified as the area of infarction by the electrocardiograph. 32 (78%) patients had at least one area of reduced perfusion with increased FDG uptake and reduced contraction representing hibernating tissue. In 13 (31%) subjects there was a large single. Of these 6 had sustained an anterior and 7 inferior infarction. 10 of these regions of hibernating tissue were directly adjacent to the infarcted area. Repeat scans were performed on 14 (34%) subjects randomly selected from the main study group, 8 at 3 months and 6 at 6 months post-infarct. Of the 13 patients who had hibernating tissue on their initial scan 6 showed no significant change, 4 showed an increase in hibernating tissue and 3 a decrease. Hibernating myocardium is of clinical significance as re-establishing adequate perfusion often restores myocardial contraction and thus improves left ventricular function. A significant proportion of patients who sustain a myocardial infarction and receive thrombolysis have areas of hibernating myocardium. However only approximately one third have a large area. In the majority of patients these areas are still present several months after infarction.
PREDISCHARGE EXERCISE TESTING IN THE PREDICTION OF CORONARY AFTER PATENCY FOLLOWING THROMBOLYSIS FOR ACUTE MYOCARDIAL INFARCTION
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212 patients (mean age 55.8 ± 9 y; range 31-74; 161 M, 51 F) received thrombolytic therapy within 6 hrs of onset of symptoms of acute myocardial infarction. Coronary artery patency was assessed angiographically at 90 mins (194/212) and 24 hrs (187/212) and defined by the TIMI scoring system (0 = Non Patent; 2.5 = Patent). A symptom limited pre-discharge exercise test (modified Bruce protocol) was performed on 148/194 and 145/187 patients. ST depression, ST elevation, T wave normalization and reported angina were compared within the Patent and Non Patent group by X² analysis. Total exercise time (SEC) and metabolic equivalents were compared using a two sample T-test and shown as a mean±SD.

90 mins Non Patent Patent (n=53) (n=95) X² P value
ST+ 22(41.5%) 35(36.8%) 0.313 NS
ST* 17(32.1%) 23(24.2%) 0.996 NS
T+ 22(41.5%) 42(45.5%) 0.157 NS
Angina 61(11.3%) 13(13.7%) 0.170 NS

24 Hrs Non Patent Patent (n=21) (n=124) X² P value
ST+ 9(42.8%) 47(37.9%) 0.186 NS
ST* 3(14.3%) 33(26.6%) 1.505 NS
T+ 7(33.3%) 55(44.3%) 0.891 NS
Angina 2(9.5%) 16(12.9%) 0.189 NS

A COMPLEX ANALYSIS OF ECG IN PATIENTS UNDERGOING THROMBOLYSIS FOR ACUTE MYOCARDIAL INFARCTION: EARLY ECG CHANGES IN RELATION TO THE RESULT OF THE TREATMENT.
Pawel Buznas, Andrzej Szafarek
Department of Electrophysiology, Silesian Center of Cardiology, Zabrze, Poland

The aim of the study was to evaluate recent electrocardiographic changes after thrombolytic treatment in patients with acute myocardial infarction (AMI). A complex, quantitative analysis of the 12-lead ECG before and after thrombolysis was performed in patients with clinical and electrocardiographic features of AMI. The results of the therapy were assessed with a coronary angiogram in the acute stage. Patients were divided into two groups (i) with unsuccessful reperfusion (TIMI grade 0, 1 or 2, group I) and (ii) with successful reperfusion (TIMI grade 3, group II). From 200 patients enrolled in the study, there were 50 in group I and 150 in group II. De- and repolarization periods were assessed in the first and second ECG. The ECG changes were significantly different with rapid evolution in the successful reperfusion group. The most prominent differences were observed from absolute value of T wave axis turn (ΔAT), absolute value of ventricular gradient turn (ΔQRSST), increase of QRS complex width (ΔQRS), increase in myocardial damage (according to Selvester's scoring - ΔSc), decrease in the number of leads with ST segment elevation (ds) as well as from relative drop of maximum ST segment elevation (index of ST segment normalization - IN).

Criteria of reperfusion were established according to the value ranges of factors showing the greatest differences. Using these criteria we could predict reperfusion with 83% sensitivity and 100% specificity. We conclude that early changes of de- and repolarization periods in the 12 lead ECG are strongly related to the result of thrombolytic therapy and their dynamics can be presented in the quantitative way.

ASPIRIN IN THE PREVENTION OF CORONARY HEART DISEASE - ARE OPPORTUNITIES BEING MISSED?
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Department of Public Health, Royal Free Hospital School of Medicine, London.

The use of aspirin in the secondary prevention of coronary heart disease is now strongly supported by clinical trial evidence. Several studies of aspirin use after hospital admission with acute myocardial infarction have now been conducted, but these provide little information on the use of aspirin in patients with coronary heart disease in the wider population. This issue has been examined in the British Regional Heart Study, a longitudinal study of cardiovascular disease in middle-aged men followed for a mean of 12.75 years. Data on aspirin use was collected using a questionnaire in autumn 1992, which was completed by 5095 (902) survivors, then aged 52-75 years. Overall, 9.2% of the study population were taking regular aspirin at least daily, while a further 2.6% were taking aspirin at least on alternate days. Of these subjects, more than half (55%) had a previous diagnosis of coronary heart disease. Among subjects with recall of a myocardial infarction (N = 565), 51.3% were taking aspirin regularly, compared with 58.7% in those with recall of a stroke (N = 208) (P = 0.08). Among subjects with recall of previous angina (N = 657), a lower proportion (44.2%) were receiving regular aspirin. However, among subjects who had previously had a coronary angioplasty (N = 58) or a coronary artery bypass graft (N = 93), the proportion receiving regular aspirin were higher (71% and 73% respectively). The results suggest that aspirin is still not received by many patients with established coronary heart disease, particularly those who are not selected for invasive forms of treatment.

DELETERIOUS EFFECT OF SMOKING ON THE ELASTIC PROPERTIES OF THE AORTA
C Stefanadis, C Vilasopoulos, C Stratos, I Kallikazaros, E Tsiamsis, S Marakas, A Sideris, L Sioris, H Boudoulas, CP Toutouzas, P Toutouzas, Athens University, Athens, Greece.

Cigarette smoking alters vascular reactivity and thus may alter the elastic properties of the aorta (Ao). To test this hypothesis, serial pressure-diameter lymphograms (figure A) were obtained from the simultaneous recordings of the thoracic Ao diameter (D) and pressure (P) before and after the initiation of smoking of one cigarette (nicotine content 1.3 mg) in 20 healthy smokers who underwent diagnostic cardiac chaterization. Ao D were measured by a Y-shaped catheter, developed in our institution, which incorporates at its distal tips a pair of ultrasonic dimension crystals (Crystal Biotech, MA). This high-definition diameter gauge was validated in in-vitro and experimental studies. Ao P were recorded by a Millar micromanometer. The pressure-diameter relationship changed significantly with smoking (figure A). Ao distensibility (2 AD/ D ADP, where AD and DP changes from systole to diastole of the Ao D and P respectively, and di-diastolic Ao D) was decreased significantly after smoking (figure B). These changes suggest that the Ao became stiffer after smoking.

This effect of smoking on the elastic properties of the aorta adds to the multiple other deleterious effects of smoking on human health.
(223) POSTER

IMPACT OF CIGARETTE SMOKING ON LONG TERM SURVIVAL AND MORTALITY FOLLOWING BYPASS SURGERY FOR ISOLATED STENOSIS OF THE LEFT ANTERIOR DESCENDING CORONARY ARTERY.

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Departments of Clinical Cardiology, Epidemiology and Biostatistics, Mater Misericordiae Hospital, Dublin, Ireland.

Cigarette smoking predicts an adverse outcome following coronary artery bypass grafting (CABG). The purpose of this study was to detail the effect of smoking on a highly select group of patients who had CABG for single vessel left anterior descending [LAD] coronary artery disease. Patients were identified from the operative records of all hospitals performing cardiac surgery in Ireland from 1984-1990. Follow up on 263 patients was by postal questionnaire or telephone interview and was complete in 100%.

RESULTS. The vital status and clinical events for all patients relating to their smoking history are tabulated below.

<table>
<thead>
<tr>
<th>Continuers</th>
<th>Starters</th>
<th>Quitters</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pt.No.</td>
<td>36</td>
<td>2</td>
<td>164</td>
</tr>
<tr>
<td>Alive</td>
<td>33 (92%)</td>
<td>2 (100%)</td>
<td>155 (95%)</td>
</tr>
<tr>
<td>Angina</td>
<td>8 (22%)</td>
<td>1 (50%)</td>
<td>57 (35%)</td>
</tr>
<tr>
<td>MI</td>
<td>3 (8%)</td>
<td>0 (0%)</td>
<td>9 (5%)</td>
</tr>
<tr>
<td>CCF</td>
<td>5 (14%)</td>
<td>0 (0%)</td>
<td>20 (12%)</td>
</tr>
<tr>
<td>Redo CABG</td>
<td>4 (11%)</td>
<td>0 (0%)</td>
<td>8 (5%)</td>
</tr>
</tbody>
</table>

CONCLUSION. Of patients with single vessel LAD disease having CABG 12.7% continued to smoke. While continuers were less likely to suffer from angina to quitters, they were more likely to die, have a myocardial infarction (MI), and to suffer from cardiac failure [CCF], or require redo CABG.

(224) POSTER

DEFECTS OF INSULIN ACTION IN PREMATURE MYOCARDIAL INFARCTION. IS Koerner, R Baliga, J Wilding, J Hulse, TJ Aitman, WS Pearl, J Scott. Royal Postgraduate Medical School, Hammersmith Hospital, London.

Prospective population studies have shown that high insulin levels constitute an independent risk factor for coronary heart disease (CHD) in Indian Asians and British whites. To test whether CHD is associated with insulin resistance, we measured insulin sensitivity (hyperinsulinaemic euglycaemic clamp, 0.05U/kg/hr), and oral glucose tolerance (OGTT), in 17 males with myocardial infarction (MI), 8 Punjabi Sikhs (PSM, age 44±2 yrs); 9 British white (BWMI, age 47±2 yrs), and 17 age matched male controls (9 Punjabi Sikh (PSC), 8 British white (BCW), of normal body weight, blood pressure, and fasting blood glucose <6.7 mmol/l). Glucose infusion rates (GIR, umol/kg/min) were lower in PSM compared to PSC (p<0.05) and lower in BWMI compared to BCW (p<0.05). Basal and two hour post OGGT glucose (GOGT0, and GOGT120, mmol/l) and insulin (IOM120 and IOCGT120, pmol/l) were similar in PSM compared to PSC, and similar in BWMI compared to BCW. Basal serum non-esterified fatty acid (NEFAOGT0) was higher in myocardial infarction patients and controls. Two hour post glucose load NEFA (NEFAT120) was higher in PSM than PSC (p<0.05), and higher in BWMI than BCW (P=0.05).

PSMI PSC BWMI BW
GIR 21±2 25±2 31±3 39±3
GOGT0 5.8±0.3 5.1±0.1 5.4±0.2 5.1±0.1
GOGT120 7.7±1.1 6.3±0.8 6.2±0.4 5.3±0.4
IOM120 124±33 75±12 188±70 109±71
IOCGT120 1000±317 674±216 393±86 235±48
NEFAT120 0.48±0.08 0.51±0.08 0.45±0.06 0.44±0.06
NEFAT120 0.39±0.02 0.06±0.02 0.18±0.05 0.06±0.02

We conclude that premature myocardial infarction, in Punjabi Sikh and British white patients, is associated with defective insulin action on carbohydrate and fat metabolism. These findings suggest that defective insulin action on carbohydrate and on fatty acid metabolism are important metabolic abnormalities in myocardial infarction and may contribute to disease pathogenesis.

(225) POSTER

A comparison of coronary risk factors in South Asians in the United Kingdom and in India: a sibling study

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People from the Indian subcontinent living abroad are reported to have an increased mortality from coronary heart disease (CHD). We have carried out a cross-sectional study of coronary risk factors in 376 randomly selected people of Indian origin in West London, UK, and in 117 of their siblings living in the Punjab, in India. The West London cohort had a greater body mass index (p<0.001), higher systolic blood pressure (p=0.0087), higher serum cholesterol (p<0.001), but lower high density lipoprotein cholesterol (p<0.05) and higher apolipoprotein B (p<0.001), and higher fasting blood glucose (p<0.05) concentrations than their siblings in the Punjab. Insulin sensitivity, derived from the homeostatic assessment mathematical model (HOMA), was decreased in men in West London compared to their siblings in the Punjab (p<0.05). Indians in West London had decreased beta cell function compared to those in the Punjab (p<0.001). By contrast, serum lipoprotein (a) concentrations were similar in both the West London and Punjabi populations, although significantly higher (p=0.01) by comparison with three populations of men and women of European descent from the UK. In people from the Indian subcontinent high serum lipoprotein (a) concentrations confer a genetic propensity to increased coronary risk. Siblings in West London have an additional, less favourable cardiovascular risk profile by comparison with the siblings in the Punjab, an adverse effect of migration.

(226) POSTER

MOLECULAR VARIANTS OF THE RENIN-ANGIOTENSIN SYSTEM DO NOT PREDICT BLOOD PRESSURE RESPONSE TO ANTIHYPERTENSIVE AGENTS

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Nuffield Department of Medicine and Department of Cardiovascular Medicine, John Radcliffe Hospital, Oxford.

Patient responses to antihypertensive agents are highly variable. Attempts to predict individual responsiveness to treatment from physiological measurements are time-consuming and of uncertain power. We therefore tested whether polymorphisms of renin-angiotensin system genes predicted patient responses to lisinopril, atenolol and nifedipine in a within-patient, placebo-controlled crossover trial using ambulatory blood pressure monitoring throughout. 67 unrelated Western European Caucasians with newly-diagnosed, untreated essential hypertension received placebo for 4 weeks followed by active drug for 4 weeks, ambulatory monitoring being carried out at the end of each 4 weeks. This cycle was repeated three times such that all subjects had received all three active drugs. Subjects were genotyped at two loci of interest: the insertion/deletion polymorphism of the angiotensin-converting enzyme gene, and the hypertension-associated M235T polymorphism of the angiotensinogen gene. The mean changes in systolic and diastolic blood pressure achieved by each agent were compared by analysis of variance across the genotypes at each locus. No significant association between the response to any drug and ACE or angiotensinogen genotypes was observed. We conclude that these polymorphisms are not helpful in predicting an individual's response to drugs of these classes.
A PROSPECTIVE STUDY TO EXAMINE THE RELATION OF SERUM LIPID SUBTRACTIONS TO THE PRESENCE AND SEVERITY OF ANGIOGRAPHICALLY DEMONSTRATED CORONARY ARTERY DISEASE: IMPLICATIONS FOR LIPID THERAPY PREVENTION STRATEGIES

R H Stables for The Brompton House Officer Audit Group. The Royal Brompton Hospital, London.

Background- There is now general acceptance of the value of 'secondary prevention' management of hyperlipidaemia in patients with established coronary artery disease (CAD). The present guidelines, including those of the American, British and European bodies, stress the importance of the measurement of total cholesterol (TC) or its low density lipoprotein subtraction (LDL), neglecting a role for high density lipoprotein subtraction (HDL) estimation. Objective- To explore the relationship between the levels of serum lipid subtractions and the presence and severity of CAD demonstrated at coronary angiography. Patients- Prospective cohort of 206 consecutive patients referred for diagnostic coronary angiography for the investigation of known or suspected CAD. Methods- De novo fasting lipid estimations were obtained on 205 subjects at the time of catheterisation. Coronary angiograms were reported by the primary operator, blinded to lipid levels. Analysis of variance and linear regression were used to explore relationships of lipid levels to two indices of disease severity: (a) The number of major epicardial vessels demonstrating at least one stenosis reducing luminal diameter by greater than 50% and (b) The total number of lesions recorded. Results- TC, calculated LDL and Triglyceride (TG) levels were found to have no association with either disease presence or severity. Values of HDL and the TC/HDL ratio were significantly related to both indices and a multiple regression model was developed to test these relationships. This revealed that independent relationships existed only for: (a) HDL and disease presence (p=0.01) (b) TC/HDL ratio and disease severity (p=0.001). All results were unaffected if patients on lipid lowering medication (n=22) and/or those with normal coronaries were excluded. Conclusions- These data suggest that the measurement of HDL levels may be of value in guiding lipid modification strategies for secondary prevention. The study group is highly selected but nevertheless is typical of the population evaluated at a cardiac centre. Conclusions cannot be generalised to a primary screening environment.

A PROSPECTIVE AUDIT OF THE MANAGEMENT OF LIPID SECONDARY PREVENTION IN PATIENTS REFERRED FOR DIAGNOSTIC CARDIAC CATHETERISATION

R H Stables for The Brompton House Officer Audit Group. The Royal Brompton Hospital, London.

Background- Despite the proven value of 'secondary prevention' management of hyperlipidaemia and coronary artery disease (CAD) many clinicians fail to recognise or adequately treat this important risk factor. Objective- To audit the lipid management of patients referred for diagnostic cardiac catheterisation for the investigation of known or suspected CAD. Patients- Prospective cohort of 206 consecutive patients referred (from a variety of primary and secondary centres) for diagnostic coronary angiography. Methods- Of the total referred, 17 were excluded. Blood tests performed, advice received and treatment prescribed. Results- 78% of patients had had their lipid levels measured. Of these only 104 (50.4%) had any idea of the result. No patient was aware of the levels of high or low density lipoprotein subtractions and in no case were these recorded in referral documentation. Conclusions- 1. Inadequate Screening: Only 137/206 (66.5%) patients had ever had their lipid levels measured. Of these only 104 (50.4%) had any idea of the result. No patient was aware of the levels of high or low density lipoprotein subtractions and in no case were these recorded in referral documentation. 2. Patient Interest: Patients who knew their total cholesterol (TC in mmol/l) result either as a value or as a 'high' or 'normal' categorisation proved accurate witnesses. ('High' group - mean TC=7.09 diet treated and =6.4 drug treated. Normal group mean TC=5.32. 'Value' group - untreated mean TC=6.03. r=0.6.p<0.01). In the 33 cases when patients reported the performance of a test but did not know any form of result, no individual had received advice or treatment despite a group mean TC=6.25. This suggests that fact may lie with the attending doctors. In comparison, of the 33 patients declaring a 'High' result, 16 had diet therapy, 13 had drug therapy in addition to any untreated. 3. Too Few Treated: Some 172/206 patients had a TC>5.2. Despite this data on primary therapy with a further 43 practising dietary modification. 4. Inadequate Treatment: In the drug treated group (n=22) the mean TC=3.9 with only 2 patients <=5.2. In the diet group (n=43) the mean TC=6.9 with only 3 patients <=5.2. Summary: This study identifies the need for more intensive management of hyperlipidaemia in secondary prevention.
A MODEL FOR CALCULATING THE COSTS OF LONG TERM DRUG THERAPY FOR LOWERING SERUM CHOLESTEROL
Authors: P. Diamond, M.B. Codd, D.D. Sugrue.

Dept. of Clinical Cardiology, Biostatistics and Epidemiology, Mater Hospital Dublin, Ireland.
Health Economics Unit, University College Dublin, Ireland.

The cost of long term drug therapy for treatment of elevated cholesterol is unknown. By combining data from the Mater Hospital Cholesterol Screening Study (normal volunteers, average cholesterol by age, 25-64, N=954), with population data (National Census 1991) the absolute numbers of individuals with cholesterol values greater than 5.6, 7 and 8mmol/l were determined. Using anticipated life expectancy by age (Irish Life Actuarial) a model for calculating lifetime costs of drug therapy was generated. (Table below).

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Total No *</th>
<th>Cholesterol mmol/l % of population</th>
<th>Life Expectancy (yrs) *</th>
<th>Total nos people Chol &gt;7 + 2 risk factors *</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-29</td>
<td>100</td>
<td>26.3</td>
<td>0.5</td>
<td>66.3</td>
</tr>
<tr>
<td>30-34</td>
<td>100</td>
<td>27.3</td>
<td>0.3</td>
<td>70.2</td>
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<tr>
<td>35-39</td>
<td>100</td>
<td>25.4</td>
<td>0.2</td>
<td>74.3</td>
</tr>
<tr>
<td>40-44</td>
<td>100</td>
<td>24.2</td>
<td>0.1</td>
<td>78.4</td>
</tr>
<tr>
<td>45-49</td>
<td>100</td>
<td>24.2</td>
<td>0.1</td>
<td>82.5</td>
</tr>
<tr>
<td>50-54</td>
<td>100</td>
<td>23.3</td>
<td>0.1</td>
<td>86.6</td>
</tr>
<tr>
<td>55-59</td>
<td>100</td>
<td>22.2</td>
<td>0.1</td>
<td>90.7</td>
</tr>
<tr>
<td>60-64</td>
<td>100</td>
<td>21.1</td>
<td>0.1</td>
<td>95.7</td>
</tr>
<tr>
<td>65-69</td>
<td>100</td>
<td>20.0</td>
<td>0.1</td>
<td>100.0</td>
</tr>
</tbody>
</table>

* National Census Data 1991
* Irish Life actuarial Data.
* Risk Factors =hypertension, previous CHD, family history of premature CHD.

Based on the above data Simvastatin 20mg daily, long term treatment Total No. people x life expectancy x annual cost (£571 )

All chol <7 £1447 Million
All chol >7 + 2 Risk Factors £380 Million

**Conclusion:** Long term drug therapy for lowering serum cholesterol is expensive. The cost of coronary events averted is considerably less. Ways of targeting lipid lowering therapy are needed.

Common mutation of the lipoprotein lipase gene protects against dyslipidaemia and coronary artery disease

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*St Georges Hospital Medical School and St Bartholomew’s Hospital Medical College, London. England. "MRC Epidemiology Unit, Penarth, Wales.

Lipoprotein lipase (LPL) is a key enzyme in lipoprotein metabolism and determines the clearance rate of triglyceride rich lipoproteins from the circulation. It also facilitates apolipoprotein and phospholipid exchange between VLDL and HDL, thereby affecting conversion of HDL₂ to HDL₃ and LDL generation derived from VLDL, clearance.

Recently, a mutation encoding a premature termination codon (Ser^**173**^-Ter) was discovered in the human LPL gene. This would yield a truncated LPL lacking the two carboxyl terminal amino acids SER-GLY. To determine the influence of this common mutation upon serum lipid and lipoprotein levels and coronary artery disease (CAD) within a representative U.K. adult male population, we analysed subjects from The Caerphilly Prospective Heart Disease Study (n=1277). All men between the ages of 45-59 (inclusive) in the Caerphilly region were selected using the electoral roll and GP records as the basic sampling frame; 89% collaborated. They were screened for CAD risk factors.

We report that possession of this mutation associates with protective lipid and lipoprotein profiles. Subjects possessing the mutation have significantly higher HDL-C (p=0.002) and apo A1 (p<0.04) levels, lower triglycerides (p=0.04) and total cholesterol/ HDL-C ratios (p=0.02); all previously established to reduce risk of CAD. We also find that this mutation is significantly less frequent amongst CAD subjects (p=0.05), relating to a 20% reduction in CAD risk amongst subjects possessing the mutation. These associations provide the first evidence for a common mutation that appears to confer beneficial lipid and lipoprotein profiles amongst the adult male population and may point to protective gene influences on CAD within populations.

SOLUBLE P-SELECTIN, COAGULATION AND LIPID CHANGES WITH HORMONE REPLACEMENT THERAPY: IMPLICATIONS FOR Atherosclerosis

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University Department of Medicine, City Hospital, Birmingham; *Department of Surgery, University Hospital of South Manchester

Patients with premature menopause constitute a group at high risk of atherosclerosis. To investigate this further, we measured sequential changes in plasma levels of the platelet adhesion molecule P-selectin (ELISA,R&D systems; which is associated with atherosclerosis), von Willebrand factor (vWF: ELISA, DAKO; a marker of endothelial dysfunction), fibrinogen (CLAUSS), fibrin Dimer (AGEN-ELISA; an index of fibrin turnover) and lipids in 22 premenopausal women (mean age 43.0 years ± 6.5) undergoing a (preliminary) surgical menopause, following hysterecotomy and bilateral oophorectomy, in whom oestrogen hormone replacement therapy (HRT) was introduced 6 weeks later. Our results are as follows: Pre- hysterectomy 6 weeks post- hysterectomy (menopausal)

P-selectin (median) ng/ml vWF (mean) µIU/ml fibrinogen (mean) g/l D-dimer (median) ng/ml cholesterol (mean) mmol/l triglycerides (mean) mmol/l

|        | 548 | 560 | 390** | 119 | 110 | 94** | 5.2 | 5.8 | 5.4 | 1.3 | 1.9 | 1.7** |

There was a significant increase in serum cholesterol and triglycerides following surgical menopause (paired t-test, p<0.01). Following HRT use, there was a significant reduction in P-selectin and vWF levels (paired Wilcoxon t-test respectively, p<0.05) compared to baseline. There were no significant changes in plasma fibrinogen and D-dimer levels. This study shows that the premature menopause is associated with elevations in serum cholesterol and triglycerides. The use of HRT results in a reduction in soluble P-selectin and vWF, suggesting beneficial effects of HRT on endothelial function and atherosclerosis. Patients undergoing a premature menopause should not be denied HRT in view of its beneficial effects in cardiovascular disease prevention.

DOES GENDER INFLUENCE ENDOTHELIAL FUNCTION IN HYPERCHOLESTEROLAEMIA?


Cardiovascular Researches Group, Departments of *Bio-engineering and Medicine, University of Wales College of Medicine, Cardiff.

The prevalence of cardiovascular disease (CVD) is relatively low in pre-menopausal women but rises after the menopause, suggesting a protective role of oestrogens. Hypercholesterolaemia (HC) is characterised by endothelial dysfunction, manifest by reduced EDRF activity. We compared the flow-related endothelium-dependent increase in brachial artery diameter during reactive hyperaemia (produced by releasing a wrist cuff inflated to suprasystolic pressure for 5 minutes), with the endothelium-independent response to sublingual nitro-glycerine (GTN 400µg) in 3 groups of 7 age-, and body mass index (BMI)-matched subjects without known cardiovascular disease (all normotensive, non-smokers, and non diabetic). Group I - HC pre-menopausal women (age 41±5 years, chol. 7.6±1.3 [SD] mmol/l), Group II - normal pre-menopausal women (age 41±5 years, chol. 5.4±0.7mmol/l), and Group III- HC men (age 41±5 years, chol. 7.8±1.4 mmol/l). Brachial artery diameter was measured by ultrasonic wall tracking (AMA Wall Track System™, resolution 3µm), blood flow with continuous wave Doppler, and reactive hyperaemia, and after sublingual GTN. Resting heart rate, BP, brachial artery blood flow and artery diameter were similar in all groups, except that artery diameter was larger in men (4.720.4mm in III cf. 3.650.4 mm in I and 3.490.4mm in II, p<0.001). During reactive hyperaemia the increase in blood flow was similar in all groups (+5765279 in I, +6031103 in II, +5895913 in III), but the increase in diameter seen in normal pre-menopausal women (4.12±2.3% in II) was abolished with HC (+1.9±2.4% in I, -0.9±2.84% in III, both p<0.01 cf. II). In contrast, the response to GTN was preserved (+20.8±5.9% in II, +19.3±6.8% in I, +13.6±5.6% in III).

Contrary to earlier reports that gender influences agonist-induced EDRF activity in resistance vessels, these results provide evidence that female gender does not protect against loss of flow-related endothelium-dependent dilatation of conduit arteries in HC.
**POSTER**

**EFFECT OF ESTRADIOL-17B ON FOREARM BLOOD FLOW IN MEN. A DOUBLE-BLIND RANDOMIZED STUDY**

M Volterrani, G M C Rosano, C M Beale, A Coats, P Collins
National Heart & Lung Institute, London, UK.

Estradiol-17b increases forearm blood flow (FFB) and reduces vascular resistance (VR) in menopausal women. However, the systemic vascular effects of this hormone in men are not known. The aim of the present study was to assess the effect of sublingual estradiol-17b ( Estrace, 1mg; SLE) or sublingual placebo (SP) upon forearm blood flow (FFB) and vascular resistance (VR) in 10 normal male volunteers (mean age 36 years). FFB and VR were measured by venous occlusion plethysmography before, 20 and 40 minutes after either SLE or SP. FFB and VR were similar before either SLE or SP (mean±SD; 5.5±1.9 vs 5.3±2.0 mL/min/100mL forearm tissue, and 17.7±6.5 vs 19.7±8.3 units respectively, P=NS). FFB and VR were the same 20 min after SLE when compared to SP (6.9±3.4 vs 5.3±2.0 mL/min/100mL forearm tissue and 15.2±7.0 vs 17.5±5.2 units respectively, P=NS). Forty min after SLE, FFB was increased when compared to SP (5.0±1.8 vs 3.6±1.3 mL/min/100mL forearm tissue, P<.05), VR was reduced by SLE compared to SP (17.5±8.0 vs 25.0±9.3 units respectively, P<.05). Blood pressure did not change throughout the study. In conclusion estradiol-17b does have acute affects on FFB and VR in men. These data suggest that the peripheral vasculature in males can respond to acute estrogen administration.

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**POSTER**

**INCREASED THROMBOTIC TENDENCY IN PATIENTS WITH SYNDROME X**

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The pathophysiology of Syndrome X [SX] (anginal pain with positive exercise test and normal coronaries on angiography) remains unclear. Microvascular ischaemia or a defective vasomotor tone have been suggested mechanisms. The purpose of this study was to compare an atherogenic or thrombotic tendency, as assessed by established metabolic and haemorheological risk markers, in patients with SX and normal controls. Serum lipids [total cholesterol, triglycerides, high density lipoprotein-cholesterol], lipoprotein(a) [Lp(a)], fibrinogen [Fib] and haematorcit [Hct] were measured in 10 female patients with angina, positive exercise thallium scans and normal coronaries on angiography SX. Similar blood parameters were measured in 9 healthy, age and weight matched female controls with no angina and normal resting 12-lead electrocardiograms. All blood samples were taken in the fasting state and analysed using conventional laboratory methods. Patients with SX had significantly elevated mean Lp(a) and Fib levels compared with controls, 53 v 8 mg/dl (p<0.01) and 299 v 250 mg/dl (p<0.05) respectively. In contrast no significant differences was observed between the lipid profiles or Hct in the 2 groups. We conclude that patients with SX have higher Lp(a) and Fib compared with controls. These observations suggest a previously unrecognised increased thrombotic tendency that may be contributory to the pathophysiology of SX.

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**POSTER**

**FIBRINOGEN AND IL-4 LEVELS ARE RAISED AND CORRELATE IN DIABETICS WITH ATHEROSCLEROSIS.**

A S Brown, J Bass, D E Jewitt, R Sherwood, J F Martin. Departments of Cardiology and Clinical Biochemistry, King's College Hospital, London.

Diabetics are known to have an increased risk of vascular disease but the underlying pathophysiological processes causing this remain largely speculative. Diabetics with vascular disease have increased circulating levels of fibrinogen, an important risk factor for ischaemic heart disease. Fibrinogen is produced from the liver. Its base line production may be determined genetically but its production is also stimulated as part of the acute phase response. Following stimulation by a wide variety of factors including interleukin-6 (IL-6). We have measured serum fibrinogen and IL-6 concentrations in 55 patients in whom the presence or absence of coronary or peripheral vascular disease was assessed by coronary or peripheral arteriography or peripheral dopplers, of these 28 were diabetic. Group I non diabetic patients admitted for aortic or mitral valve replacement with normal coronary arteries, Group II diabetics with no vascular complications, Group III non diabetics with coronary artery disease, Group IV diabetics with vascular disease. Fibrinogen was measured by immunoassay on a Cobas Bio analyser (normal range 170-400mg/dl) and IL-6 by a solid phase enzyme immunoassay technique, with a lower detection limit of 0.3pg/ml and an upper limit of normal of 2.3pg/ml.

<table>
<thead>
<tr>
<th>GROUPS</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrinogen (SI)/mg/dl</td>
<td>29(24)</td>
<td>260(50)</td>
<td>335(32)</td>
<td>598(40)*</td>
</tr>
<tr>
<td>IL-6 (SE) pg/ml</td>
<td>0.6(0.3)</td>
<td>2.9(0.8)</td>
<td>5.5(1.4)</td>
<td>7.9(1.5)*</td>
</tr>
</tbody>
</table>

*p<0.05 Mann Whitney U

We found that patients with atherosclerosis had raised levels of IL-6, in patients with diabetes and atherosclerosis this increase was greater and was associated with significantly higher fibrinogen levels. Furthermore IL-6 levels correlated with fibrinogen levels (r=0.53, p=0.0001) suggesting this cytokine may have an important intermediary role in the process of inflammation associated with vascular disease and that this response is exaggerated in diabetics.

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**POSTER**

**INSULIN RESISTANCE IN POSTMENOPAUSAL WOMEN WITH SYNDROME X WHO DO NOT RESPOND TO ESTROGON THERAPY.**

IF Godsland, GMC Rosano, AJ Prouddier, DC Lindsay, NS Peters, P Sarrel, P Collins, P Poole-Wilson, JC Stevenson. Wynn Institute for Metabolic Research and Department of Cardiac Medicine, National Heart and Lung Institute, London, U.K.

In women, the onset of Syndrome X (angina-like chest pain, ischaemic appearing ST depression and angiographically normal coronary arteries) occurs in the perimenopause and may be associated with typical menopausal symptoms suggesting that estrogen deficiency contributes to development of the syndrome.

Twenty-one postmenopausal women with syndrome X received detailed baseline metabolic investigations prior to entry into a double-blind, placebo-controlled, crossover trial of the effects of transdermal estradiol therapy on hemodynamic and cardiological end-points (exclusions from the original study cohort of 25 included 2 non-Caucasians, and 2 grossly obese). Insulin sensitivity (SI, Inversely related to insulin resistance) was measured by modelling analysis of intravenous glucose tolerance test glucose and insulin profiles.

After 2 months of therapy, 12 women showed an improvement in time to ≥1mm ST segment depression on treadmill exercise testing whilst on oestrogen compared with their time on placebo therapy (responders). The other 9 women showed no such improvement (non-responders). At baseline, insulin sensitivity was 126% higher in the responders compared with the non-responders (median SI 2.53 v 1.12 min-1.U-1.ml, p=0.02). The responders also had a 3-fold shorter time since menopause (median 4.5 v 14.0 years, p=0.04) and lower body mass index (24.3 v 27.1kg.m-2, p=0.05). Otherwise there were no significant baseline differences. In multivariate analysis insulin sensitivity emerged as the principal predictor of difference in time to ≥1mm ST segment depression between placebo and oestrogen treatment phases.

Responsiveness to estrogen in postmenopausal women with syndrome X appears to be greatly diminished in those who are insulin resistant.
British Heart Journal

(239) POSTER

SYSTEMIC ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH SYNDROME X.
J Goodfellow, M W Ramley, L A Luddington, S T Gorman, C H Jones, M J Lewis, and A H Henderson. Cardiovascular Sciences Research Group, *Department of Bio-engineering, University of Wales College of Medicine, Cardiff.

Whether Syndrome X (SX) (angina, positive exercise test, normal coronary arteriograms) is associated with systemic vascular dysfunction, and if so whether this reflects endothelial dysfunction remain unresolved questions. We studied 7 carefully characterised patients with SX (age 56±7 SD yr, 2 male, all with reversible myocardial thallium perfusion defects). Patients with risk factors known to be associated with endothelial dysfunction (smokers, BP >150/90 mmHg, diabetics, chronic renal control 6.5 mmol/l) were excluded. Patients with coronary artery disease (≥50% stenosis in ≥2 coronary arteries) (CAD) and normal subjects (C) formed control groups (both: age- and sex-matched, n = 7). Brachial artery diameter responses to reactive hyperaemia (flow-related, endothelium-mediated) and to sublingual glyceryl trinitrate (3 min after 400 µg GTN) were measured using a high resolution (3 µm) ultrasonic wall tracking system (AMA Wall Track System™).

Resting blood flow (43±24, 32±20, 51±42 ml/min, respectively in SX, CAD, C) and diameter (4.60±0.22, 4.44±0.24, 4.20±0.20 mm) were similar in all groups. Hyperaemia and GTN-induced increases in flow were each similar in all groups (+562±186, +605±101, +567±276 with reactive hyperaemia, +115±21, +117±25, +119±28% with GTN). The increase in brachial artery diameter seen in C during reactive hyperaemia (+7.60±4.12%) was lost in SX and CAD (+0.54±3.12, -1.87±4.14% respectively, both p<0.001 cf. C). The GTN-induced increase in diameter was similar in all groups (+14.74±2.85, +15.56±2.8%, +16.84±2.6%).

This study demonstrates reduced flow-related vasodilatation in systemic conduit arteries in patients with SX and CAD, consistent with systemic endothelial dysfunction.

(240) POSTER

PLASMA ENDOTHELIN-1 CONCENTRATION IN PATIENTS WITH ABDOMINAL AND NORMAL CORONARY ARTERIOGRAMS.

Patients with angina and normal coronary arteriograms (NCA) have reduced coronary flow reserve and abnormal endothelium dependent coronary vasodilator responses. Endothelin-1 (ET-1), a potent vasoconstrictor, is an important modulator of microvascular blood flow and may play a pathophysiological role in such patients. We determined the plasma level of ET-1 in 40 consecutive patients with angina and NCA (30 female, 56±8 years) and 21 normal controls (17 female, 53±7 years) and determined its relation to clinical exercise parameters. Patients with hypertension, left ventricular hypertrophy and/or coronary spasm were excluded. Thirty five patients had ≥1 mm ST segment depression during exercise. Left bundle branch block (LBBB) was present in 4 patients at rest and in 1 during exercise. Peripheral venous blood was sampled after 20 minutes supine rest. Plasma ET-1 was measured using radioimmunoassay (Nichols Institute B.V.). Mean plasma ET-1 (pg/ml) was significantly higher in patients (3.84±1.25 versus 2.88±0.71):

In patients with "high" (> control mean +1 SD) ET-1 levels (n=23), the time to onset of new pain during exercise was significantly shorter (6.21±3.9 versus 9.03±3.9 mins, p<0.001). Of the 5 patients with LBBB, 4 had plasma ET-1 > 4.0 pg/ml.

Conclusion: Plasma ET-1 is elevated in patients with angina and NCA and may be important in the pathophysiology of the disease.

(241) POSTER

ENDOTHELIUM-DEPENDENT AND ENDOTHELIUM-INDEPENDENT CORONARY VASODILATION IN SYNDROME X.
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The aim of this study was to investigate both endothelium-dependent and endothelium-independent vasodilation in patients with angina, a positive exercise test, and normal coronary angiograms (Syndrome X). We infused the endothelium-independent vasodilator papaverine and endothelium-dependent vasodilator acetylcholine in to the left coronary artery of 32 patients with Syndrome X and in 15 control subjects (patients with atypical chest pain, negative exercise test, and normal coronary angiograms). The changes in coronary blood flow were measured with an intracoronary 3F Doppler catheter positioned in the proximal left anterior descending coronary artery (LAD) and diameter of the LAD was assessed using quantitative coronary angiography. The mean increase in coronary blood flow in response to a 10 µg dose of papaverine was significantly less in the Syndrome X group (180 ± 76% vs 410 ± 60%, p< 0.01). Acetylcholine, given at doses of 1, 3, 10, and 30 µg per minute increased coronary blood flow in a dose-dependent manner in both the Syndrome X and the control group. However, the increase in coronary blood flow was significantly lower (p< 0.01) in the Syndrome X group (10 ± 10, 40 ± 34, 55 ± 70, and 124 ± 89%) as compared to the control group (70 ± 50, 204 ± 90, 354 ± 120, and 362 ± 80%). The results of our study have shown that both endothelium-dependent and endothelium-independent dilatation of the coronary microvasculature is impaired in Syndrome X patients suggesting a dynamic abnormality of coronary microvascular function.

(242) POSTER

REGIONAL BRAIN ACTIVATION COMPARED IN SILENT AND PAINFUL MYOCARDIAL ISCHAEMIA.
SD Rosen, E Pauleus, P Nihoyannopoulos, D Tousoulis and PG Camici. MRC Clinical Sciences Centre and Royal Postgraduate Medical School, Hammersmith Hospital, London.

Why silent (ie painless) myocardial ischaemia is silent is unclear. Using positron emission tomography, we measured regional cerebral blood flow (rCBF) changes as an index of neuronal activation during painful and silent myocardial ischaemia. Two groups were studied: Group A - 9 patients (7 male, age 61(7) years, mean (SD)) with angina, ischaemic changes on the exercise electrocardiogram (ECG) and angiographic coronary artery disease; and Group B - 9 patients (all male, age 62(7) years) with a positive stress echo angiogram and angiographic coronary artery disease, but no angina during myocardial ischaemia. No patient had diabetes or other systemic disease. Myocardial ischaemia was induced with intravenous dobutamine. The end-points were angina with ischaemic ECG changes in Group A or painless myocardial ischaemia, confirmed by ECG and echo, in Group B. rCBF changes during myocardial ischaemia were compared to baseline conditions and to placebo. PET images were transformed into a standard stereotactic space and comparisons made across conditions by Statistical Parametric Mapping. During myocardial ischaemia, there were rCBF increases bilaterally in the thalamus, basal frontal and prefrontal and anterior cingulate cortices in Group A and in the thalamus and basal cortex in Group B. rCBF increases were greater in the prefrontal cortex in angina compared to silent ischaemia. In silent ischaemia, the thalamus is activated and may act as a gate to affect pain signals. Frontal cortical activation appears necessary for the sensation of pain. Abnormal central processing of the afferent pain messages may have an aetiological role in silent myocardial ischaemia.
HAEMODYNAMIC CHANGES IN CORONARY CIRCULATION WITH MYOCARDIAL STUNNING

XY Jin, JR Pepper, DG Gibson
Royal Brompton Hospital, National Heart & Lung Institute, London

Coronary blood flow velocity has been found to increase during the first 6-12 hrs after aortic valve replacement as local myocardial function is injured. To investigate the underlying mechanisms in coronary circulation, we studied 13 patients (age 65±13 ±5SD yrs, 7 male, with normal coronary arteries undergoing isolated aortic valve replacement (using blood cardioplegia), before bypass and 30 mins after release of aortic cross clamp with bypass off. Blood flow velocities were measured in proximal left anterior descending coronary artery (LAD) by transthoracic echocardiography, and simultaneously left ventricular (LV) and aortic root (Ao) pressures by micromanometers, allowing Ao-LV pressure drop (P Ao-LV) to be derived continuously. Coronary flow velocities fell linearly with P Ao-LV during mid and late diastole, though extrapolated zero velocity occurred consistently at P Ao-LV above zero, defined as 'zero flow tissue pressure'. The effective pressure drop (P e) supporting coronary flow (Q; P Ao-LV - P e) was thus always less than P Ao-LV. Results: With 100 mins cardioplegia and 30 mins reperfusion, anterior wall thickening fraction decreased from 22±2% to 8±2% (p<0.01); peak Ao-LV coronary flow velocity (53±8 to 93±19, cms/s) and velocity time-integral (from 18.2±5 to 27.6±6, cm²/s) were both significantly greater (p<0.01) than pre bypass. Mean aortic diastolic pressure was unchanged (62±12 vs 63±12, mmHg) as LV end diastolic pressure (14±7 vs 13±10, mmHg), but P e fell strikingly from 27.9±7 to 12.7±14 mmHg (p<0.01), and P e thus rose from 18.8±6 to 36.2±12 mmHg (p<0.01).

The effective proximal resistance, defined as the ratio of P e and mean Ao-LV diastolic flow velocity, was unchanged (0.5±0.8 vs 0.47±0.15, mmHg/cms²). Conclusion: Diastolic Ao-LV coronary flow velocity is determined by a pressure significantly greater than that in the left ventricle, which falls by approximately 50% early after reperfusion. The associated increases in coronary flow velocity can be explained by this fall, with no alteration in calculated proximal resistance. The changes in vascular dynamics associated with reduced local myocardial function are likely to result from the injury to the mechanisms coupling local perfusion to metabolic activity.

CORONARY AUTOREGULATION IS MAINTAINED IN LEFT VENTRICULAR HYPERTROPHY

D R Wallbridge, SM Cobbe
Department of Medical Cardiology, Royal Infirmary, Glasgow

Left ventricular hypertrophy (LVH) is associated with an increased risk of cardiovascular morbidity and mortality. Previous studies have shown that patients with LVH develop ECC changes and left ventricular dysfunction during acute hypotension, and suggest that the lower end of autoregulation may be shifted upwards. The aim of this study was to measure left coronary blood flow (velocity) and flow reserve at baseline and during acute hypotension in subjects with LVH. We studied 15 patients with normal epicardial coronary vessels: 8 with aortic stenosis and 7 with LVH due to hypertension (mean echo LV mass index 106 vs 210 g/m², p=0.002). Coronary blood flow velocity (CBFV) was measured using a Judkins-style Doppler-tipped catheter at rest and during maximal hyperaemia (induced by intracoronary injection of adenosine) during acute hypotension with sodium nitroprusside, using a physiological range of pressures defined by prior ambulatory monitoring. Coronary artery diameter was measured using calipers and a projected image. For both groups, coronary blood flow velocity remained relatively constant over a wide range of physiological diastolic blood pressures and showed a steep relationship with diastolic blood pressure during maximal hyperaemia with intracoronary adenosine. No lower limit of autoregulation was identified in either group. Coronary blood flow was calculated as:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Coronary Flow</th>
<th>Control</th>
<th>LVH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td>Absolute (ml/min)</td>
<td>83.5±29.5</td>
<td>106.4±27.6</td>
</tr>
<tr>
<td></td>
<td>Per LVMass (ml/min/g)</td>
<td>0.38±0.09</td>
<td>0.26±0.09</td>
</tr>
<tr>
<td>Hyperaemia</td>
<td>Absolute (ml/min)</td>
<td>412.0±55.2</td>
<td>419.6±61.0</td>
</tr>
<tr>
<td></td>
<td>Per LVMass (ml/min/g)</td>
<td>2.02±0.26</td>
<td>1.16±0.50</td>
</tr>
</tbody>
</table>

In conclusion, the results are consistent with an inadequate blood supply to the hypertrophied heart, but no upward shift of the lower end of autoregulatory range could be demonstrated.

ROLE OF Na,K+ ATPASE PUMP IN HYPOXIC VASORELAXATION OF CORONARY ARTERIES

A Yazdani Butt, Motoshi Takao, A Tuan Dinh Xuan, George Cremona, Tim W Higenbottam, Papworth Hospital, Cambridge

Hypoxic vasodilatation of coronary arteries (CA) may protect myocardium from ischemic injury distal to CA stenosis. To study the phenomenon we have used 57 porcine CA rings from 17 animals and 22 human CA rings from 9 patients undergoing transplant surgery for cardiomyopathy (n=3), primary pulmonary hypertension (n=1), rheumatic heart disease (n=1) and coronary artery disease (n=4). Hearts were obtained immediately after death of the animal or explanation of the human heart. Conduit coronary arteries were carefully dissected. Rings (2-5mm in diameter and length) were studied in pairs, with (E+) and without (-E-) endothelium. Isometric tension was studied in organ baths filled with 20 mls of Krebs-Ringer bicarbonate solution at 37°C. Initially the solution was bubbled with 95% O2 and 5% CO2 to achieve PO2 of 73.5±2.3 kPa. At a stable basal tone prostaglandin F2 alpha (10^-7 to 10^-5 M) was used to achieve a stable plateau of contraction. Then the rings were treated with either nothing (control) or with ouabain (oua) (10^-6 M) which inhibits Na,K+ ATPase pump. After obtaining a stable plateau of tension the bubbling gas mixture was changed to 95% N2 and 5% CO2 to give a final PO2 of 8.7±0.3 kPa.

The results are as follows:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum Relaxation to Hypoxia (Percent of control)</td>
<td>80%</td>
</tr>
<tr>
<td>Porcine CA Rings</td>
<td>Human CA Rings</td>
</tr>
<tr>
<td>Control</td>
<td>Oua (10^-6 M)</td>
</tr>
<tr>
<td>E+</td>
<td>99.4±5.7</td>
</tr>
<tr>
<td>E-</td>
<td>115±6±13.4</td>
</tr>
<tr>
<td>(n=10)</td>
<td>(n=3)</td>
</tr>
<tr>
<td>Mean values ± SEM; *p&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

Ouabain inhibited relaxation to hypoxia in both human and porcine CA rings. Na,K+ ATPase pump may have a role in hypoxic vasorelaxation of conduit coronary arteries.

ABNORMAL BLOOD PRESSURE RESPONSE DURING EXERCISE IS A MARKER OF RISK OF Sudden death IN YOUNG PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY

N Sadoul, K Prasad, ABK Slade, PM Elliott, L Pei, RC Saumarez, WJ McKenna. Department of Cardiological Sciences, St. George's Hospital Medical School, Cranmer Terrace, LONDON, UK.

Abnormal blood pressure response (BPR) on exercise occurs in a third of patients with hypertrophic cardiomyopathy (HCM) especially the young and is often associated with family history of sudden death. To assess the prognostic significance of this finding, we prospectively evaluated 167 patients (107 male) aged <40 yrs (mean 26.5±8 years), using maximal symptom limited exercise test [Bruce 151] between Jan 1992 and Feb 1994. Results: 100 patients had a normal BPR defined as rise of >20 mm Hg from baseline to peak exercise whereas 67 exhibited an abnormal BPR. During a mean follow up of 35±21 months (range 6-92) sudden cardiac death (SCD) occurred in 13 patients; 3 with normal BPR and 10 with abnormal BPR (p<0.005). This relationship was independent of the other accepted risk factors i.e., non-sustained ventricular tachycardia (NSVT) on Holter, syncope and family history of SCD. Among other patients (n=154), 3 died from other causes (endocarditis, heart failure, mitral valve replacement) and one patient was transplanted. The SCD group did not differ significantly from the survivors in terms of age, family history, syncope or NSVT and achieved a similar degree of cardiovascular stress as assessed by maximum heart rate (HR) attained.

We conclude that an abnormal blood pressure response on exercise in young patients with HCM is associated with an increased risk of sudden cardiac death and is independent of the other accepted risk factors.
PACED ELECTROGRAM FRACTIONATION IN HYPERTROPHIC CARDIOMYOPATHY. RESULTS IN 101 PATIENTS
RC Saumarez, N Sadoul, AKB Slade, WJ McKenna. St George's Hospital Medical School, London SW17 ORE.

Increased duration of paced right ventricular (RV) electrograms in Hypertrophic Cardiomyopathy has been shown in an initial study to correlate with the risk of ventricular fibrillation (VF). The changes in electrogram duration with pacing stimulus prematurity discriminated patients into two groups. VF survivors and those with no risk factors (nRF) for sudden death (SD). These "original" groups have been tested prospectively in a further 64 patients. Of 64 patients with HCM, 3 had documented VF, 1 had witnessed SD and is assumed to have had VF, 25 had non-sustained VT on ambulatory ECGs (NSVT), 21 had a family history of SD (FHSD) and 14 had nRF. They were studied by pacing 1 RV site with a decremental sequence and recording electrograms from 3 other RV sites. The delay of each fractionated potential in the electrogram was determined relative to a pacing stimulus of increasing prematurity. These measurements were repeated by pacing each ventricular site in turn. The electrograms were characterised by two parameters: the S1S2 interval at which delay starts to increase and the change in electrogram duration between an S1S2 of 350 ms and VERP. Three VF patients lay within the original VF group while only 6/60 non VF patients lay within this group, discriminating between VF patients and the remainder (p<0.007). 11 of 14 noRF patients lay within the original nRF group and only 8 of the remaining 50 patients also lay within the nRF group, discriminating between the nRF patients and the remainder (p<0.0005). Most of the NSVT and FHSD patients lay between the original VF and nRF groups with 5/25 NSVT and 1/31 FHSD patients lying in the original VF group. Most patients with FHSD or NSVT lay between these groups. Pooled data from the original and current studies allows definition of a new VF group which includes all patients with VF (n=9), 8/30 patients with VT and 3/31 patients with FHSD. This new group may be used as a criterion for a prospective trial in the technique for the prediction of SD.

FAMILIAL HYPERTROPHIC CARDIOMYOPATHY WITH WOLFF-PARKINSON-WHITE SYNDROME MAPS TO A LOCUS ON CHROMOSOME 7q3
C MacRae, N Ghaisas, S Donnelly, HC Watkins, K McGarry, E Rowland, WJ McKenna, JG Seidman, CE Seidman. Harvard Medical School, Boston, MA, USA, Our Lady's Hospital, Navan, Eire and St George's Hospital, London, UK.

Familial hypertrophic cardiomyopathy (FHC) is a genetically heterogeneous disorder with four known loci and evidence of at least one other locus. We have previously identified disease causing mutations in three sarcomeric contractile protein genes. The earliest descriptions of FHC recognized an association with the Wolff-Parkinson-White syndrome although the exact nature of this relationship has remained enigmatic. In those families in which both disorders are found there appears to be a distinct phenotype with a predisposition to complete heart block and prominent myocardial fibrosis. To identify the underlying gene defect responsible for this phenotype we studied the molecular genetics of a large Irish kindred in whom hypertrophic cardiomyopathy, the Wolff-Parkinson-White syndrome and complete atrioventricular block segregation in a manner consistent with a single autosomal dominant disorder. After excluding the four known FHC loci a random genome search was performed. Our genetic linkage studies map the gene defect causing this disorder to human chromosome 7q3 with a maximum two-point LOD score of 7.80 at α = 0. These data also confirm that the diverse phenotypes within this family are indeed the result of a single mutation. While this is the fifth locus demonstrated for FHC it represents the first locus described for the Wolff-Parkinson-White syndrome. Several candidate genes are known to be located within this region of chromosome 7. The elucidation of the molecular basis for the disease within this kindred will shed light on the mechanism by which both these conditions arise and in particular provide insights into the development of the conduction system and atrioventricular regions of the heart.

PACING MODE AND ATRIAL FIBRILLATION: 1517 PACED YEARS FOLLOW-UP OF 1068 PACEMAKER IMPLANTS
DM Walker, J Radovan, R Chase, T Edwards, JM Morgan, IA Simpson, HH Gray, KD Dawkins. Wessex Regional Cardiothoracic Centre, Southampton General Hospital, Southampton.

DDD pacing has been shown to reduce the rate of spontaneous atrial fibrillation (AF) and flutter (AFL). However reservations about this implantation mode include the perceived high rate of atrial lead failure or displacement, and the need for system review or reprogramming to VVI mode as a result. To address these issues, we prospectively assessed the incidence of AFL/AF and the requirement for system revision/re-programming due to atrial lead problems. Data were collected from March 1992 to November 1994, comprising 1068 new implants by experienced operators with a total follow-up of 1517 paced years. In this period, there were 272 DDD implants (mean age 62.5 ± 14.3, 164M:397F) with a total follow-up of 333 paced years. Only 22 (8.1%) of these DDD systems have subsequently required re-programming to VVI mode, either due to the development of chronic AFL/AF (3.0%) or failure of the atrial lead to sense or pace (5.1%). A further 4 atrial leads required repositioning due to displacement, but are now functioning correctly (1.5%). 16 DDD implants were performed in patients with paroxysmal AFL/AF, and of these 8 are now asymptomatic. In comparison over the same period there have been 771 VVI implants (mean age 74.6 ± 10.8, 425M:342F) with a total follow-up of 1155 paced years. Of these 249 (32.3%) were implanted in patients with AFL/AF. Of the remaining 522 patients with P-wave activity at implantation, 36 (6.9%) are now in chronic AFL/AF, compared with only 3% for DDD pacing (p = 0.03). Finally there were 25 VDD implants (mean age 70.0 ± 5.2, 14M:11F) with a total follow-up of 29 paced years. There are no new cases of AFL/AF recorded to date. The overall incidence of ventricular lead problems in the same population was 3.8% (41/1068), comprising 3.3% of DDD ventricular leads (9/272) and 4.2% in VVI systems (32/771). The major causes of failure were high threshold (54%), fracture (22%) and displacement (12%).

Conclusion 1. We confirm that dual chamber pacing significantly reduces the incidence of AFL/AF, 2. Atrial lead displacement/failure to sense or pace is minimal. 3. These data support a more aggressive implant strategy in favour of DDD pacing.

FREQUENT REPROGRAMMING IS NECESSARY TO OPTIMISE PACING THERAPY IN HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY

Dual chamber pacing with short atrioventricular delay (AVD) to obtain complete right ventricular capture (CVC) is an effective therapy for refractory symptoms in hypertrophic obstructive cardiomyopathy (HOCM). This study reports the initial pacing parameters and subsequent changes required to maintain efficacy, 34 consecutive patients were implanted between August 1988 and July 1994 with the following pacemakers: ELA Chorus 1.2 & RM, n = 19, Biotronik Physios n = 8, Medtronic Elite, Minuet, Thera-DR n = 6, Intermedics Relay n = 1. Patients were divided by normal (Group 1: n=29) or impaired (Group 2: n=5) atrioventricular conduction. At implantation, mean maximum sensed AVD was 64±25 ms in Group 1 and 158±25 ms in Group 2. After a mean follow-up of 10.2 months 33 patients remain alive whom 23 required reprogramming. 9 Group 1 patients implanted with shorter AVD to allow CVC reducing the mean AVD to 85±20 ms. Group 2 AVD remained unchanged. Mode changes were required in 9 patients: DDD to DDDR n=6, DDD to VVIR n=3 (due to permanent atrial fibrillation). 7 patients required increased upper tracking limit to maintain CVC on exercise.

Conclusion: Reprogramming is frequently needed to maintain the effectiveness of pacing therapy in HOCM. Despite short initial AVD, patient with normal AV conduction may require further shortening of AVD as well as increased upper tracking limit and the DDDR mode to maximise CVC.
(251) POSTER

DIAGNOSTIC CARDIAC CATHETERISATION AND EMERGENCY CARDIAC SURGERY
TA Millane, B Bridgewater, MT Jones, NH Brooks
Regional Cardiothoracic Unit, Wythenshawe Hospital, Manchester

Proliferation of cardiac catheterisation laboratories in units without immediate access to cardiac surgery has raised questions about safety. Aims: To review recent diagnostic cardiac catheterisation practice at a regional cardiothoracic unit to establish the rate of referral for emergency cardiac surgery and to investigate outcome with a view to considering similar events were they to have occurred in a unit without immediate access to cardiac surgery.


Results: Twelve patients were referred for emergency surgery as a direct result of events occurring during diagnostic cardiac catheterisation (0.12%). Mean age 59 years (37-71), 4 were female. All but one were elective cases, 8 performed by non-consultant or visiting staff. Case note review revealed few distinguishing clinical features prior to catheterisation. Complications precipitating emergency surgery were severe myocardial ischaemia in 4 patients, profound hypotension in 3 (one from cardiac tamponade) and cardiac arrest in 5 patients requiring full cardiopulmonary resuscitation. Four patients had proximal 3 vessel disease, 3 had right coronary artery dissection, and 3 had associated left main stem stenosis. One patient had a post-infarction VSD and another received an inadvertent intramyocardial injection. All patients survived to leave the operating theatre. There were 3 post-operative deaths: two within 24 hours of surgery, three of the 5 patients massaged onto bypass left hospital alive. These 12 patients represented 25% of all emergency referrals from the catheter laboratory.

Conclusions: In this study which is in keeping with National data, 1:1000 patients undergoing elective diagnostic catheterisation required emergency cardiac surgery. Despite optimal conditions, the mortality was 25%. It is unlikely that any would have survived outside a surgical unit, which would have resulted in 2 avoidable deaths per year from one unit alone. The requirement for urgent surgery is unpredictable, and, unlike complications of PTCA, non-operative techniques are rarely of benefit. Operators and patients in centres not equipped for emergency surgery should be aware of this small, but significant extra risk.

(252) POSTER

APPROPRIATENESS OF CORONARY ANGIOGRAPHY AND REVASULARISATION IN A REGION WITH A HIGH DISEASE PREVALENCE
R H Robson, J Piknenay, S S Furniss, D S Reid
Cumberland Infirmary, Carlisle and Cardio-Thoracic Dept, Freeman Hospital, Newcastle upon Tyne

Some studies have suggested that coronary angiography and revascularisation procedures may be undertaken inappropriately. We attempted to assess this, and the equity of accessibility, in a Region with a high prevalence of coronary artery disease and a low intervention rate. Patient selection criteria for coronary angiography and revascularisation were agreed and applied retrospectively by case-note review to coronary angiograms undertaken with a view to revascularisation within the Region in the financial year 1991 - 1992. 1,380 case-notes were audited, 23 were untraceable. The number of angiograms per million population per District ranged from 754 to 1376. There was a significant negative relationship (P = 0.0075) between the distance of the District Hospital from the single centre undertaking angiography and the angiography rate per District. Much of this difference was due to patients with unstable angina, but the relationship remained in patients with stable angina. The proportion of patients investigated by angiography with unstable angina per District ranged from 10 - 40%. Overall, 82% of patients were taking double or triple therapy. 40% were found to have 3 vessel or left main stem disease. 7% of patients did not meet the criteria for stable angina but were considered to have unstable angina. 55% of patients investigated underwent emergency or elective revascularisation and satisfied the selection criteria. This study confirms that coronary angiography and revascularisation procedures were undertaken appropriately, except that accessibility was inequitable and it is likely that procedures were not made available to many patients who might have benefited.

(253) POSTER

Cardiac Catheter Complications related to Left Main Stem Stenosis
J. Kovac, D.P. de Bono, Department of Cardiology, University of Leicester.

Diagnostic cardiac catheterisation is a safe diagnostic procedure but subsets of patients constitute higher risk groups. We report complications associated with left main coronary stenosis reported to the CECC audit database. Of 88,735 reported procedures between September 1990 and April 1994, 940 (1.05%) were associated with a complication. 54 complications (5.7%) were associated with left main coronary disease. Of these 24 (48%) were associated with cardiac arrest during the procedure and 6 (12%) with delayed cardiac arrest. 22 patients (44%) died within 1 month of the procedure, of whom 12 died in the catheter laboratory. Urgent CABG was attempted in 36 patients (66%) of whom 27 survived at 1 month. Left main stenosis is found in between 2% and 5% of diagnostic coronary arteriograms. The overall complication rate is low, but the mortality rate associated with complications when they do occur is high. Urgent CABG is associated with a survival rate of 75%.

(254) POSTER

ASYMPTOMATIC RESTENOSIS AFTER CORONARY ANGIOPLASTY: AN UNCOMMON OCCURRENCE
Department of Cardiology, University of Leicester and THe Cardiothoracic Centre, Liverpool.

Many symptom free patients undergo investigation following coronary angioplasty (PTCA) because of suspected restenosis, consuming a considerable amount of medical time and resources. To investigate whether patients with asymptomatic angiographic restenosis (defined as >50% net luminal diameter loss) after PTCA remain symptom free at follow up, we reviewed the records of 339 patients entered into a randomised trial of subcutaneous heparin in restenosis prevention after PTCA. Early (<4 months) angiographic follow up was available for 299 patients (88.2%). Restenosis of one or more of the dilated vessels was present in 138 patients (46%) and 41 (27.7%) of these were symptom free without medical therapy at the time of angiography. There were 29 men and 12 women, median age 56 years (range 35-70). Nineteen patients had single vessel disease and 20 (49%) a history of previous myocardial infarction. At median follow up of 9 months (range 6-36), only 4 of the 41 patients (9.75%) remained asymptomatic without need for revascularisation or medical therapy. A further 9 (21%) were symptom free only with drug therapy or following a second revascularisation procedure. Sixteen patients (39%) reported grade I angina and 12 (30%) grade II angina. Ten of the 41 patients (24.4%) underwent revascularisation either by repeat PTCA (n=7) or coronary artery bypass surgery (n=3). Thirty two patients (78%) were taking 1 or more antianginal drugs.

Conclusion: the majority (>90%) of patients with asymptomatic early angiographic restenosis following PTCA develop a recurrence of symptoms at follow up necessitating reintroduction of medical therapy or a revascularisation procedure. Symptom recurrence should thus be used as the primary guiding factor in determining the need for repeat investigation following coronary angioplasty.
The Cardiothoracic PRIMARY Moriss, EXPERIENCE K H

The directional atherectomies presented below.

either favoured in the time restenosis, a number of vessels dilated of 133 vessels and 222 (20%) thought did also be with 1994 revascularisation, proliferation from intimal and was accelerated atherosclerosis reflecting the time. However, special training is required to optimise results and minimise complications and there are important cost implications.

A NOVEL DEVICE TO REDUCE DISCOMFORT DURING ARTERIAL SHEATH REMOVAL FOLLOWING INTERVENTIONAL PROCEDURES

S Gupta, REA Smith, RJ Wainwright, T McIntosh, MR Thomas. Department of Cardiology, King’s College Hospital, London.

Removal of arterial sheaths is associated with local pain and discomfort. A novel device has been developed to facilitate infusion of local anaesthetics in the subcutaneous tissues prior to sheath removal. This device is a coiled tube with a proximal infusion port and distal pores, and is mounted onto percutaneous introducer sheaths. A prospective study to assess the efficacy of the device was performed. Of 61 consecutive patients undergoing Coronary Angioplasty (PTCA) 23 had the device inserted (Device group) at the time of PTCA. Prior to sheath removal these 23 patients received 10ml of 1% lignocaine via the infusion port. The remaining 38 patients had no device inserted and were randomly allocated to 2 control groups. Control group A (n=19) received 10ml of 1% lignocaine injected subcutaneously via a 23-gauge needle around the sheath prior to its removal, and control group B (n=19) received no local anaesthetic. All 61 patients received premedication of 5mg diamorphine and 10mg metoclopramide intravenously. A visual analogue pain scale graded 1 to 5 (1=no pain; 5=severe pain) was used to compare degree of patient discomfort before (PRE) and during sheath removal/arterial compression (POST). Results comparing the grading of pain (mean ± SEM) by all 3 groups are shown in the table. The device was inserted in only 22 of these 23 patients.

A novel experience of Laserwire coronary angioplasty in chronic total occlusions

Since the introduction of coronary angioplasty (PTCA) the treatment of totally occluded coronary arteries (TOA) has remained a problem. Despite published success rates of 50-80%, the finding of TOA at angiography often leads to surgery. The spectranetics Model 018-003 Prima Coronary Occlusion System is comprised of 3 components; a 0.018" laserwire, support catheter and introducer. 12 optic fibres of 45um encased within the laserwire shaft transmit the excimer laser energy to the distal tip of the device. Using the guide catheter the laser wire is positioned in contact with the TO and the laser activated. The laser wire (LW) is then advanced allowing it to used as a guidewire. LW angioplasty was performed in 7 pts with TIMI 0 flow chronic TO (age 56-60 months, mean 16), 2 left anterior descending arteries (LAD), 2 right coronary arteries (RCA), 2 circumflex (Cx) and 1 graft to the RCA. Previous conventional PTCA had failed after 25-65 min (mean 42 min). Using a 60 mildm/sec fluence, 5 of 8 occlusion were crossed after 12-45sec laser time (mean 26 sec). All 5 were then successfully followed by conventional PTCA using the LW as a guidewire. In the unsuccessful cases 1 patient suffered perforation of the coronary artery (RCA) without any clinical sequelae and in the second case it proved impossible to cross the RCA lesion. No major complication (MI, surgery or death) occurred. Preliminary data suggests that technology may play a role in otherwise untreatable coronary artery occlusion. A European randomised trial is in progress.

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THE POTENTIAL DEMAND FOR AND FEASIBILITY OF IMMEDIATE PTCA FOLLOWING ACUTE MI IN A HOSPITAL WITHOUT ON-SITE CARDIAC SURGERY

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

Since the advent of thrombolytic therapy with its proven benefits for acute MI, there has been a search for an alternative equally effective treatment for those patients in whom thrombolysis is contra-indicated. Recent evidence suggests that immediate PTCA may be a suitable alternative treatment. We therefore set out to determine the potential demand for immediate angioplasty in our hospitals and to explore the feasibility of transferring such patients to the regional cardiothoracic surgical centre some 25 miles away.

In two teaching hospitals in 1989 and 1990 7855 patients were admitted with a suspected acute MI. 3211 patients were admitted within twelve hours (and were therefore suitable for thrombolysis), but only 2926 were admitted to coronary care units (thrombolysis is not administered on our medical wards at present). 771 patients had an 'initial working diagnosis' of acute MI and 579 of these patients received thrombolysis. Of the 192 patients who did not receive thrombolysis this was an appropriate decision in 24 cases and these 24 patients would be potential candidates for immediate PTCA. The other patients either died soon after admission or should have been given thrombolytic therapy. Of the 297 patients were felt to have absolute contra-indications to thrombolysis on admission. 96 of these had an 'initial working diagnosis' of acute MI and would also be candidates for immediate PTCA.

The total number of patients who should have been considered for immediate PTCA in 2 years is 120. We would anticipate transferring one patient per week to the regional cardiothoracic surgical centre. With such demand, this an emergency PTCA service seem a feasible option for patients with an acute MI who cannot have a thrombolytic agent.

THE BENEFITS OF FAST TRACK CORONARY ANGIOPLASTY


Percutaneous coronary angioplasty (PTCA) may be performed immediately following diagnostic cardiac catheterization ('fast track') or as a second new procedure on a subsequent day ('conventional'). We performed a retrospective study of the PTCA procedures performed at UCL hospitals during 1993 to establish the influence of the two PTCA protocols on outcome, radiation exposure and inpatient stay.

One hundred and twenty two patients (88 males and 34 females, mean age 56.5) who underwent PTCA were studied and their details summarized in the table. P values are derived from unpaired t tests. Figures are expressed as proportions or mean ± standard error of mean.

CONVENTIONAL FAST TRACK P value

<table>
<thead>
<tr>
<th>Condition</th>
<th>Patients</th>
<th>Unstable angina</th>
<th>Restenosis</th>
<th>Total lesions angioplastied</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTCA</td>
<td>87/11</td>
<td>23/48 (48%)</td>
<td>18/48 (37.5%)</td>
<td>42/51 (82.4%) NS</td>
</tr>
<tr>
<td>CAGB</td>
<td>27/2.8%</td>
<td>9/46 (17.4%) NS</td>
<td>7/46 (15.2%)</td>
<td>0.035</td>
</tr>
<tr>
<td>Total screening time</td>
<td>22.3 ± 2.0 mins</td>
<td>14.5 ± 1.1</td>
<td>0.0004</td>
<td></td>
</tr>
<tr>
<td>Nights in hospital</td>
<td>6.0 ± 0.7</td>
<td>3.3 ± 0.3</td>
<td>0.006</td>
<td></td>
</tr>
</tbody>
</table>

Lesion morphology, number of vessels attempted, seniority of operator and the number of PTCA balloons used were similar in both groups (data not shown).

In comparison to conventional PTCA, fast track PTCA had similar angiographic success rates with significantly decreased inpatient stay and screening times. It therefore reduced immediate hospital costs and radiation exposure. However, fast track PTCA had a higher requirement for repeat PTCA and CAGB within the following 6 months probably because there were a higher proportion of patients with unstable angina and restenosis in this group. These results suggest that patients who are likely to benefit from PTCA should be consented and scheduled for this in addition to routine coronary angiography.

DURING ROUTINE CORONARY ARTERY SURGERY, AORTIC CROSS CLAMPING AND INTERMITTENT VENTRICULAR FIBRILLATION IS ASSOCIATED WITH LESS PERI-OPERATIVE MYOCARDIAL DAMAGE THAN CRYSTALLOID CARDIOLYSE.

AP Banning*, F Musumeci, J Tovey*, L Davies*, J Kuo, WJ Penny*, Departments of Cardiology*, Biochemistry* and Cardiothoracic Surgery, University Hospital of Wales, Cardiff.

Previous comparisons of myocardial protection techniques during coronary artery surgery have been limited by the lack of a sensitive and specific marker of subclinical perioperative myocardial damage. Plasma levels of cardiac specific enzymes Troponin T (TnT) and the MB isofrom of creatinine kinase (CK-MB) are sensitive markers of myocardial injury. We enrolled patients (n=64, 12 female) undergoing elective coronary artery bypass surgery into a prospective randomised comparison of crystalloid cardioplegic solution (28°C) and intermittent fibrillation with aortic cross clamping (37°C). Plasma samples were collected pre-operatively, immediately post-operatively, 4 hours for 24 hours and daily thereafter. Levels of TnT, total creatinine kinase (CK) and CK-MB were assessed. Peak levels and area under the time activity curve for each cardiac enzyme were determined. Groups were comparable for age, sex, extent of disease and number of arterial and venous grafts performed. Compared to intermittent fibrillation with aortic cross clamping, crystalloid cardioplegia was associated with lower ischaemic and by-pass times (57 vs 38 min, p<0.001) and 108 vs 87 min, p<0.001). Non-specific ECG changes occurred more commonly post-operatively (day 7) following cardioplegia (48% vs 31%, p<0.01). More peri-operative myocardial injury as evidenced by release of TnT and CK-MB occurred with cardioplegia.

Max TnT TnT area Max CK-MB CK-MB area

| Cross clamp | 2.62±.9 | 7153±** | 252±9 | 352±60 |
| Cardioplegia | 2.8±2 | 1259±13 | 353±4 | 1100±570 |

*p<0.05, **p<0.01 Cross clamp vs cardioplegia, (mean±SD)

Intermittent fibrillation with aortic cross clamping is a more effective method of myocardial preservation than crystalloid cardioplegia during elective coronary artery surgery.

ISCHAEMIA DURING BYPASS SURGERY DOES NOT PRODUCE ANTI-Α MYOSIN ANTIBODIES


Background - Myocardial damage results in release of cardiac antigens. Antibodies to α-myosin (non cardiac specific) have previously been reported in 16% of patients after myocardial infarction (MI) and in 38% following bypass surgery (Eur Heart J 1991; 12D: 88-94; Am J Cardiol 1985; 56: 631-633), but the prevalence of antibodies against human cardiac specific α-myosin has not been reported in these clinical contexts.

Method - To test the hypothesis that ischaemia can produce cardiac autoimmunity, we assessed anti-α myosin antibody (Ab) levels (titre 1/320) in 30 consecutive patients (age 64 ± 11, male) before and 1.9 ± 0.4 months after bypass surgery. Twenty-four patients received coronary artery bypass grafts and 6 had valve replacement. Six patients had had MI 2.5 ± 4 years previously, 19 patients smoking and 11 were hypertensive. Antibody levels were also assessed in 203 normals (age 45 ± 16, 103 male) with no evidence of ischaemic heart disease.

Results - Mean anti-α myosin Ab levels (absorbance at 450 nm ± SEM) were no different in preoperative patients who had previous MI and in those who had not (0.14 ± 0.02 vs 0.17 ± 0.03, p=0.7). Mean bypass time was 74 ± 21 mins. and cross clamp time was 33 ± 17 mins. Two of 30 (7%) patients had abnormal levels pre- and the same 2 postoperatively (p = NS). Mean Ab level did not rise at follow-up (0.16 ± 0.02 vs 0.19 ± 0.04; p=0.5), and there was no association with post-operative Ab levels and either bypass time or cross clamp time. The proportion of patients with abnormal Ab levels (7%) was not higher than in normal individuals (4/203 (2%), p=0.4)

Conclusion - There is no evidence that ischaemia induced cardiac damage resulting from either MI or bypass surgery leads to production of cardiac specific anti-α myosin antibodies, which to date has only been reported in dilated cardiomyopathy and polyendocrinopathy.
OUTCOME OF LEFT MAIN CORONARY DISEASE IN A NEW REGIONAL CENTRE
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Left mainstem (LMS) disease has a high mortality and revascularisation with coronary artery bypass grafts (CABG) improves prognosis. We have reviewed the outcome of patients (pts) presenting with LMS disease defined as a stenosis ≥50% from Jan 93 to Oct 94 in our unit. 2055 pts had coronary angiography and 134 (6.5%) pts were identified as having LMS disease. In 103 pts data were available for audit. 7 pts were excluded because of previous CABG. Thus 96 pts had native LMS disease (11 females). The mean age was 61 (39-78) with a mean duration of symptoms of 57 ± 60 months (1-276). 91 patients were referred for CABG with 4 patients continuing medical management and one death prior to referral. The mean time to wait for CABG was 56 ± 65 days (1 - 360). 74 patients had surgery with 3 (4%) postoperative deaths; 4 pts have died waiting for surgery. Nine pts are on the waiting list and 4 pts have refused operation. All CABG pts had LIMA grafts with 20 having RIMA grafts and the mean number of vein grafts was 2.2 ± 0.9 (0-5). The mean ITU stay was 1.7 ± 1.4 (1-14) days and postoperative hospital stay 8 ± 4.6 (3-28) days. There were no clinical predictors of preoperative death but postoperative mortality was associated with increasing age (61 ± 8 v 74 ± 5 years, p = 0.0025) and a trend towards a lower mean ejection fraction (61 ± 16 v 41 ± 36 %, p >0.06) 26 pts presented with acute coronary syndrome before waiting time to CABG 27 ± 40 days v 92 ± 125 days (p = 0.01).
Conclusion: LMS disease is common in our referral population and carries a significant mortality. Risk factors for postoperative deaths are increasing age and impaired left ventricular function. The unacceptable delay in waiting for surgery was attributable in part to the institution of an angiographic service 12 months before a full surgical service and we would advocate simultaneous development of cardiological and cardiological surgical services in future.

EARLY EXPERIENCE WITH A NEW MITRAL ANNULOPLASTY RING - THE SCULPTOR RING
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Left ventricular shape and function are better preserved in mitral valve repair than replacement as chordal preservation maintains valvulo-ventricular interaction. The contribution of annular contraction to this interaction is unknown. The new partly rigid and partly flexible "D" shaped Sculptor ring (S) is physiologically designed to mimic normal annular shape and movement pattern, unlike the rigid Carpentier-Edwards rings (CER) and fully flexible Duran rings. We reviewed 206 consecutive patients who underwent mitral valve repair with ring annuloplasty by one surgeon, 25 with Sculptor and 164 with Carpentier-Edwards rings. A subgroup of 12 patients in the CER group underwent annuloplasty in the same period as the SR group (Jun 93 - Mar 94). Mean follow-up in the SR group, CER group and CER subgroup was 5.8, 36.2 and 7.9 months respectively. Mortality and morbidity rates in the first post-operative year for the SR group and the CER group respectively were: in-hospital mortality 0.0% vs 2.4% (p>0.05), significant recurrent mitral regurgitation (grade III or IV) 12.0% vs 3.7% (p>0.05), re-operation 4.0% vs 3.7% (all were for mitral regurgitation), endocarditis 0.0% vs 2.4%, systemic thromboembolism 0.0% vs 5.5%, major anti-coagulation-related bleeding 8.0% vs 4.3%, ventricular arrhythmia 8.0% vs 3.0%, haemolytic anaemia 4.0% vs 0.0%, NYHA class III or IV heart failure 18.0% vs 7.9%. The CER subgroup suffered 0% deaths and 0% morbidity, suggesting that the differences cannot be accounted for by the use of historical controls. Outcome was satisfactory overall. Although outcome appeared worse in the SR group, the differences were not statistically significant (p>0.05 in all cases, Fishers exact test). Although no definite conclusions can be made, use of the Sculptor ring should be confined to closely-followed trial groups of patients until more information is available.
POSTER

MAGNESIUM SULPHATE IN UNSTABLE ANGINA: A DOUBLE BLIND RANDOMIZED TRIAL

Magnesium (Mg²⁺) has been shown to reduce coronary spasms, have favorable hemodynamic effects, inhibit platelet function, reduce arrhythmias, reduce catecholamine secretion and to be protective during experimental acute myocardial ischemia.

Sixty-two consecutive patients with unstable angina (with ECG changes) were randomized (double-blind) to Mg²⁺ (8 mmol bolus, then 3 mmol/h for 24 hours) or placebo. All patients received aspirin, β blockers, iv nitrates and heparin, provided no contraindications existed.

Four 12 hour urine collections were started at study entry for estimation of catecholamines (n=30) or β thromboglobulin (n=26). Baseline characteristics and extent of coronary disease were similar in both groups. Serum Mg²⁺ rose from 0.84 ± 0.03 to 1.69 ± 0.05 mmol/l (mean ± SEM) in the Mg²⁺ group. CKMB release was less in the Mg²⁺ group at 6 and 24 hours (28.3 ± 7.4 vs 6.6 ± 1.2 ng/ml at 6 hrs, p < 0.05). Regression of T wave changes on the 24 hour ECG (compared with admission) occurred more frequently in the Mg²⁺ group (11 patients vs 0 patients, p < 0.005). On 48 hour Holter monitoring, a similar proportion had transient myocardial ischemia (TMII) in the two groups (11 (39%) vs 10 (39%) respectively), however there were fewer episodes of TMI in the Mg²⁺ group (37 vs 54, p < 0.005) with a median total duration of 31.45 vs 81.15 mins respectively (ns). Frequency of ventricular ectopics and non-sustained ventricular tachycardias were similar in both groups. Adrenaline and noradrenaline excretion were lower in the Mg²⁺ group in the first 12 hour sample (1.05 ± 0.20 vs 1.61 ± 0.41 and 9.99 ± 2.05 vs 18.48 ± 3.13 ng/mmol creat respectively, p < 0.05). Urinary β thromboglobulin was similar in both groups in all collections. Thus Mg²⁺ reduces CKMB release, ECG progression and catecholamines in the acute phase of unstable angina with no effect on β thromboglobulin excretion. A larger scale trial investigating the effect of Mg²⁺ on mortality is warranted.

POSTER

A MULTI-CENTRE TRIAL OF DISOPYRAMIDE, ATENOLOL, AND PLACEBO FOR PAROXYSMAL ATRIAL FIBRILLATION
F D Murgatroyd, D M O’Farrell, J P Foran, S J Kelly, D E Ward, A J Camm, for the Controlled Randomized Atrial Fibrillation Trial Investigators. St George’s Hospital Medical School, London.

Class la drugs and β-blockers are commonly used to treat symptomatic paroxysmal atrial fibrillation (PAF), and patients with “vagal” and “adrenergic” patterns of PAF onset are held to respond to anticoagulogenic and β-blocking agents, respectively. However, neither class has been subjected to controlled clinical trials in this condition.

CRAFT-2 was a double blind three-way crossover comparison of disopyramide (Dp) (initial dose 100mg daily), disopyramide (Dp) (initial dose 450mg daily), and matched placebo (P). The primary endpoint was the time to the first and second attacks of PAF, documented by transtelephonic monitoring. All patients completed a symptom questionnaire to identify vagal and adrenergic patterns of PAF onset. 75 patients from 7 hospitals were screened, and 30 were randomized; their clinical characteristics closely approximated those of 334 patients with PAF in the CRAFT registry. The numbers of patients with 0 and 2 attacks of PAF were 0, and 1, respectively. On At, these were 6 and 7, and on Dp 5 and 6, respectively. The median times to the first and second attack were 4.2 and 7.5 days on P, 4.4 (p = 0.08) and 16.4 (p = 0.03) days on Dp, and 12.4 (p = 0.007) and 29.1 (p = 0.008) days on At, respectively. The mean (SD) heart rates (bpm) during attacks were 130 (21) on P, 135 (26) on Dp, (p=NS), and 115 (23) on At (p = 0.02). Dose reductions due to side-effects were required in 0, 2, and 4 cases, and treatment withdrawal was required in 0, 1 and 1 cases during P, Dp, and At treatment, respectively. There was no clear relationship between ataxonomic patterns of symptom onset and the response to treatment.

We conclude that disopyramide and especially atenolol reduce the frequency of symptomatic episodes of PAF. The efficacy of atenolol may relate to symptom reduction because of a lower heart rate, but that of disopyramide is likely to be a true antiarrhythmic action. Symptom onset pattern does not easily predict individual therapeutic responses.

MODERATED POSTER

PRE-HOSPITAL ADMINISTRATION OF ASPIRIN TO PATIENTS WITH SUSPECTED ACUTE MYOCARDIAL INFARCTION DOES NOT IMPROVE OUTCOME
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The ISIS-2 trial has shown that in-hospital treatment of suspected acute myocardial infarction (AMI) patients with aspirin is almost as effective as treatment with streptokinase in reducing 35 day mortality. We carried out a prospective, randomised, non-blind, controlled study of the effect of administration of a single oral dose of 300mg aspirin to patients with suspected AMI prior to transportation to hospital on 35 day mortality. The study was carried out over an eighteen month period by front line ambulance crews based at 15 London Ambulance Stations. 1850 patients with suspected acute myocardial infarction aged over 30 years were screened for eligibility. 1652 were randomised by the ambulance crews. 599 were allocated to a strategy of pre-hospital aspirin and 653 allocated to control (no aspirin). 980 (98%) of those allocated to the treatment group received the medication.

At 35 days there were 91 deaths in the aspirin group (9.1%) compared with 56 (8.6%) in the control group. The absolute increased risk 0.5% (95% confidence interval -2.25% to 3.3%) was not significant. The majority of deaths were due to cardiac causes 77 (85%) in the aspirin group and 47 (84%) in control. There were no major side effects attributable to pre-hospital aspirin. During long term 12 - 28 months follow up, there were 213 deaths (21.3%) in the aspirin group and 152 (20.2%) in the control group. This 1.1% increase in the risk of death (95% confidence interval -2.9% to 5.1%) was not significant.

We conclude that a policy of pre-hospital administration of aspirin to patients with suspected acute myocardial infarction is safe but does not improve outcome.
(271) MODERATED POSTER

INTERNATIONAL JOINT EFFICACY COMPARISON OF THROMBOLYTICS (INJECT): RETEPLASE VS UROKINASE IN ACUTE MYOCARDIAL INFARCTION


Department of Cardiovascular Medicine, University Hospital, Nottingham*, Boehringer Mannheim, Germany **; Universitätsklinikum Benjamin Franklin, Berlin, Germany §.

Reteplase (r-PA) is a non-glycosylated recombinant plasminogen activator containing the kringle-2 and protease domains but lacking the finger, epidermal growth factor and kringle-1 domains. It has a longer half-life than native t-PA and the 20 MU dose administered as two 10 MU boluses separated by 30 minutes has been shown to achieve a 90 minute patency rate of 85%. The objective of the INJECT trial was to compare the efficacy and safety of this r-PA regimen with standard regimen Streptokinase (1.5 MU over 60 minutes) in patients with acute myocardial infarction receiving treatment within 12 hours of symptom onset. A double-blind, randomized design was employed and standard inclusion/exclusion criteria for thrombolysis applied. The primary endpoint was 35 day survival. Target recruitment was 6000 patients which was achieved from September 1993 - 94 inclusive. All 333 patients in the 18 countries participated. This paper will present the results of INJECT and thus provide a detailed characterization of the efficacy and safety (including mortality) of Reteplase, a second generation direct plasminogen activator in comparison with Streptokinase.

(272) MODERATED POSTER

THROMBOLYSIS WITH ALTEPLASE FOR MYOCARDIAL INFARCTION: RISK-BENEFIT, TIME WINDOW AND 'EARLY HAZARD'

R.G. Wilcox, A. Charlesworth, A.M. Skeene* Department of Cardiovascular Medicine, University Hospital and Department of Mathematics*, University of Nottingham, Nottingham.

An overview of the large placebo controlled mortality trials of thrombolysis in acute myocardial infarction gives guidance about patient selection and risk benefit ratios. However, as Streptokinase has been numerically the most studied its effects dominate the overall analysis, particularly the increased risk of death on days 0-1 (early hazard) and the decrement of benefit with time to treatment up to 24 hours. This paper examines the combined data from the only two placebo controlled mortality trials with Alteplase (ASCET and LATE) to ascertain risk-benefit ratios, effective time window and early hazard. Of 10,724 patients randomised within 24 hours, 72% (68%) had an abnormal ECG on admission and were treated within 3 hours of admission.

Mortality at 35 days was 8.7% Alteplase and 11.8% placebo, p=0.00003. Relative reduction in mortality was 28% for those treated 0-6 hrs. 29% 7-12 hrs. and 23% 13-24 hrs.

The risk of death on days 0-1 were 3.4% vs 4.0% Alteplase (ASCET) 1.7% vs 2.5% placebo and 2.8% vs 2.4% (LATE >12 hrs). 35 day stroke rates were 1.48% Alteplase and 1.12% placebo (ASCET) 0.76% vs 0.78% Stroke risk did not change with time to treatment. Thus treatment with Alteplase results in a sustained benefit from 0-24 hrs with no early hazard and with a small constant increased stroke risk. Different thromblytics may have different effective time windows and hazards.

(273) MODERATED POSTER

PATTERNS OF ST-SEGMENT RECOVERY AFTER ACUTE MYOCARDIAL INFARCTION: EFFECT ON INFARCT SIZE AND VENTRICULAR REMODELLING


The General Infirmary at Leeds

Reperfusion of the infarct-related artery is an important determinant of infarct size, ventricular dysfunction and mortality following acute myocardial infarction. ST-segment resolution is a useful non-invasive marker of reperfusion but interpretation of reperfusion may be complicated by episodes of ST re-elevation, the significance of which is unclear. We studied 302 patients admitted with acute myocardial infarction and monitored using continuous 12-lead electrocardiography. Infarct size was measured by cumulative enzyme release and left ventricular volume and function by echocardiography. We identified two common patterns of ST-segment re-elevation following thrombolytic therapy: 1) a sudden increase in ST elevation shortly after the onset of treatment that preceded a rapid decrease in ST elevation indicating reperfusion (paradoxical elevation) 2). Transient and often repeated re-elevations of the ST segment that occurred after initial resolution (ST occlusion).

Pattern Infarct size % End diastolic volume (%)
A. No resolution 25 1299 (149) +23.9 (17.4)*
B. No paradoxical elevation 99 886 (75) +4.3 (7.4)*
C. Paradoxical elevation 54 897 (66) +2.9 (3.9)*
D. No occlusion 88 798 (67) -0.3 (4.1)*
E. Occlusion 89 891 (70) +14.2 (6.1)* p<0.05 v B-E =NS v E p<0.004 v C p<0.9 v E p<0.3 v E

These findings confirm that failure of ST resolution is associated with both an increase in infarct size and adverse remodelling. Paradoxical ST elevation accompanying reperfusion is linked with negative ST segment change, possibly reflecting reperfusion injury. This however does not result in greater susceptibility to ventricular dilatation presumably because of the protective effect of successful reperfusion. In contrast, ST occlusion does not influence infarct size but is associated with adverse remodelling, possibly reflecting less stable reperfusion.

Conclusions: The mechanisms and prognostic implication of increases in ST segment elevation seen after thrombolytic therapy for acute myocardial infarction differ according to the timing in relation to ST occlusion.

(274) MODERATED POSTER

ELECTROCARDIOGRAPHIC EVIDENCE OF REPERFUSION INJURY IN ACUTE MYOCARDIAL INFARCTION

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The aim of the study was to assess myocardial injury in relation to the result of thrombolytic treatment in patients with acute myocardial infarction (AMI). Myocardial injury was measured according to Selvester's QRS scoring system before and after thrombolysis treatment (Sc1-Sco). The ST-segment trend is often assessed by episodes of ST re-elevation, the significance of which is unclear. We studied 302 patients admitted with acute myocardial infarction and monitored using continuous 12-lead electrocardiography. Infarct size was measured by cumulative enzyme release and left ventricular volume and function by echocardiography.

In the first few hours after starting thrombolytic treatment an increase of myocardial injury (counted as Sc1-Sco) was more prominent in the group2 (2.7±2.4 vs 1.6±1.9, p<0.001). During the next 4 weeks there was no increase of the infarct size (Sc1-Sco) in group2 and a further increase in the group1 (1.7±2.0 vs 0.7±1.8, p<0.001). The total increase of injury (Sc1-Sco) was significantly higher in group2 (4.5±3.7 vs 2.6±4.2, p<0.001).

We conclude that the myocardial reperfusion injury can be assessed by using QRS scoring system. The total amount of the myocardial injury in the reperfusion group is smaller than in the non-reperfusion group.
(275) MODERATED POSTER

A COMPARISON OF INITIAL AND REPEAT THROMBOLYsis FOR EARLY REOPENING AS CRITERIA OF REPERFUSION

MM El-Omar, GYH Lip, H Singh, M Been
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There is limited data on the usefulness of repeat thrombolytic therapy for early reinfarction (<1 month). Using simple ECG changes as markers of reperfusion we compared the outcomes after first (T-1) and repeat (T-2) thrombolysis in 40 patients with early reinfarction (24 male, 16 female, mean age 61.8 years ± 10.6 years). Reinfarction was defined in the same territories as the initial infarcts, and occurred at a median period of 3.0 days (range 0-61) following T-1. Streptokinase (SK) was given to 39 and 20 patients on initial and repeat thrombolysis respectively; the rest received atepatepsia (nPA). ECG's immediately before and at a standard time after the commencement of each thrombolytic agent (2.5 hours for SK and 4 hours for nPA) were analysed. ECG parameters measured were the maximal ST elevation of any lead (STmax), and the sum of ST segment elevations (STT), R waves (ER), Q waves (QO) and their ratios (ΣRQ) in the infarct-related leads. The table shows the number of patients who achieved each of the ECG changes listed post T-1 & T-2:

<table>
<thead>
<tr>
<th>ECG change</th>
<th>T-1 all</th>
<th>T-1 EF</th>
<th>T-2 SK</th>
<th>T-2 nPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;25% reduction STmax</td>
<td>20</td>
<td>22</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>&gt;50% reduction STmax</td>
<td>23</td>
<td>16</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>&gt;25% reduction STT</td>
<td>30</td>
<td>24</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>&gt;25% reduction SR</td>
<td>22</td>
<td>18</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>&gt;25% increase ΣO</td>
<td>9</td>
<td>13</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>&gt;25% reduction ΣRQ</td>
<td>21</td>
<td>22</td>
<td>9</td>
<td>13</td>
</tr>
</tbody>
</table>

There were no significant differences between the T-1 and T-2 groups, or the T-2 SK and T-2 nPA subgroups of any of the ECG changes listed (X²-test, p=NS). Coronary angiographic data were available in 12 patients post T-2 prior to discharge. A reduction of >25% in STmax predicted angiographic vessel patency in 50% of patients (6/12), whilst a reduction of >50% predicted patency in 92% (11/12).

Conclusion: Repeat thrombolysis with SK or nPA for early reinfarction achieves comparable rates of reperfusion to those following initial thrombolysis. A reduction of >50% in STmax post-thrombolysis was most predictive of angiographic vessel patency.

(276) MODERATED POSTER

S-NITROSOGLUTATHIONE INHIBITS ACTIVATION OF PLATELETS IN UNSTABLE ANGINA.

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Activation of platelets, with platelet thrombus formation in the coronary artery, is a major factor in the pathogenesis of unstable angina (UA). Despite anti-platelet treatment with aspirin, patients with UA are still at increased risk of recurrent angina and myocardial infarction. The aim of this study was to investigate whether systemic platelet activation persists despite aspirin treatment in UA and whether this could be inhibited using the nitric oxide donor S-nitrosothioglutathione (GSNO). We studied 10 patients with new onset or recently worsening angina, having pain at rest or on minimal exertion and ST/T changes on ECG, being treated with aspirin. Venous blood was analysed using flow cytometry to determine platelet surface expression of P-selectin and Glycoprotein (GP) IIb/IIIa (indicating the degree of platelet activation). GSNO was then infused systemically, the dose being titrated to give a fall in mean arterial pressure of no more than 10 mmHg. Following a maximum of 45 mins infusion, a further venous blood sample was taken to measure platelet activation. Results (mean±SEM) were compared with 10 age-matched normal volunteers. P-selectin expression was 1.1±0.1% in normals compared with 2.54±0.2% in the UA group at baseline (p<0.01), falling to 1.26±1% after GSNO infusion (p<0.01). GP IIb/IIIa expression was 91±4 arbitrary units of relative fluorescence in normals compared with 103±4 in the UA group at baseline (p<0.05), falling to 94±3 after GSNO infusion (p<0.01). These results demonstrate systemic platelet activation in patients with UA despite aspirin treatment. This activation can be inhibited using a dose of GSNO that has only a small effect on blood pressure.

(277) MODERATED POSTER

DOSE-DEPENDENT EFFECTS OF ASPIRIN ON VASODILATATION AND PLATELET AGGREGATION

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Vasoconstrictor and vasodilator prostanoids are synthesised by human vascular cells (1) and administration of exogenous prostanoids alters the tone of human isolated blood vessels in vivo and vasoconstrictor and vasoconstrictor endogenous derived constrictor and relaxant factors have been described (2). Despite these observations there is no direct evidence for production of vasoactive amounts of prostanoids in humans, in vivo, and cyclo-oxygenase inhibitors may alter, in any, direct effect on the tone of most adult human blood vessels. In the present study we have explored the effects of the prostanoid precursor, arachidonic acid (AA), in superficial hand veins of healthy volunteers, and determined the effects of cyclo-oxygenase inhibitors on the responses seen.

Methods Subjects lay supine in a temperature-controlled (±0.1°C) laboratory with one hand placed on an angled support above the level of the heart. Drugs or physiological saline were infused continuously (0.25ml/min) through a 22G butterfly needle placed in a dorsal hand vein. The diameter of the vein was recorded 5-10mm downstream from the tip of the needle by recording the linear displacement of a lightweight probe placed on the skin overlaying the summit of the vein, when the pressure in a constricting cuff placed on the upper arm was lowered from 40 to 0mmHg (3). Results are expressed as mean ± SEM.

Results In veins pre-constricted by a continuous infusion of noradrenaline (20-160μg/ml), AA (20μg/ml) caused a maximal dilatation of 77±4% (n=5; p<0.05). Locally infused aspirin (10μmol/ml) for 30min abolished the dilator response to AA (dilatation to AA 0.6±20%; aspirin at a dose of 7.5μg/kg test before the study did not affect the response to AA whereas 1μg aspirin abolished the dilatation (dilatation after aspirin: 75μg 72±20%; n=3, Ig 29±19% n=3). The effects of this inhibition persisted at 24h (dilatation 7±4% (p>0.05) but by 5 days the dilator response had returned to 72±19% of the control dilatation. Paracetamol (1g) had no effect on AA-induced dilatation. Discussion The results of this study show that exogenous AA causes dilatation of human blood vessels in vivo. These effects were blocked by aspirin indicating that local generation of prostanoids accounted for the dilatation and suggesting that endogenous prostanoids may be produced in amounts sufficient to produce profound vasoconstriction. Low dose oral aspirin did not inhibit the dilatation to AA although it did inhibit ex vivo platelet aggregation (data not shown). In contrast, high dose aspirin abolished the dilatation. This study demonstrates that the effects of aspirin are dose dependent and we were able to identify a dose of aspirin which abolished AA-induced platelet aggregation without affecting AA-induced vasodilatation.


(278) MODERATED POSTER

Resternotomy for bleeding after cardiac surgery: A marker for morbidity and mortality.

Department of Cardiothoracic Surgery, St. George's Hospital, London.

Over a two year period from 1st January 1992 to 31st December 1993, of 2221 patients undergoing cardiac surgery in our unit, 85 (3.8%) were reopened for bleeding (9 patients more than once). Resternotomy for coronary cases was 2.3% but was more than 3 times as likely in valve cases (odds ratio 3.4, 95% confidence interval 2.1 to 5.4). Previous cardiac surgery was commoner amongst resternotomy patients than the remainder (18% vs. 9% respectively, P=0.018). An identifiable source of bleeding was found in 57 of the 85 patients (67%) but a concurrent coagulopathy was common (45 patients). Resternotomy patients, as a group, had higher preoperative risk scores (Parsonnet) than other patients (P<0.001), stayed longer in the intensive therapy unit (ITU) (P<0.001) and had greater requirements for intra-aortic balloon counterpulsation (14% vs. 3%) and haemofiltration (9% vs. 0.001 and P<0.01 respectively). 19 resternotomy patients (22%) died in hospital, a proportion significantly greater than the risk assigned to this group of patients preoperatively (12.8%) (P=0.008). In contrast, the observed mortality for the 2136 patients (5.5%) was significantly less (8.3%) (P=0.00006).

Multiple forward stepwise logistic regression confirmed resternotomy for excessive bleeding after cardiac surgery to be a significant independent predictor of prolonged ITU stay (P<0.00001), the need for intra-aortic balloon counterpulsation (P<0.0001) and death (P<0.0001).
A prospective randomised trial of a heparin-coated cardiopulmonary bypass circuit

MJ Unsworth-White, P Kallis, D Cowan, JA Toose, D Bevan, T Treasure. Cardiothoracic Unit, St. George’s Hospital, London

The bleeding diasthesis after cardiac surgery is believed to be the result of the interaction between blood and the surfaces of the bypass circuit. It has been hoped that heparin-coated surfaces will be more haemocompatible. We have tested this hypothesis in a prospective randomised trial of two cardiopulmonary bypass circuits. 63 patients awaiting first time elective coronary artery bypass surgery were randomised the day before surgery to one or other of two Baxter bypass circuits. The circuits were identical except that one was coated with heparin using the Duraflow® technology. Only the right atrial basket (Ross) and the aortic cannula remained uncoated. All patients were anti-coagulated with heparin to a similar target whilst on bypass to maintain the ACT greater than 400 seconds. Heparin was reversed with protamine on a 1:1 basis at the end of bypass. Blood loss and transfusion requirements for blood and colloid were recorded. Haemostatic variables including platelet surface markers, von Willebrand’s Factor and extrinsic pathway activation markers were measured throughout the procedure for the first 38 patients.

Groups were well matched for bypass and cross clamp times, total number of grafts performed, age, sex and body surface area. Blood loss and transfusion requirements were not significantly different between the two groups and there were no differences in the haemostatic parameters measured.

<table>
<thead>
<tr>
<th>Un-coated circuit (N=32)</th>
<th>Coated circuit (N=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median postop blood loss (IQR)</td>
<td>1000ml (660)</td>
</tr>
<tr>
<td>Median blood transfusion requirement (IQR)</td>
<td>3 units (1)</td>
</tr>
</tbody>
</table>

Heparin coating of the bypass circuit made no impact on bleeding or blood requirements when standard anti-coagulation was employed during cardio-pulmonary bypass.

(281) MODERATED POSTER

THROMBOGENESIS AND PLATELET ACTIVATION IN CHRONIC ATRIAL FIBRILLATION: EFFECTS OF ULTRA-LOW DOSE WARFARIN AND ASPRIN THERAPY

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Chronic atrial fibrillation (AF) is an arrhythmia which is associated with a high risk of stroke. To determine the effects of ultra-low dose warfarin and aspirin therapy on thrombogenesis in AF, we measured sequential changes in plasma fibrin D-dimer (an index of thrombogenesis, AGENT-ELISA) and beta-thromboglobulin (β-TG, a measure of platelet activation, AMERSHAM) in 51 patients (34 male, 17 female; mean age 70.4 years ± s.d. 7.4) with chronic AF before and at 2 and 6 weeks following randomisation to either 1mg warfarin or 300mg aspirin (Phase 1). All patients were then started on standard warfarin therapy, aiming for a target INR of 1.5-2.5 (Phase 2) with samples at 2 and 6 weeks afterwards.

Pretreatment results were compared to 26 healthy controls in sinus rhythm (16 male, 10 female; mean age 72.7 years ± 9.9). Baseline (pretreatment) β-TG and D-dimer levels in patients with AF were significantly elevated compared to controls in sinus rhythm (β-TG: 181 vs 91 ng/ml, median difference 79 ng/ml, paired Wilcoxon test, p<0.001; D-dimer: 220 vs 100 ng/ml, median difference 106 ng/ml, p<0.0001). In phase 1, there were no significant changes in median levels of fibrin D-dimer or β-TG, despite warfarin 1mg or aspirin 300mg. However, with standard warfarin therapy (Phase 2), there was a reduction in median β-TG at 6 weeks (207 vs 172 ng/ml; p<0.025) and a sequential reduction in median D-dimer levels, which was significant at 2 weeks (220 vs 193ng/ml; p<0.001) and at 6 weeks (220 vs 110 ng/ml; p<0.001) when compared to baseline levels. This study demonstrates that patients with AF have increased intravascular thrombogenesis and platelet activation when compared to patients in sinus rhythm. Introduction of ultra-low dose (1mg) warfarin or aspirin 300mg does not significantly alter these markers, although standard warfarin therapy does reduce β-TG and D-dimer levels. This is consistent with the beneficial effect of warfarin in preventing stroke and thromboembolism in patients with AF.

(280) MODERATED POSTER

HAEMOSTATIC AND HAEMODYNAMIC ABNORMALITIES ARE ASSOCIATED WITH LEFT ATRIAL SPONTANEOUS ECHO CONTRAST, WITHOUT LEFT ATRIAL THROMBUS

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Spontaneous echo contrast (SEC), or "smoke", seen in the left atrium (LA) at transoesophageal echocardiography (TOE) has been implicated as an independent risk factor for embolic events, particularly in non-rheumatic atrial fibrillation (NRAF). The mechanisms of SEC formation, in relation to thrombosis are, however, not fully understood. At TOE we identified SEC in 44 of 72 subjects with NRAF, not on anticoagulants. LA thrombus was identified in 12 patients,(11 of whom had SEC), these subjects were excluded from analysis. Peak blood velocity was measured at three sites in the left atrium (LA) using a pulsed wave Doppler technique, and venous blood was sampled for coagulant proteins, and markers of haemostatic activity. Subjects with SEC had reduced LA appendage (LAA) outflow velocity (0.19 vs 0.34 m/s, p<0.001), Mid-LA velocity (0.22 vs 0.35 m/s, p<0.001) and LA outflow velocity (0.40 vs 0.54 m/s, p=0.001) compared to those without. SEC subjects also had elevated levels of von Willebrand Factor (1.54 vs 1.14 IU/ml, p=0.01), thrombin-antithrombin complexes (3.98 vs 3.12 mcg/ml, p=0.02) and β-thromboglobulin (37 vs 33 IU/ml, p=0.04). Multiple logistic regression identified Mid-LA (p<0.001) and LAA (p=0.002) velocity as independent correlates of SEC. Haemostatic abnormalities are associated with SEC, even without LA thrombus at TOE, although the phenomenon appears to be predominantly associated with diagnosis of blood in the left atrium. The findings suggest that, in the absence of anticoagulants, NRAF patients with SEC are in a "hypercoagulable" state.
INCREASES Cardiology, University

Segments

Table

frees cells and locally produced growth factors and free radicals for instance, recently apoptosis (programmed cell death) has been shown to occur in all the component cells of the atherosclerotic plaque. We studied cell death in cultured human smooth muscle cells derived from individual coronary plaques (5) retrieved by atherectomy and normal aorta (4) from cardiac transplant donors, in high (20%) and low (0%) serum conditions. Cells from normal vessels showed no death in high serum, but 2.7% (±0.3) (mean, SEM) of cells died over 24 hours after withdrawal of serum survival factors. In contrast, 8.6% (±1.0) of plaque cells died even in high serum, and death increased to 16.8% (±2.8) after serum withdrawal. Death was characterized of apoptosis as demonstrated on time-lapse videomicroscopy, electron microscopy and DNA electrophoresis. IGF-1 and PDGF (0.1-100 ng/ml) were shown to act as concentration-dependent survival factors for both normal and plaque-derived cells, suppressing apoptosis by 78.2% (±5.2) and 50.0% (±6.2) respectively at the highest concentrations. IGF and bFGF had no survival effect at any concentration. Stable expression of bel-2, a proto-oncogene implicated in protection against apoptosis, via a retrovirus promoter suppressed death of both cell types in low serum, and plaque cell apoptosis in high serum. To what extent does bel-2 expression correlate with bel-2 activity? bel-2 expression is regulated by expression of specific genes and the local cytokine environment. Apoptosis may be important in cell turnover in normal arteries and the increased apoptosis observed in plaque VSMCs may contribute to plaque breakdown.

72 kDa proA 68 kDa active A 95 kDa proB

95 kDa gelatinase A and 92 kDa gelatinase B mRNA were detected in scarified plaques, an in-vitro model of arterial injury, and interestingly in normal arteries, too. However, gelatinase A expression in normal arteries was much lower than in scarified plaques. In scarified plaques, gelatinase A mRNA was maximal at 7.2 hours after injury, followed by a rapid decline. Gelatinase A mRNA expression in normal arteries was much lower and the time-course of gelatinase A expression in normal arteries was much lower and the time-course 1-2 5k16 0.6±0.6 0.9±0.9

13-14 129±22 54±18* 39±17*

Values are mean±SEM (n=12) * p<0.05 vs 1-2 days

The Table shows that there was constitutive activity of progelatinase A that was increased during neointima formation. Deamidatic activity of gelatinase A also occurred. Secretion of gelatinase B was also greatly increased during neointima formation. Activation of gelatinase A and induction of gelatinase B in cultured smooth muscle cells was stimulated during neointima formation and probably frees cells to respond to locally produced growth factors.

Vascular smooth muscle cell proliferation is an important component of angioplasty restenosis. Recently, genetic strategies have been shown to suppress neointima formation in animal models of arterial injury, including the use of antisense oligonucleotides to c-myc or sense c-myc oligonucleotides applied in a pluronic gel to the adventitial surface of the rat carotid artery after balloon catheter injury. At 2 days, antisense c-myc treatment suppressed medial replication to 2.5% (20.8) vs. 7.7% (21.6) and 7.0% (21.1)(Mean, SEM) for sense and gel alone respectively (n=6)(p<0.05).

However, no difference was present between antisense and control groups in proliferation rates in the media at 4 days or in the intima at 14 days. Antisense c-myc treatment suppressed neointimal area at 14 days by 34.3 % vs. gel alone, or 67.8% vs. sense treatment (p<0.05 for both treatments). There was no difference in the rates of migration of cells into the intima between groups, as assessed by the number of cells appearing on the arterial surface in an en face preparation of the artery at 4 days. In addition, no effect of antisense on endothelial cell replication could be demonstrated, despite demonstrating penetration of the oligonucleotides to the luminal surface using biotinylated oligonucleotides. Antisense c-myc oligonucleotides suppressed c-myc mRNA induction to 2 hours after injury on Northern analysis, but this difference had disappeared by 4 days. We conclude that antisense c-myc suppresses early medial replication following injury to the rat carotid artery, but does not suppress endothelial cell proliferation or smooth muscle cell migration since it is sufficient alone to suppress neointima formation at 14 days. Thus, a single application of antisense c-myc oligonucleotides may maintain arterial patency after injury.

IN VASCULAR SMOOTH MUSCLE CELLS.

HYPOXIA-INDUCED GENE EXPRESSION IN VASCULAR SMOOTH MUSCLE CELLS.

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Structural changes in the arterial wall may alter the distribution of oxygen and result in hypoxia of vascular smooth muscle cells (VSMC) within the tunica media. The molecular response to such oxygen deprivation is poorly understood. This study investigated the effect of hypoxia on expression of Vascular Endothelial Growth Factor (VEGF) and the nuclear proto-oncogene c-myc in an in-vitro model of VSMC. c-myc is a transcription factor involved in the regulation of cellular proliferation. The expression of this proto-oncogene is upregulated when cells are stimulated to re-enter the cell cycle. VEGF (also known as Vascular Permeability Factor) acts specifically on endothelial cells to stimulate their proliferation. It is potently induced by hypoxia in malignant cells, an effect considered to be responsible for mediating tumour angiogenesis, growth and metastases. It also promotes monocyte migration through the endothelium and increases its permeability. The above processes are known to be important in atherosclerosis. First passage, confluent and quiescent cultures of rabbit VSMC were incubated in humidified environmental chambers at 37 °C under controlled oxygen tensions (0-21% O2). Levels of mRNA for VEGF were measured by Northern blot analysis. Hypoxia resulted in a marked upregulation of VEGF (>20-fold) in a concentration-dependent and time-dependent manner. Increased levels of VEGF were detected within thirty minutes of hypoxia and continued to increase for up to 24 hours. The combination of a suboptimal hypoxic stimulus (2.5% O2) and the mitogen platelet-derived growth factor (PDGF) resulted in a striking increase in VEGF expression suggesting a synergistic interaction between the two stimuli. In contrast, c-myc was not induced by hypoxia and in the presence of PDGF was similar under both hypoxic and normal oxygen tensions. These results suggest that hypoxia is not a direct proliferative signal for VSMC. They do however suggest that VSMC may have a direct role as mediators of atherogenesis by responding to a hypoxic microenvironment with the production of VEGF. This multifunctional molecule has important biological effects on the endothelium that may be important both in early atherogenesis and in the late clinical presentation of advanced atherosclerotic plaque.
THE ROLE OF THE VASCULAR RENIN-ANGIOTENSIN SYSTEM IN THE REGULATION OF AORTIC WALL THICKENING AND COLLAGEN DEPOSITION: STUDIES IN THE HETEROGENEOUS TGR(mRen-2)27 RAT.

HE Montgomery, LA Kiernan*, JE Bishop*, JJ Mullins+, GF Laurent*, JR McEwan (Hatter Institute, University College Hospital, London; *Stoke Mandeville and National Heart and Lung Institute, London; +AFRC Centre for Genome Research, Edinburgh.)

Background: Hypertension causes aortic medial hypertrophy with associated accumulation of collagen in the aortic wall. Local (autocrine/paracrine) renin-angiotensin systems have been implicated in generating these changes. We have investigated this involvement by studying the hypertensive transgenic TGR(mRen-2)27. Heterozygote animals show expression of the murine renin gene in diverse tissues including the aorta, and are hypertensive. Methods: Three groups of animals (six per group) were compared: (i) Hypertensive heterozygote male transgenic rats (TGRs) (ii) Normotensive Sprague-Dawley rats of the same strain as the transgenic stock (iii) TGRs rendered normotensive by the administration of the angiotensin converting enzyme inhibitor Ramipril (1mg/kg/day in drinking water from age 28 days). Systolic blood pressures were measured under light halothane anaesthesia every 3 days using the tail-cuff method. On day 70, the animals were exsanguinated, tissues pressure perfusion-fixed, and collagen content and concentration per unit length of desiccating thoracic aorta assessed by high performance gasliquid chromatography. A further piece of aorta was dehydrated, set in araldyte, cut into 2micrometer sections, stained and aortic wall medial area assessed by computer morphometry. Results: After 28 days, the blood pressures of untreated TGRs rose (up to 300mmHg maximum). Medial area was greater in untreated TGRs than controls. However, it was lower in those TGRs treated with Ramipril (0.624mm2) than in controls (0.935mm2)(p<0.05). Aortic collagen content was significantly lower in untreated TGRs at high weight (334mg/g) than controls (33mg/g) (p<0.01), but was higher in treated TGRs(419mg/g) than in either untreated TGRs (p<0.001) or controls (p<0.01). However, aortic collagen content per unit area was identical in all groups. Conclusions: Activity of the Ren-in-angiotensin system in the aortic wall of young hypertensive animals: (i) Does not play an important role in regulating collagen deposition, (ii) Does increase aortic medial hypertrophy probably by increasing the size of the vascular smooth muscle cell compartment.

Doppler Myocardial Imaging: Mean Myocardial Velocity and Velocity Gradient in Normal Subjects

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Using an ultrasound scanner modified for Doppler Myocardial Imaging (DMI), maximum mean velocity (MV) and velocity gradient (VG) were measured across the myocardium during the cardiac cycle (CC) in 36 volunteers (age 21-73 yrs; heart rate 67±10 b/min). Mean myocardial velocity was the average value of velocity estimates throughout the myocardium and MV was defined as its peak value over one cardiac phase. VG was defined as a gradual spatial change in the value of velocity estimates. All measurements were taken from DMI M-mode images of left ventricular (LV) posterior wall. 3 CC were analysed for each volunteer and each CC was divided into 6 phases: atrial contraction (AC), isovolumetric contraction (IC), ventricular ejection (VE), isovolumetric relaxation (IR), rapid ventricular filling (VF) and diastasis (D). IC and IR were subdivided into 2 parts a and b, due to changes in the direction of the myocardial movement. The normal range of MV and VG in these phases have been found. Results are expressed as mean and standard deviation (Mean ±SD).

Mean AC ICa VE IRa IRb VF D ±SD
MV -3.2 ±2.0 -1.5 +4.4 +1.8 -1.8 -6.6 ±1.1 cm/s ±0.2 ±1.8 ±1.3 ±1.5 ±1.2 ±1.1 ±2.4 ±0.5 VG ±2.5 ±0.0 ±2.1 +3.9 +1.4 ±0.9 ±6.0 ±0.0 cm/s ±1.9 ±0.1 0.2 ±0.2 ±2.4 ±1.5 ±0.8 ±2.7 ±0.0 * (p<0.01), (%) (p<0.001), ** (p<0.001) ±, indicates that myocardium is moving towards the centre of LV; ~, away from the LV. mean VGSD: +, indicates that subendocardium is moving faster than subepicardium, ~, subepicardium is moving faster than endocardium. Linear regression shows that MV and VG increase with increasing age of normal subjects during AC (p<0.001). However, VG decreases (p<0.01) with age during VF. These findings are in agreement with haemodynamic abnormalities responsible for LV diastolic dysfunction in ageing hearts defined by the analysis of blood flow using spectral Doppler. It shows that MV and VG DMI measurement can be used as a diagnostic tool in assessment LV diastolic function.

ASSESSMENT OF CARDIAC PHYSIOLOGY BY TISSUE DOPPLER ECOCARDIOGRAPHY: A COMPARISON WITH PRESSURE RECORDINGS DURING CARDIAC CATHETERISATION.

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Tissue Doppler echocardiography (TDE) reveals characteristic patterns of myocardial tissue velocities within systole and diastole which are not well understood. The purpose of this study was to determine if these velocity patterns are related to the different physiological phases of the cardiac cycle as determined by invasive haemodynamics. Recordings of left ventricular/aortic and left ventricular/pulmonary wedge pressures were obtained simultaneously with apical TDE images. A total of 120 cardiac cycles from 12 patients (mean age 58 yrs) undergoing cardiac catheterisation were analysed. Time intervals were measured from the R-wave to the end of conventionally defined physiological phases for haemodynamic (haemo) studies (see table), and to the major interfaces of tissue velocity colours on TDE M-mode images.

In conclusion, tissue Doppler echocardiography has the potential to accurately assess the different physiological phases of the cardiac cycle, which until now could only be invasively determined. By this means, it may be possible to quantify regional diastolic function.

DOPPLER MYOCARDIAL IMAGING IN THE EVALUATION OF NORMAL AND ABNORMAL VENTRICULAR DEPOLARISATION

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Doppler Myocardial Imaging (DMI) is a new ultrasound technique in which standard blood pool Doppler algorithms are modified to detect myocardial motion. From this information, intraventricular velocities and regional variations in myocardial acceleration can be derived. Thus, both normal and abnormal patterns of myocardial acceleration could be identified as could the presence and precise location of foci of abnormal ventricular contraction. To determine the normal ventricular acceleration sequence, 30 normal patients were studied by 2-D and M-mode Grey scale imaging and then by DMI (2-D, pulsed and Doppler and M-mode) modalities. This data was compared with myocardial velocity and acceleration information from patients with VVI (12 pts) and DDD (9 pts) pacemakers, with unifocal VPB's (3 pts.), with RBBB (5 pts) and LBBB (7 pts) and with ventricular pre-excitation (11 pts - 3 right, 5 left posterior, 3 left lateral bypass tracts). The combination of DMI Velocity and Acceleration mapping using 2-D, M-mode and pulsed DMI techniques consistently identified specific normal and abnormal sequences of myocardial acceleration which accurately reflected the mode and timing of electrical depolarisation. Abnormal early regional acceleration associated with either WPW bypass or unifocal VPBs were accurately located, as were the immediate changes induced during the monitoring of radiofrequency ablation. This information was only in part available from standard grey-scale ultrasound imaging. Conclusion: DMI should become an important adjunct to the non-invasive investigation of abnormal myocardial depolarisation including the real-time monitoring of radiofrequency ablation.
**FLOW AUGMENTATION**

The degree of coronary flow augmentation by IABP is not fully defined. The feasibility of using TOE to measure coronary flow velocity parameters in the proximal left anterior descending coronary artery (LAD) has been demonstrated, but the technique has not gained widespread clinical application. To address these issues we studied 6 ventilated male patients at 2.2 ± 1 days post angiography and emergency coronary bypass surgery who had IABP in situ using TOE to determine coronary flow. Of the 6, one had proximal occlusion of the LAD which was not vein grafted (infarct related vessel), one had occlusion of the left main stem artery, with a vein graft to the LAD, and the remainder had patent vessels. TOE was performed using conventional equipment and LAD Doppler flow parameters (Peak, mean and velocity-time integral (VTI) of flow measured both with and without mechanical support.

<table>
<thead>
<tr>
<th>Results</th>
<th>Mean arterial pressure (mmHg)</th>
<th>Peak flow (cm/s)</th>
<th>Mean flow (cm/s)</th>
<th>VTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>IABP off</td>
<td>70 ± 15</td>
<td>43 ± 14</td>
<td>27 ± 8</td>
<td>12 ± 4</td>
</tr>
<tr>
<td>IABP on</td>
<td>81 ± 17</td>
<td>62 ± 21</td>
<td>40 ± 14</td>
<td>20 ± 7</td>
</tr>
<tr>
<td>p ns</td>
<td>-0.03</td>
<td>-0.02</td>
<td>-0.01</td>
<td></td>
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</tbody>
</table>

VTI increased by a mean of 71%, mean flow by 69% and peak flow by 45%. A characteristic rapid or late diastolic flow velocity increase was seen, depending on balloon inflation settings. Little augmentation was seen in the patient with LAD occlusion. In the patient with revascularised mainstem occlusion, biphasic, predominantly positive (retrograde) flow was detected, with overall values and increases in peak (47%) and VTI (36%) similar flow to that seen with patent vessels, thereby demonstrating vein graft patency by inference.

Conclusions: 1) IABP causes significant increases in LAD coronary flow. 2) Vein graft patency may be demonstrated by inference using TOE. 3) Coronary flow velocity measurement using TOE may offer further clinical potential for the adjustment of IABP setting to optimise augmentation of flow.

**MYOCARDIAL "CONTRAST REFLOW": IS IT A BETTER PREDICTOR OF IMPROVEMENT IN LEFT VENTRICULAR FUNCTION FOLLOWING ANGIOPLASTY (PTCA) THAN QUANTITATIVE ANGIOGRAPHY?**

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Demonstration of myocardial echo contrast reflow and the status of the epicardial coronary anatomy following PTCA have both been independently utilised to predict improvements of myocardial contractile function. However, these two observations have not been compared in the same patient. Fourteen patients underwent intracoronary contrast echo (ICCE) using sonicated omnipaque contrast medium and digital densitometric analysis of echo data before and after angioplasty or successfully performed PTCA. Quantitative analysis of index artery minimal luminal diameter (MLD) was performed. Global and regional left ventricular function was assessed by ejection fraction (EF) and wall motion index score (WMI) prior to the procedure and again at 1 month.

The myocardial contrast effect immediately pre and post angioplasty was assessed blindly and independently at the end of the study period. In 10 patients myocardial echo contrast reflow was demonstrated following the procedure while 4 had no reflow.

<table>
<thead>
<tr>
<th>Echo data</th>
<th>EF</th>
<th>WMI</th>
<th>MLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td>Reflow</td>
<td>51.4%</td>
<td>54.3%*</td>
<td>1.40</td>
</tr>
<tr>
<td>No reflow</td>
<td>50.1%</td>
<td>43%</td>
<td>1.588</td>
</tr>
</tbody>
</table>

*P<0.05

There was no significant difference in MLD of the index epicardial coronary artery following the procedure in the two groups. However ICCE evidence of "no reflow" correlated with either no change or a deterioration in EF and WMI score. Conversely in those patients where reflow was demonstrated there was a significant improvement in EF and WMI at 1 month. ICCE provides a novel and useful method of assessing functional changes and hence myocardial viability following PTCA. It appears more reliable than angiographic analysis of the epicardial coronary status.

**ECHOCARDIOGRAPHIC MYOCARDIAL CONTRAST ENHANCEMENT WITH PRESSURE RESISTANT BIODEGRADABLE MICROSPHERES**


Myocardial two-dimensional contrast echocardiography using direct intracoronary injection of sonicated contrast media can allow semi-quantitative evaluation of regional myocardial perfusion. However sonicated microbubbles are inconsistent in size, have a short half-life and are destroyed by compression within the left ventricle so that they cannot be used for intravenous use. Ultravue® (Delan: Nottingham, UK) is a new contrast agent consisting of stable air-filled albumen microspheres of consistent diameter (900-3.5 μm in diameter) capable of withstanding pressure of 200 mmHg. In this study we evaluated its efficacy for causing myocardial contrast enhancement. Ultravue was injected into the left ventricle of 7 open-chest pigs. Short axis images of the left ventricle were obtained with a 5 MHz transducer placed directly on the heart. Contrast enhancement of the myocardium was assessed by videodensitometry (0-256 grey scale) and also on a visual scale as follows: 0: no contrast; 1: faint contrast partially filling the ventricular myocardium; 2: contrast filling the entire myocardium; 3: dense contrast filling the entire myocardium; 4: excessive contrast. A total of 42 injections (50-300 x 10^6 microspheres in 2ml of water) were administered. Ultravue showed consistent myocardial enhancement (visual scale ≥2 and ≥30 U/pixel increase in image enhancement) at dosages of 275 x 10^6 microspheres. We conclude that Ultravue reproducibly provides myocardial enhancement of intensity suitable for clinical application.

**SHOULD ALL ELECTIVE CORONARY STENTS BE IMPLANTED VIA THE BRACHIAL APPROACH? AUDIT OF A SINGLE CENTRE EXPERIENCE OF STENTING FROM THE FEMORAL AND BRACHIAL ROUTES**


Coronary stenting is known to improve outcome after coronary angioplasty (PTCA). In order to assess the benefits of the brachial over the femoral approach we audited all stent procedures in our unit between December 1992 and September 1994. We compared duration of stay (nights following procedure) and vascular complication rates in a total of 155 patients aged (mean ±SD) 58 ± (10) years. Fifty procedures were in the left anterior descending, 24 circumflex, 57 right coronary and 24 in vein grafts. Almost half (44%) of elective stents were implanted via the brachial approach, whilst the majority (88%) of non-elective stents were implanted via the femoral approach. There were 19 cardiac complications (2 deaths, 11 myocardial infarcts, 6 CABG during admission).

<table>
<thead>
<tr>
<th>RESULTS</th>
<th>n = Duration of stay</th>
<th>Vascular complication rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(nights after stent)</td>
<td></td>
</tr>
<tr>
<td>Femoral</td>
<td>102 8 (±5)</td>
<td>12%</td>
</tr>
<tr>
<td></td>
<td>P&lt;0.001</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Brachial</td>
<td>53 5 (±3)</td>
<td>0%</td>
</tr>
<tr>
<td>Elective stent</td>
<td>107 6 (±4)</td>
<td>3%</td>
</tr>
<tr>
<td>Non-elective</td>
<td>48 9 (±5)</td>
<td>17%</td>
</tr>
</tbody>
</table>

In hospital stay and complication rates following coronary stent implantation are significantly reduced when the brachial approach is employed in preference to the femoral. Elective stenting is associated with a short in hospital stay and low complication rate due in part to the high frequency of brachial procedures in this group. In conclusion, the data from this audit supports the use of the brachial approach where possible for coronary stent implantation.
PLATELET DEPOSITION ON POLYMER COATED STENTS IS REDUCED BY PRE-COATING WITH AN ANTIPLATELET-FIBRINOLYTIC CONJUGATE

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Thrombotic stent occlusion remains a significant problem despite use of antplatelet and anticoagulant drugs; use of these agents also increases bleeding complications. Drug-eluting stents could serve as local delivery devices, obviating the need for systemic anticoagulation. To investigate platelet deposition on such stents we perfused 1cm segments of commercial polymer-coated stainless steel stent wire, adsorbed with antplatelet and fibrinolytic agents, with rabbit blood containing $^{111}$I-labelled platelet aggregates. Polymer coated stents without adsorbed agents (Nil) were compared with stents adsorbed with one of 5 agents: monoclonal anti rabbit platelet glycoprotein IIb/IIIa receptor antibody (AZ1), urokinase (UK), urokinase chemically conjugated to AZ1 (Conj), antibody of irrelevant specificity but same subunit as AZ1 or inactivated urokinase. Adsorption was achieved by immersing the stent wire segments into a 1mg/ml solution of each agent for 24 hours at 37°C. (optimal conditions in preliminary experiments). Platelet deposition was assessed from in-vitro activity on stents. Results:

<table>
<thead>
<tr>
<th>Agent</th>
<th>Mean (sd) platelets/cm wire x10$^{4}$ P (value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nil</td>
<td>385.1 (27.1) 440.8 (28.1) -- --</td>
</tr>
<tr>
<td>AZ1</td>
<td>364.8 (39.6) 301.4 (29.7) 0.020 0.002</td>
</tr>
<tr>
<td>UK</td>
<td>351.6 (31.2) 470.0 (36.8) NS NS</td>
</tr>
<tr>
<td>Conj</td>
<td>289.7 (31.2) 184.8 (25.5) 0.009 0.009</td>
</tr>
</tbody>
</table>

Stents adsorbed with control antibody or inactivated urokinase did not significantly differ from polymer-only stents. Conjugate-adsorbed stents did not significantly the least platelet deposition than AZ1-adsorbed stents at both 2 hours (P<0.02) and 4 hours (P<0.01). Conclusion: antplatelet-fibrinolytic conjugates adsorbed onto polymer-coated stents retain their efficacy and reduce platelet deposition more effectively than antplatelet agents alone in vitro. These agents may thus reduce stent related thrombosis and improve further in vivo evaluation.

MECHANISM OF BENEFIT OF STENTING IN FAILED PTCA

SG Ray, IM Penn, DR Ricci, J Barri, MB Bancini, CE Beller, B O'Neill, C Foster, D Almond, C Lazzam, L Roy, G Barbeau Vancouver Hospital, British Columbia, Canada.

The Trial of Angioplasty and Stents in Canada (TASC II) is a randomised multicentre study comparing the strategies of stenting (n=21) and prolonged perfusion balloon inflation (PPB, n=22) as initial bail-out therapy in failed PTCA. Quantitative analysis was used to compare the angiographic outcomes of these strategies. 40/43 patients had analyzable angiograms. Results:

<table>
<thead>
<tr>
<th>Pre randomisation</th>
<th>Post randomisation</th>
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<tbody>
<tr>
<td>MLD (mm) %</td>
<td>MLD (mm) %</td>
</tr>
<tr>
<td>Stent n=21</td>
<td>1.2±0.5 59%</td>
</tr>
<tr>
<td>PPB n=19</td>
<td>1.2±0.6 60%</td>
</tr>
<tr>
<td>P</td>
<td>ns</td>
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</table>

1) Stenting was more effective as bail-out therapy especially in treating lesions of greater diameter. Above: stent pre 1/22, post 1/21, PPB pre 5/19, post 5/19 (p<0.001). 2) Angiographic results with successful PPB were inferior to stenting: % stenosis: 30±6±20; MLD 1.2±0.3 (p=0.05 stent MLD) due to greater recoil in the PPB group: PPB 0.6±0.34mm (p=0.05 stent recoil). 3) Stenting following failed PPB was successful in 9/10 attempts with equivalent angiographic results to primary stent bail-out: % stenosis 24±8±8, MLD 2.5±0.4mm, but procedure time was longer 152±65.3mins v 114±8±13.4mins (p<0.05). Summary: This study confirms the benefit of stenting in improving immediate results of failed PTCA by reducing elastic recoil and closing complex dissections. Crossover to stenting following failed PPB gives angiographic results comparable to primary bail-out stenting at the expense of increased lab time.

PRINCIPAL PRIMARY STENTING FOR LONG CORONARY ARTERY LESIONS: AN EXPERIENCE WITH THE 18mm PALMZ-SCHZ STENT

NMK Robinson, RJ Wainwright King's College Hospital Medical School, London

Eighteen patients (17 men) with mean age 55 (range 41-79) years were included in this study. Eleven patients had angina at rest and 7 angina on minimal exercise. Long lesions of >15mm (confirmed on Quantitative Coronary Angiography) received a long (18mm) stent delivered with a stent delivery system (SDS) as an elective procedure. Mean lesion length was 16.9mm (range 15.3-18.2). Of the lesions treated, only 1 was a simple (Type A) lesion. The remainder were complex lesions. Predilation was performed with 8 long and 10 standard length balloons. One stent could not be delivered through a tortuous proximal right coronary artery and 1 patient had 2 long lesions treated with separate long stents. Stentining contributed to complete revascularisation in 10 patients but was salvage (treatment of target lesion in patients felt unsuitable for surgery) in 7 patients. The primary success rate for stent delivery was 18 out of 19 lesions. Mean pretreatment stenosis was 90% (range 75-99%) and all immediate post stent stenoses were <10%. Mean length of stay was 6 (range 3-9) days. One patient required bypass surgery due to a distal obstructive dissection. No anticoagulation was required in 3 patients after an excellent angiographic result using 4mm balloons. At 6 month follow-up 11 of the 16 patients successfully stented were asymptomatic, 4 had angina on severe exertion and 1 had died of non-cardiac causes (renal failure and sepsicaemia). Follow-up angiography has been performed in 10 patients at 6 months. At the stent site, 6 have stenoses of <10%, 1 of 30% and 3 have asymptomatic restenoses of >90%.

In conclusion, primary stenting with an 18mm Palmez-Schz stent and an SDS is practicable, allowing treatment of long coronary artery lesions. The 30% restenosis rate is greater than that expected for elective stenting of simple lesions (Benestent Study) but compares favourably with restenosis rates following coronary balloon angioplasty to complex lesions.

UNSTABLE ANGINA IS NOT A CONTRAINDICATION TO INTRACORONARY STENT INSERTION

NMK Robinson, MR Thomas, RJ Wainwright, DE Jewitt King's College Hospital Medical School, London

Complications following insertion of intracoronary stents may be related to thrombosis within the coronary artery. Acute ischaemic syndromes are associated with higher rates of acute complications following balloon angioplasty but their effect on outcome following stent insertion is less clear.

We assessed clinical outcome, complications and 6 month symptomatic status in 110 consecutive patients treated with 110.5 Palmez-Schatz stents. These were delivered electively and for threatened vessel closure. Patients with abrupt vessel closure were excluded. All patients had TIMI 2 or 3 flow prior to stent insertion. Unstable angina (UA) was defined as new onset or accelerating angina and always included rest pain. 58 patients were stented in the setting of UA (mean age 56 years, range 35-76) and 52 patients in stable angina (SA) (mean age 58 years, range 35-73). Event rates of myocardial infarction (MI), subacute stent thrombosis (SAST), coronary artery bypass graft surgery (CABG), and patients transfused (Tx) were similar in the 2 groups (p=NS for all, Chi square analysis). Patients may have contributed to more than one lesion. In conclusion, the outcome following insertion of a Palmez-Schatz stent with maintained TIMI flow is not affected by the intracoronary conditions associated with unstable angina. Therefore, unstable angina should not be considered a contraindication to intracoronary stenting.
Prolonged hospital stay, meticulous anticoagulation, and a high number of local puncture site complications are the main drawbacks of coronary stenting. In 100 consecutive patients we have tested a simplified post implant management designed to shorten hospital stay without increasing the risk of subacute thrombosis or bleeding complications. All patients had suboptimal results due to elastic recoil or type 2 to 3 dissections. The decision for stenting was always made during angioplasty. There were no pre selected cases. A total of 123 Johnson & Johnson PS-153 stents (24 half stents, 87 full stents and 12 tandem stents) were implanted using high pressure balloons with implantation pressures exceeding 14 bar. The mean reference vessel diameter was 3.2 ± 0.6mm final balloon size at maximum pressure was 3.4 ± 0.3mm. In 73 cases a short balloon was used for the final dilation. Only in 10 patients was the procedure complimented by intravascular ultrasound.

The ACT at the time of implant was 346 ± 48 seconds, no further intravenous heparin was given. All sheaths were removed the same day and a FemoStop compression device was left in situ at low pressures for 8 ± 3.5 hours. The patients were discharged on day 1 (48 patients) or 2 (52) on low molecular weight heparin 5,000 units SC for 7 days, self administered after instruction. Warfarin was started the day of the procedure and given for 6 weeks and regulated to an INR of 2.5 to 3.5 while the patient was out of hospital. All patients received Aspirin 75mg per day and a calcium antagonist. There was 1 subacute thrombosis which was successfully treated by thrombolysis at 16 hours after implant secondary to a non covered distal dissection. We observed 1 femoral false aneurysm responding to compression. 1 patient died 10 days after the procedure from late haemorrhage due to dissection of the iliac artery. We conclude that a short hospital stay does not increase the risk of thrombotic and bleeding complications after stenting. Stenting with good primary result has an extremely low subacute thrombosis rate. Intravenous heparin after stenting is unnecessary.