3rd Biennial Meeting

The Association for European Cardiovascular Pathology

8th - 10th October 2008

Institute of Physics
76 Portland Place
London W1B 1NT

FINAL PROGRAMME
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Welcome to London

On behalf of all British Cardiovascular Pathologists welcome to the 3rd Biennial meeting of our Association. We hope that you will be pleased with the venue we have selected. It is very popular with many different medical societies and is right in the centre of London. The different lecture rooms are named after distinguished Physicists and we are in the Rutherford Room. Nearby is the Rosalind Franklin room. She contributed greatly to the discovery of the structure of DNA. Her early death precluded her consideration for a Nobel Prize. A recent biography of her was a best seller and alluded to the poor treatment she received from her male colleagues!

As usual there are three themes to our meeting. Arterial disease will be featured on Wednesday afternoon. The British Heart Foundation lecture will be given by Mark Hanson who holds a BHF chair in Cardiovascular Science in Southampton. He heads a multidisciplinary unit which studies how the environment in utero and early life influences disease in later decades. The afternoon concludes with a short symposium on transplantation pathology organised by Annalisa Angelini and Margaret Burke.

It is now 50 years since a British forensic pathologist Donald Teare published his account of the pathology of hypertrophic cardiomyopathy. This has prompted a special edition of Heart which has just been circulated. We are especially grateful to Perry Elliott for his contribution to the Cardiomyopathy Symposium on Thursday. The Cardiomyopathy Association has sponsored this and made registration for Pathologists and Cardiologists in training free of charge. Just before lunch Malcolm Alison will give the Pathological Society lecture entitled “Stem cells: every organ should have some!” The “Path Soc”, as it is sometimes called, is the academic face of Pathology in Great Britain and Ireland. It is strongly committed to the support of general and academic training in histopathology.

A poster round will be held during the latter part of the Thursday lunch interval. The afternoon programme includes the customary “What is it?” clinicopathological cases. There are then three general presentations on topical issues in Cardiovascular Pathology. Kim Suvarna through his contacts as an examiner at the Royal College of Surgeons has organised an evening reception in their Hunterian Museum. We had hoped to hold the reception in the Royal College of Pathologists but it is in the process of a major redevelopment.

Michael Ashworth and Yen Ho are the organisers of the Friday morning symposium on Congenital Heart Disease. The Cardiovascular Society lecture on Grown Up Congenital Heart Disease will be given by Michael Gatzoulis. The meeting will conclude with a practical demonstration and there will be an opportunity for “hands on” examination of specimens. It is a crowded programme but we hope you will enjoy it. Special thanks to those who agreed to give poster rather than platform presentations!
The organisation of this meeting began nearly a year ago when Mary Sheppard, Margaret Burke and I met at St Pancreas station, strikingly redeveloped as the new Eurostar Terminal. We presented our proposals to the AECVP Board meeting in Amsterdam in January and then co-opted Michael Ashworth, Martin Goddard and Kim Suvarna. Allard van der Wal and Cristina Basso have been virtual members of the group with their frequent and always positive messages. In Southampton our Education Co-ordinator, Sara Pender has done most of the day to day secretarial work. Two administrators from the National Histopathology Training Schools, Jane Axtell and Susan Cossins are kindly helping on the registration desk.

Very many thanks to you all.

Patrick J Gallagher
President AECVP (2006-8)

General Information

Registration
The Registration Desk is in the ground floor foyer very close to the main entrance of the Institute of Physics. The opening hours are

- Wednesday 8th October 11.00 hrs to 17.30 hrs
- Thursday 9th October 08.00 hrs to 17.00 hrs
- Friday 10th October 09.00 hrs to 14.00 hrs

The registration fee for the meeting is £100 or €120. We can accept payment in Sterling or Euros or by cheques payable in Sterling to “The Pathology Meetings Account”. Please ensure you receive a receipt for your registration fee. There is no registration fee for Pathologists or Cardiologists in training. The registration fee includes lunch and tea and coffee. These will be served in a large area in the lower ground floor. Posters will also be displayed in this area.

The meeting has educational approval from the Royal College of Pathologists. Please sign the attendance sheets at the registration desk each day and collect a certificate at the end of the Conference.

Transportation in London
The nearest underground stations are Regent’s Park or Great Portland Street, both less than 5 minutes walk from the Institute of Physics. Underground fares are expensive. If you plan to use either the Underground or London Buses significant savings can be made by purchasing an Oyster card. There is a refundable deposit of £3. Some of these are available for purchase at the registration desk or you can buy them at Underground stations. If you wish to take a taxi simply signal to one with the yellow light above the windsreen illuminated.

Social Programme
All delegates are warmly invited to attend a reception at the Hunterian museum of the Royal College of Surgeons from 18.30 to 20.30 on Thursday 9th October. This is a unique collection of anatomical and pathological specimens in an elegant setting. We suggest that you take taxis to the Royal College which is in Lincoln’s Inn Fields. A taxi can take up to 5 passengers. The fare from the area of the meeting to the Royal College would be about £12. The nearest underground station is Holborn. Lincoln Inn Fields is within easy walking distance of Covent Garden, a popular tourist destination with many shops and restaurants.
Emergency Services

All emergency services respond to a 999 telephone call. The nearest 24 hour Accident and Emergency Department is at University College Hospital, about 800m from Portland Place. There is also an Accident and Emergency Department at St Thomas’s Hospital, opposite the Houses of Parliament. NHS Direct is a free advisory service that can also provide the names of doctors, dentists and pharmacists. Their telephone number is 0845 46 47.

Tourist Attractions

Dr Samuel Johnson (1709-84), the author of the first English dictionary memorably said, “No Sir, when a man who is tired of London he is tired of life, for there is in London all that life can afford”. There is still something for everyone. Oxford Street is close to the conference venue. It is full of shops most of which stay open late on Thursday evening. A visit to up market stores such as Harrod’s in Knightsbridge or Fortnum and Mason’s in Piccadilly will be a memorable and expensive experience. They both have a variety of excellent restaurants and large food halls. The London Eye is featured in the cityscape of this booklet. You get an incredible view of Central London, especially the Houses of Parliament. If you are staying over the week end consider a boat trip down the River Thames to Greenwich, perhaps with a visit to the Maritime Museum. Central London is often crowded but usually safe and closely policed. Watch out for the inevitable pick pockets.

The Association for European Cardiovascular Pathology

The primary purpose of the Association for European Cardiovascular Pathology is to promote the practice of cardiovascular pathology in all parts of the European continent. Membership is open to all physicians or scientists with an interest in cardiovascular pathology. The need for a European Association was identified in the early 1990s. We began life as a European School for Cardiovascular Pathology. Through the efforts of Anton Becker and the support of the Academic Medical Centre in Amsterdam we held annual meetings in Amsterdam from the mid 1990’s until 2003. The School was then transformed into the Association for European Cardiovascular Pathology with a legally registered constitution and by laws. We organise our own biennial meeting in the Autumn. Previous meetings have been in Padua (2004) and Aarhus (2006). In alternate years we contribute to the European Society of Pathology meeting. We have a close and productive relationship with the ESP Board and their organising committees. We have a large input into the next ESP meeting which will be held in Florence in September 2009. Our own next Biennial Meetings will be in Lisbon (2010), Paris (2012) and Amsterdam (2014).

You are warmly invited to join our Association. Membership fees are only € 50 per year and are waived for Pathologists in training or early career grade scientists. A significant proportion of our income is used to provide travel grants for younger colleagues to attend our meetings. If you would like to join please visit our web site, AECVP.org or contact our Secretary-Treasurer (a.c.vanderwal@amc.uva.nl).

President
Patrick J. Gallagher, UK (2008)

Past Presidents
Gaetano Thiene, IT (2006)
Anton E Becker, NL (2004)

President elect
Ulrik Baandrup, DK (2010)

Secretary Treasurer
Allard van der Wal, NL (2008)

Councillors
Patrick Bruneval, FR (2008)
Mary Sheppard, UK (2009)
Ivana Kholova, FI (2010)

Standing Committees

Education
Ulrik Baandrup, DK Chair (2008)
Margaret Burke, UK (2008)
James Kirkpatrick, DE (2008)

Membership
Annalisa Angelini, IT Chair (2008)
Rainer Bohle, DE (2008)
Kim Suvarna, UK (2008)

Nominating
Gaetano Thiene, IT Chair (2008)
Rosa H de Gouveia, PR (2008)
Paul Forries, FR (2008)

Web Master
Cristina Basso, IT (2008)
Wednesday 8th October

12.00 Registration and Lunch

13.30 Symposium on Vascular Pathology
Chairpersons
Professor Patrick Bruneval, Paris and
Dr Kim Suvarna, Sheffield

British Heart Foundation Lecture
Professor Mark Hanson, Southampton
Developmental Influences on Vascular Disorders
Dr J-P Duong van Huyen, Paris. Maternal diabetes, salt sensitive hypertension and renal function
Dr Chris Torrens, Southampton. Effect of statin therapy on developmental vascular disease

1.00 Break

15.00 Free Papers
Ageing, smooth muscle cells and vascular pathobiology
Orlandi A. Rome IT
Atherosclerotic plaque macrophage infiltration does not help identify coronary death individuals.
Dalager S., Kristensen I. B., Paaske, W. P., and Falk, E. Aarhus DK
Lymphatic vasculature is increased in cholesterol rich and calcified atherosclerotic lesions.
Kholová I., Dragneva G and Ylä-Herttuala S. Kuopio FI

16.00 Symposium on Transplantation Pathology
Chairpersons
Drs Ulrik Baandrup (Denmark) and Margaret Burke (London)
Dr Martin Goddard, Cambridge. The 2005 ISHLT revision of the working formulation for cardiac allograft rejection
Professor Annalisa Angelini, Padua. The ISHLT revision: a proposal for a Europe wide audit?
Dr Desley Neil, Birmingham. C4d and antibody-mediated rejection in cardiac allografts: more questions than answers?
Dr Margaret Burke, Harefield. C4d methodology and interpretation- is standardization feasible?
Close

19.00 AECVP Board Meeting
Royal Society of Medicine, Wimpole Street
Thursday 9th October

09.30  Cardiomyopathy Association Symposium
       Chairpersons
       Professor Paul Fornes, Rheims and Dr Mary Sheppard, London
       Professor Gaetano Thiene, Padua. Classification and nomenclature of cardiomyopathies
       Dr. Sanjay Prasad, London. Imaging in cardiomyopathy
       Dr. Perry Elliott, London. HOCM and unexplained left ventricular hypertrophy
       Break
       Professor Cristina Basso, Padua. Arrhythmogenic right ventricular cardiomyopathy
       Professor Gilda Caruso, Bari IT
       Tako-tsubo Cardiomyopathy.
       Dr. Sanjay Sharma, London. Risk stratification in cardiomyopathies

15.45  Break

16.00  Topical Issues in Cardiovascular Pathology
       Chairpersons
       Drs Ivana Kholova, Finland and Allard van der Wal, Amsterdam
       Dr Martin Goddard, Cambridge. Graft arterial disease: atherosclerosis or not?
       Dr Adrian Chester, Harefield, London. Aortic Valve Tissue Engineering: Myth or reality?
       Professor Tony Lehr, Lausanne. Training in histopathology: a European perspective

17.00  Announcements from the AECVP Board

18.30  Reception Hunterian Museum Royal College of Surgeons

12.00  Pathological Society Lecture
       Chair Professor Gaetano Thiene, Padua
       Professor Malcolm Alison, Imperial College London
       Stem Cells: every organ should have them!

12.45  Lunch
       (A poster round led by Martin Goddard and Tony Lehr will start at 13.30 hrs)

14.15  Case Presentations What is it?
       Chairpersons
       Drs Rosa Henriques de Gouveia, Lisbon and Patrick J. Gallagher, Southampton

Presentations by:
       Allard van der Wal, Amsterdam
       Rahul Bhobe & Kim Suvarna, Sheffield
       Michael Ashworth, London
       Robert Ainsworth, Glasgow
       Junaid Patel & Mary Sheppard, London
       Rosa Henriques de Gouveia, Lisbon
### Friday 10th October

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<td>09.00</td>
<td>Symposium on Congenital Cardiovascular Pathology</td>
<td>Chairpersons Dr Michael Ashworth and Professsor Yen Ho, London</td>
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<td>Dr Andrew Cook, London. How morphology correlates with ultrasound</td>
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<td>Dr Andrew Taylor, London. Imaging of congenital heart disease</td>
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<td>09.45</td>
<td><strong>Cardiovascular Society Lecture</strong></td>
<td>Chair Professor Cristina Basso, Padua</td>
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<td>Professor Michael Gatzoulis, London – Grown-up Congenital Heart Disease</td>
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<td>10.30</td>
<td>Break</td>
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<tr>
<td>11.00</td>
<td>Free papers</td>
<td>Chairs Drs Andrew Cook and Andrew Taylor, London</td>
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<td></td>
<td>Myocyte necrosis as first manifestation of arrhythmogenic right ventricular cardiomyopathy in desmoglein-2 transgenic mice</td>
<td>Pilichou K and others, Padua IT &amp; Amsterdam NL.</td>
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<td>Diagnostic problems in heterotaxy syndromes: sonography vs. autopsy</td>
<td>Niszczota C, Koleśnik A, Szymkiewicz-Dangel Warsaw, PL.</td>
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<td>Morphometry of the fetal atrioventricular septum in Spatio-Temporal Image Correlation (STIC) 4D echocardiography – preliminary data</td>
<td>Koleśnik A Warsaw PL.</td>
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<td>11.30</td>
<td>Drs Michael Ashworth, Yen Ho and Karen McCarthy, Demonstration of congenital heart defects: pre- and post surgical intervention.</td>
<td>Following the demonstration and during lunch, there will be opportunities for delegates to examine specimens “hands on”</td>
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<td>13.00 – 14.00</td>
<td>Lunch and Specimen viewing</td>
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Poster Presentations

1. Theoretical model of functioning of the heart-aorta system in the normal state and in pathology
   
   Lubov Batoroeva, .
   Research Center of Reconstructive Surgery, Siberian Branch of the Russian Academy of Medical Sciences (RAMS), Irkutsk, Russia.

2. Angiogenesis modulation in ischemic conditions through hypoxia upregulated ECM-interacting angiopoietin-like 4
   
   A Cazes1,2, C Chomel1, A Galaup1, E Gomez1, S Le Jan1, L Muller1, S Germain1 and C Monnot1
   INSERM U833-College de France, Paris1
   Pathology Department, Hopital Europeen Georges Pompidou, Paris, France2

3. A case of segmental mediolytic arteriopathy following lung transplant
   
   NU Khan, HM Doran, Departments of Transplant and Pathology, University Hospital of South Manchester NHS Foundation Trust, UK.

4. Obesity as a primary risk factor for sudden cardiac death. Case-control study
   
   J Lucena1, A Rico1, M Santos1, A Fernández2, R Marin1, R Vazquez2.
   Forensic Pathology Service, Institute of Legal Medicine, Seville1, Research Unit, University Hospital of Valme, Seville2.
   Cardiology Service, University Hospital of Puerta del Mar, Cadiz, Spain3

5. Fatal pulmonary thromboembolism in an 8 year-old child with nephrotic syndrome and prothrombin 20210 mutation
   
   J Lucena1, A Rico1, M Santos1, R Gutierrez2, C Martinez2, E Barrero1.
   Forensic Pathology Service, Institute of Legal Medicine, Seville1, Haematology Service, University Hospital of Valme, Seville2, Forensic Histopathology Service, National Institute of Toxicology and Forensic Sciences, Seville, Spain3

6. Undiagnosed phaeochromocytoma and sudden death due to myocardial ischaemia in a 38 yr old woman
   
   J Lucena1, A Rico1, M Saritos1, A Sanchez2, R Gonzalez-Campora2, M Blanco1.
   Forensic Pathology Service, Institute of Legal Medicine, Seville1, Anatomical Pathology Department, University Hospital of Macarena, Seville, Spain3

7. Two cases of cardiac arteriovenous malformations complicated by a local angioproliferative process
   
   L.B. Meijer-Jorna1, R.B.A. van der Brink2, A.C. van der Wal3.
   Department of Pathology1 and Department of Cardiology2, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

8. Presence of a distinct neural component in congenital vascular malformations relates to the histological type and location of the lesion
   
   L.B. Meijer-Jorna, C.M.A.M. van der Horst, A.C. van der Wal
   Academisch Medisch Centrum, University of Amsterdam, The Netherlands

9. Acute thrombosis of coronary arteries and juvenile sudden death: the calcium score does not predict the presence of unstable atherosclerotic plaques.
   
   S Rizzo1, S. Romano1, A. Abudureheman1, A. Morra2, P. Greco2, G. Thieme1, C. Basso1
   University of Padua, Padua, Italy1 and Euganea Medica, Padua, Italy2

10. Alcohol and arrhythmic cardiac death: A prospective and retrospective study of post mortem cases
    
    A H. Templeton1, K. Carter1, N. Sheron2, P. J. Gallagher1, C. Verrill1.
    Department of Pathology1 and Liver Research Group2, University of Southampton UK.
Abstracts of Oral Presentations:

The ISHLT revision: a proposal for a Europe-wide audit?

Annalisa Angelini
Cardiovascular Pathology, University of Padua, Padua, Italy

In late 2005 an Expert Group of the International Society for Heart and Lung Transplantation, led by Dr Susan Stewart, published its long-awaited revision of the 1990 Working Formulation for biopsy diagnosis of acute cellular rejection (Stewart et al JHLT 2005;24:1710-20). A recommendation was that the revised system should be audited to assess reproducibility, shown to have been a problem with the more complex 1990 system. After preliminary discussions with other AECVP transplant pathologists, a transplant working group has been set up to start collaboration between heart transplant pathologists and to create an European Network of Pathologists. The aim of the present study was to assess reproducibility and strength and weakness of ISHLT 2005 new revised Working Formulation for biopsy diagnosis of acute cellular rejection. A call for participation has been sent out in March 2008. Thirty European Centres agreed to take part to the study: Italy (6), Spain (7), United Kingdom (6), France (3), Switzerland (1), Germany (1), Portugal (1), Netherlands (1), Belgium (1), Denmark (1), Finland (1), Czech Republic (1), Turkey (2). Each centre is asked to produce 10 cases which should include different diagnosis and pathological features to cover all the aspects of the classification. Padua will serve as core centre receiving the cases and coding them anonymously and performing the statistical evaluation. The study will be performed on an electronic base with the use of a tele-pathology system.
Abstract

Arrhythmogenic Right Ventricular Cardiomyopathy

Cristina Basso
University of Padua Medical School, Padua, Italy

Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is a genetically determined heart muscle disease associated with ventricular arrhythmias and sudden death, particularly in the young and athletes. The prevalence in the general population has been estimated from 1 in 2000 to 1 in 5000. Inheritance is typically autosomal dominant with low penetrance and variable expressivity and causative mutations mostly in genes encoding proteins of desmosome have been identified. The pathognomonic histologic feature is fibro-fatty replacement of the ventricular myocardium, an injury-repair process following myocyte death, which is no longer considered exclusive of the RV as to support the term arrhythmogenic cardiomyopathy. The clinician should be aware of the possibility of ARVC/D in young individuals with palpitations, syncope or aborted sudden death, left bundle branch block morphology ventricular arrhythmias and T wave inversion in precordial leads on 12 lead ECG. Clinical diagnosis may be achieved by demonstrating function and structure changes of the RV, ECG depolarization and repolarization abnormalities, ventricular arrhythmias and fibro-fatty replacement through endomyocardial biopsy. Although highly specific, the standardized diagnostic criteria lack sensitivity for early disease and their primary application remains in establishing a diagnosis of ARVC/D in probands. The main target is the early detection of concealed forms, which are also at risk of life-threatening arrhythmias and in which electrocardiographic and imaging abnormalities are often subtle or even absent. This underscores the potential role of gene mutational analysis in identifying asymptomatic affected family members of genotyped probands. Restriction of physical exercise, antiarrhythmic drug and beta-blocker therapy, and ICD are life-saving. Risk stratification of patients who would benefit from one or a combination of the above therapies represents the clinical challenge.

Abstract

C4d methodology and interpretation—is standardization feasible?

M M Burke, Harefield Hospital, Royal Brompton & Harefield Hospitals London, UK.

Antibody-mediated rejection (AMR) in the heart causes primary graft dysfunction and is associated with accelerated graft vascular disease (chronic rejection). Diagnosis of clinical AMR requires the demonstration of circulating de novo donor-specific HLA and/or non-HLA antibodies and deposition of antibody and complement C4d in the graft in the presence of graft dysfunction. However at a NIH conference to define AMR in solid organ transplantation, Takemoto et al (Am J Transplant 2004;4:1033-41) also defined latent, silent and sub-clinical forms whose diagnosis depends on various combinations of circulating donor-specific antibody, complement deposition in the graft and tissue damage in the absence of graft dysfunction.

Central to diagnosis of tissue damage is reliable and reproducible demonstration of C4d as a marker of complement deposition in the graft. The 2005 revision of the ISHLT Working Formulation for the diagnosis of cardiac allograft rejection incorporates criteria for the diagnosis of AMR. Staining for C4d and macrophages using immunohistochemistry is a key part of that process but confusion exists regarding its methodology, the significance of the different patterns of staining and their correlation with parameters of graft function and with outcome.

It is essential to standardize methodology and interpretation of C4d staining and its clinical significance to facilitate multicentre studies of diagnosis and treatment. As a first step and to share individual centres’ practice and experience we propose that a questionnaire addressing the above issues is circulated amongst European cardiac transplant pathologists under the aegis of the newly-established Transplant Working Group of the AECP. The results may provide the basis for a recommended approach to this aspect of biopsy diagnosis of AMR in cardiac allografts.
Abstract

Tako-tsubo Cardiomyopathy
Dipartimento di Anatomia Patologica, Università degli Studi di Bari, Italy

We report the case of a 51 year old black woman with a history of hypertension and dyslipidemia hospitalized because of the sudden onset of angina-like chest pain and dyspnoea. ECG showed marked precordial T-wave inversions suggestive of acute myocardial ischemia. The patient underwent cardiac catheterization that revealed mild epicardial coronary artery stenosis, systolic ballooning of the apex and hypercontraction of the basal segment. A diagnosis of Tako-tsubo syndrome was made and two weeks later, after the complete resolution of the wall motion abnormality, the patient was discharged.

A month later, during a Holter ECG test, the patient had a new episode of dyspnoea and died of ventricular fibrillation. The autopsy documented mild left ventricular hypertrophy and marked non occlusive coronary atherosclerosis. Histologically the myocardium showed diffuse contraction band necrosis and areas of subendocardial and intramural previous myocardial infarction. A mild T lymphocytic infiltrate was found around epicardial nerves.

Tako-tsubo syndrome was first described in 1991 in Japan and only small numbers of cases have been reported. Although the exact pathogenesis of Tako-tsubo cardiomyopathy remains unclear, various mechanisms have been proposed. As far as we know this is the first autopsy study of a patient who has died as a consequence of a tako-tsubo cardiomyopathy. Generally this syndrome has generally a favourable outcome and only few studies performed on endomyocardial biopsies are reported in literature.

This study brings a novel contribution to the clarification of the pathogenesis of this rare syndrome. The presence of a lymphocytic perineural infiltrate documented at autopsy could suggest a role for inflammation. It may explain the particular sensitivity to increased levels of catecholamines, suggested as one of the mechanisms of microvascular spasm.

Aortic valve tissue engineering: myth or reality?
A. Chester, Heart Science Centre, Imperial College/National Heart and Lung Institute, Harefield Hospital, Harefield, Middlesex UK

The goal to tissue engineer replacement blood vessels, myocardium and heart valves each present a unique series of challenges. Heart valves in particular require a structure that resembles the native valve while being strong enough to instantly withstand the haemodynamic forces generated by the heart.

Tissue engineering heart valves is an ambitious project and will rely on a multidisciplinary approach. Knowledge and techniques from biologists, engineers, material scientists and clinicians are being combined to make advances towards the goal of providing an implantable, living valve that is able to grow with the patient and recapitulate the complex function of the native valve.

The first steps in this process involve the choice of an appropriate and readily available cell source, which may include stem cells. These cells then need to be combined with a biological or synthetic material that will act as a scaffold. The scaffold needs to be non-toxic to the cells, non-immunogenic and ideally degradable once implanted into the body. The cells and the scaffold are combined to form a tissue construct. The tissue construct must then be conditioned ex-vivo to give it the desirable mechanical properties that will allow it to be durable enough to survive in the circulation.

Some of these steps have been achieved but at the current time a significant amount of work is still required to fulfil all the requirements described above. Similar, but distinctly different approaches are being taken by a number of groups worldwide and time will tell if their efforts will fulfil the theoretical benefits offered by the use of stem cells and tissue engineering.
Abstract

**Atherosclerotic plaque macrophage infiltration does not help identify coronary death individuals**

Dalager S., Kristensen I. B., Paaske, W. P., and Falk, E.

Department of Pathology, Aarhus University Hospital (NBG), Aarhus, Denmark

**Background**

On a group level, it is well established that macrophage infiltration is increased in atherosclerotic plaques from individuals with acute coronary events. In an autopsy study, we wanted to investigate the potential utility of macrophage infiltration as a diagnostic tool on an individual level.

**Methods**

Coronary, carotid, and femoral artery segments from 27 coronary death individuals were compared to those from 71 non-coronary death individuals. We identified the largest plaque in each artery and quantified plaque area and macrophage area (identified by immunohistochemistry as CD68 positivity quantified by digital image analysis).

**Results**

Individuals dying from coronary causes had larger plaque areas in all arteries (P<0.05). Overall, the median intimal macrophage areas were 0.03 mm² (0.6% of intima area) in the coronary arteries, 0.2 mm² (2.4%) in the carotid arteries, and 0.002 mm² (0.07%) in the femoral arteries. The absolute intimal macrophage area was significantly increased in the coronary and femoral arteries in coronary death individuals but overlaps were wide (P<0.05). The same tendency was observed in the carotid arteries but the significance was lost after Bonferroni adjustment.

The ability to correctly identify coronary death individuals was evaluated by logistic regression models for plaque area alone and in combination with macrophage area. Classification accuracy was expressed as the area under the receiver operating characteristic curve (AUC) but inclusion of macrophage area did not result in significant increases in the AUC in any of the examined arteries (≤0.02) compared to the models with plaque area alone.

**Conclusion**

On a group level, we confirmed that intimal macrophage area is increased in most arteries from coronary death individuals but the utility as a diagnostic tool on the individual level is questionable.

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Abstract

**Coronary Artery Vasculopathy – atherosclerosis or not?**

MJ Goddard  Papworth Hospital, Cambridge UK

It is generally true, that more names we give something the less we really know about it as successive authors try to capture the essence of the disease in its name. Thus the narrowing of the coronary arteries that characterises the chronic rejection process has at various times been called coronary artery vasculopathy, graft associated arteriosclerosis, transplant related atherosclerosis and transplant vascular disease to name a few. There are similarities and differences between this chronic rejection process and native atherosclerosis and this talk will briefly cover:

- Epidemiological and risk factors
- Morphology and distribution
- Intimal neovascularisation

Insights into the differences between the two diseases may allow us to better understand the underlying pathological processes and hence raise potential therapeutic targets. Continuing work related to:

- The origin of intimal smooth muscle cells
- The role of the microvasculature of the vasa vasorum

will be presented and their contribution to the pathogenesis of chronic rejection discussed.

Delegates will be invited to answer the question – atherosclerosis or not?
Abstract

Grading Rejection in Cardiac Transplantation
MJ Goddard, Papworth Hospital, Cambridge, UK.

In the early days of cardiac transplantation and following the introduction of the Caves cardiac bioprome which allowed endomyocardial biopsies to be performed, many of the pioneering centres developed their own grading systems of cardiac rejection. With the support of the International Society for Heart and Lung Transplantation and under the guidance of Margaret Billingham, a standardised grading system was introduced and adopted by transplant centres throughout the world. Published in 1990, it proved a very successful system. However, as with any grading system, there are weaknesses and in 2004 the ISHLT undertook a revision of the system reflecting a better understanding of the pathological processes and the significance of different findings to produce a simplified version.

The talk will cover
- The pathological principles of rejection grading
- The old and revised grading system
- Winners and losers in the revision
- An introduction to humoral (antibody-mediated) rejection

The talk will be designed to appeal to a wide audience and no previous transplant pathology experience is required!

Abstract

Lymphatic vasculature is increased in cholesterol rich and calcified atherosclerotic lesions
Ivana Kholová, Galina Dragneva, Seppo Ylä-Herttuala
Department of Biotechnology and Molecular Medicine, A.I. Virtanen Institute, University of Kuopio, Finland

Background
Lymphatic vessels provide the only means for removal of plasma proteins that escape the blood and enter the interstitium. Lymphatic vessels play a role in the pathogenesis of several diseases, such as lymphedema, inflammation, transplant rejection, and cancer. Despite the importance of vasculature in many pathological conditions very little information is available about lymphatic vessels in normal and atherosclerotic coronary arteries.

Methods
Vasculature was assessed by immunohistochemistry with CD 31 and lymphatic endothelium markers D2-40 and LYVE-1 in 20 adult coronary arteries obtained at autopsy.

Results
In progressive atherosclerotic lesions, we observed lymphatic growth in calcified and fibrous plaques in 29% of studied lesions. The areas with lymphangiogenesis were morphologically rich in scattered calcium deposits and cholesterol crystals, however characterised by low or no cellular infiltrate. In progressive atherosclerotic lesions, blood vessels were more frequent (76%). Furthermore, blood vessels were distributed differently in various progressive atherosclerotic lesions. In adventitia, lymphatic vessels accompanied vasa vasorum in both nonatherosclerotic and atherosclerotic arteries.

Conclusions
Progressive atherosclerotic lesions rich in calcium and cholesterol crystals revealed lymphangiogenesis. Nevertheless, progressive atherosclerotic lesions were accompanied more frequently by blood than lymphatic vessels.
Abstract

Morphometry of the fetal atrioventricular septum in Spatio-Temporal Image Correlation (STIC) 4D echocardiography – preliminary data

Adam Kolesnik
Department of Anatomy, Center of Biostructure Research, Medical University of Warsaw, Poland

Background
Examination of fetal heart became a standard part of routine sonographic assessment of fetal development, especially in cases when obstetrical sonographic screening provides indications for fetal echocardiography. Contemporary four-dimensional echocardiography methods are getting more and more popular. The study aimed to assess usefulness of 4D echocardiography in morphometric studies of normal fetal atrioventricular septum (AVS).

Methods
Morphometric analysis of AVS was performed offline using 4D View software on 50 volume files acquired during routine echocardiographic examination of fetuses aged 18-34 weeks using GE Voluson 730 Expert equipment. Files were stored using STIC modality, which allows for reconstruction of cardiac cycle basing on series of heart rate-gated images. TUI (Tomographic Ultrasound Imaging) was used for measurements of height and thickness of AVS.

Results
TUI allowed for reconstruction of 5 perfectly perpendicular slices of AVS equally distributed along this structure in three phases of cardiac cycle. Attachments of leaflets of atrioventricular valves were best visible when the valves have closed completely. Measurements were easiest to perform in the slice situated in the middle of the AVS.

Conclusions
STIC 4D echocardiography showed to the highly valuable method of offline morphometric assessment of echocardiographic data of normal fetal hearts. Planes of measurement and phase of the cardiac cycle are replicable thanks to multiplanar reconstruction and TUI method. Analysis of STIC files can improve standardization of echocardiographic measurements.

Abstract

C4d and antibody-mediated rejection in cardiac allografts: more questions than answers?

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Aim
To audit C4d staining and its relationship to clinical symptoms and the presence of donor specific antibodies (DSA).

Methods
C4d staining had been performed routinely on all endomyocardial transplant biopsies between May 2004 and May 2008 and graded prospectively as 0: negative, 1: weak, 2: moderate or 3: strong staining of interstitial capillaries, other staining patterns were noted. Clinical details were obtained retrospectively. Luminex beads were used for DSA detection and characterization.

Demographics
There were 1443 biopsies in 163 patients with a median age of 49 (14-65), 132 (81%) were males. 90 (54.9%) were transplanted for dilated cardiomyopathy (DCM) and 55 (33.5%) for ischaemic heart disease (IHD). The median time post-transplant (tx) of the biopsies was 171 days (0-5806 days) with each patient having a median of 4 (1-40) biopsies.

Results
Grade 0 C4d staining was present in 1037 (71.9%), grade 1 in 177 (12.3%), 2 in 147 (10.2%), 3 in 46 (3.2%), 36 (2.5%) ungradeable/missing. The highest C4d grading for an individuals biopsy series was a median of 1 (0-3) with 48 (29.3%), 35 (201.3%), 57 (34.8%) and 21 (12.8%) having a highest grade of 0 to 3 respectively. Persistent strong C4d staining was present in 6 (3.7%) of which 4 (66.7%) had a DSA and 5 were symptomatic, in 1 patient the c4d preceeded symptoms. 7 had a single biopsy only a median of 7.9 (3-10.8) years post-tx which showed mod/strong C4d, 3 (42.9%) of these had a DSA. A single patient with a DSA had persistent perimyocyte C4d staining only. 13 (11.7%) patients, 15 (78.9%) male, were found to be positive for DSA a median of 2668 days (0-4581) post-tx. 5 (26.3%) were asymptomatic, 14 (73.7%) symptomatic: 3 had symptoms attributed to ischaemic heart disease/graft vasculopathy and 6 heart failure, dizziness or syncope. 13 (68.4%) DSAs were class II and 6 (31.4%) mixed class I and II. 7 (36.8%) of the DSA positive patients have died; the median time to death was 3.4 (2.9-12.6) years post-tx; a median of 232 (7-839) days after detection of the DSA.

Conclusions
Persistent C4d suggests a DSA. Most DSAs occur late and are class II and a late biopsy with mod/strong C4d staining should prompt a search for a DSA. Perimyocyte C4d staining should not be ignored.
Abstract

Aging, smooth muscle cells and vascular pathobiology
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Epidemiological, autopsy and experimental studies suggest a close link between arterial aging and the clinical manifestation of atherosclerosis, supporting a role of aging as an independent risk factor for atherosclerosis. A variety of structural and biochemical age-related changes occur in the arterial wall with aging. One relevant change with aging is a progressive intimal thickening that is typically diffuse in large human arteries such as the aorta, whereas in coronary vessels it appears eccentric and develops early along with bifurcations. In the tunica media, thickness progressively increases, paralleled by a decrease of cellularity and an increase in glycosaminoglycan and collagen accumulation, whereas the relative elastin content decreases. Areas of progressive calcification are also encountered. In myocardial microvasculature, an endothelial dysfunction also occurs that is likely to contribute to fibrotic myocardial remodelling observed with aging. Smooth muscle cells (SMCs) represent the major arterial cell population. As aging occurs, SMCs progressively migrate from the tunica media and accumulate into the tunica intima. Myointimal thickening may represent the site where low-grade atherogenic stimuli cause earlier development and more severe lesion progression. Intimal SMC accumulation is characterized from a switch from a differentiated to a synthetic phenotype, with reduced cytoskeletal myocytic markers and the expression of new proteins. Aging also associates to changes of SMC proliferative and apoptotic behaviour and response to growth factors, such as transforming growth factor-β1. The alteration of SmC proliferative and apoptotic behaviour and response to growth factors, such as transforming growth factor-β1. The alteration of SmC properties represents a crucial event in the arterial pathobiology, since it contributes to the remodelling and decline of vascular function with aging and favours the progression of atherosclerosis. Increased knowledge of biomolecular mechanisms regulating these events helps to develop new strategies aimed at contrasting the adverse effect of vascular aging.

Abstract

Myocyte necrosis as first manifestation of arrhythmogenic right ventricular cardiomyopathy in desmoglein-2 transgenic mice
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Background
Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a desmosomal cardiomyopathy characterized by ventricular arrhythmias, sudden death and structural alteration of the myocardium. Recently, mutations in the desmoglein-2 (DSG2) gene have been associated with ARVC. The aim of this study was to generate a mouse model of DSG2-related ARVC and to investigate the pathophysiological mechanisms involved in the disorder.

Methods
For cardiac-selective expression, we cloned cDNA sequences encoding WT and mutant (N266S) dsg2 downstream of the murine alpha-MHC promoter. Phenotypic characterization was performed by electrophysiology (4-lead surface ECG), echocardiography (M-mode, B-mode and Doppler), epicardial mapping, histology, electron and confocal microscopy in the two transgenic (Tg) lines expressing comparable levels of transgene.

Results
Tg-NS mice displayed a high incidence (30%) of sudden death at young age (12-20 weeks). ECG analysis on 10 week-old Tg-NS mice demonstrated prolonged QRS-duration and spontaneous ventricular arrhythmias compared to WT and Tg-WT mice (mean QRS 15±1.0 ms vs 10±0.9 ms; n=12 each; p<0.0001). Echocardiographic investigation (M-mode, B-mode, Doppler) showed decreased left ventricular (LV) fractional shortening (LV%FS 13.50±7.70 vs 34.77±4.95; n=5; p<0.002) and increased LV end-systolic and end-diastolic dimensions in Tg-NS mice. Isolated Langendorff-perfused hearts showed conduction slowing and increased arrhythmia inducibility in both ventricles of Tg-NS mice (arrhythmia inducibility: 8/10 in Tg-NS vs. 1/10 in WT/Tg-WT; p=0.0016). Myocyte necrosis was an early histopathologic feature in Tg-NS hearts, marked also by evans blue staining already at 2-3 weeks of age.

This was accompanied by inflammatory infiltration and calcification, followed by fibrosis with biventricular aneurysms at about 4-5 weeks.

Conclusions
Transgenic mice over-expressing the dsg2 mutation N266S recapitulate pathognomonic features of the human ARVC phenotype and provide novel insight into mechanisms underlying DSG2-related ARVC.
Abstract

Diagnostic problems in heterotaxy syndromes: sonography vs. autopsy

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Background

Visceral heterotaxy syndromes (VHS) are defined as abnormalities of determination of left-right symmetry usually described as left or right atrial isomerism (LaI, RAi). However, some cases which do not follow classical patterns and may cause diagnostic problems. The aim of study is to determine whether there are features which can be helpful or misleading in diagnosis of VHS.

Methods

The study was based on 6 cases of VHS diagnosed sonographically and/or on autopsy. The results of ultrasound and post-mortem examinations were re-evaluated and compared.

Results

Three of 6 cases were described as LAI on sonography. The diagnosis was based on morphological features of atrial situs ambiguous, interruption of IVC with azygos vein continuation and complete heart block. One case of RAi was not diagnosed in utero, but it was described on postnatal echocardiography. Two cases were not classified as VHS on ultrasound. The autopsy confirmed diagnosis of 3 cases of LAI. None of them presented polisplenia and in one case the spleen was hypoplastic. In one case diagnosed prenatally as TOF, post-mortem examination revealed isomorphic right atrial appendages, atypical lobation of lungs and asplenia. The last fetus presented otocephaly, which is associated with mutation of SHH gene and LAI. The only features of heterotaxy on autopsy were isomorphic left lungs and main bronchi.

Conclusions

Although there are characteristic features of left and right isomerism, these symptoms can present various forms and simple associations can be misleading. Terms like polisplenia or asplenia seem to be irrelevant. In some cases extracardiac features of VHS can be seen only in autopsy.

Abstract

Imaging of congenital heart disease

Andrew Taylor, UCL Institute of Child Health & Great Ormond Street Hospital for Children

Over the last five years there has been a sea change in the imaging pathways used to investigate patients with congenital heart disease. Prior to 2003 in our own Institution, patients would undergo an echocardiogram, and, if diagnostic, the appropriate management pathway would be followed. For example, a patient with a large ASD seen at echocardiography would be referred for surgical closure of the septal defect. However, if echocardiography was not able to resolve the diagnostic problem, a cardiac catheter was performed. This obviously entailed a general anaesthetic in most patients, an interventional procedure with the potential to damage vascular access, and potentially long screening times with high radiation doses. Since 2003, we have introduced a second tier of investigations: Cardiovascular magnetic resonance (MR) and computed tomography (CT) imaging. Thus, if echocardiography cannot resolve the diagnostic problem, the patients will now be referred for cardiovascular MR/CT. Diagnostic cardiac catheterization is now reserved for those patients where there remain diagnostic dilemmas, when measurement of pressure is essential (for example in the assessment of pulmonary vascular resistance), or when echocardiography suggests that there may be a lesion that requires treatment and a diagnostic/query procedural catheter is performed. Over this time period, we have seen a gradual increase in the number of cardiovascular MR and CT investigations, and interestingly, the overall number of diagnostic tests we perform has also increased significantly.

In this presentation, I will outline the role of cross-sectional imaging in the management pathway of patients with congenital heart disease, both children and adults.
Abstract

Classification and nomenclature of cardiomyopathy
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Cardiomyopathies are disease of the myocardium with cardiac dysfunction. Myocardial damage due to coronary, valve, congenital heart diseases as well as systemic or pulmonary hypertension is excluded.

Cardiomyopathies may be primary, when the disease is confined to the heart muscle, or secondary, where the heart muscle is involved in the setting of systemic disease. In terms of etiology, the disorders may be genetic, acquired or mixed acquired-genetic. Inflammatory cardiomyopathy is an example of acquired heart muscle disease.

Cardiac dysfunction may be divided into mechanical (with systolic or diastolic impairment) or electrical (with arrhythmias or conduction disturbances). Moreover, cardiomyopathies may present with or without structural abnormalities.

Dilated, hypertrophic, arrhythmogenic and restrictive cardiomyopathies clearly present with structural abnormalities. In case of hereditary disorders, they show mutations of genes coding defective proteins of the cytoskeleton (dilated), sarcomere (hypertrophic and restrictive) and desmosome (arrhythmogenic). The genetically determined atrio-ventricular block (Lenègre disease) has been proven to be a genetically determined fibrosis of His bundle and bundle branches due to sodium channelopathy.

Other genetically determined cardiomyopathies with electrical dysfunction and structurally normal heart are characterized by ion channel disease, usually presenting with ECG abnormalities:

- the long and short QT syndrome with abnormal QT interval, mostly due to potassium channelopathies;
- the Brugada syndrome with ST segment elevation, due to sodium channelopathy;
- the catecholaminergic polymorphic ventricular tachycardia, with normal basal ECG and ventricular tachyarrhythmias on effort or emotion, due to calcium ryanodine receptor 2 gene defect at the smooth sarcoplasmic reticulum.

The concept of cardiomyopathy with structural abnormalities, means that in vivo imaging techniques should be accomplished for the diagnosis, whereas ECG should be employed for the diagnosis of cardiomyopathies without structural abnormalities.

Mutational analysis by genetic screening is becoming mandatory as routine diagnostic tool in hereditary diseases.

Abstract

Effect of statin therapy on developmental vascular disease
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In the rat, dietary protein restriction during pregnancy results in raised blood pressure and endothelial dysfunction in the offspring. Statins have pleiotropic actions beyond their lipid lowering effects, including increasing NO bioavailability and reduction of oxidative damage. We tested the effect of statin treatment in our cholesterol-independent model of endothelial dysfunction.

Wistar rats were fed a control (C; 18% casein) or protein restricted (PR; 9% casein) diet throughout pregnancy and returned to standard chow postpartum. At weaning a subset of the PR group were given atorvastatin (FRS, 10 mg/kg/day) in the drinking water. At 475 days of age male offspring were sacrificed by CO2 inhalation. Small mesenteric arteries were mounted in a myograph and relaxation to aCh and Sodium Nitroprusside (SNP) were assessed. Samples of artery were also frozen for molecular biology. Differences were assessed by one-way ANOVA. Significance was accepted at p<0.05.

In the PR offspring endothelial-dependent vasodilation to ACh was blunted compared to controls and restored by statin treatment. Similar responses to were seen to the NO-donor SNP. Mesenteric artery levels of eNOS mRNA were similar between the groups but levels of Superoxide Dismutase were significantly reduced in the PR group compared to C and restored in the PRS group (p<0.05).

This data suggests that chronic atorvastatin therapy may restore endothelial function and NO bioavailability through modulation of oxidative pathways in this model.

This work was supported by the British Heart Foundation & Pfizer
Abstracts of Poster Presentations:

**Theoretical model of functioning of the Heart–Aorta system in the normal state and in pathology**

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This research presents an original theoretical model of cardiovascular system functioning: in normal state and in deficit of aortal compliance.

We suppose to consider working aorta as a sphere with all the time variable contour, but not as a cylinder structure.

In the research we designate additional hemodynamic mechanisms, which promote blood kinetics through elastic vessels, that allows to reduce myocard load considerably.

We show the conditions for “ideal” functioning Heart–Aorta system. In such conditions the system should work almost without energy loss.

We give a self-contained functional dynamic structural unit of blood stream system. This unit is “Artery wall – Blood” and it is an essential condition of perfect vessel functionality.

In this research we show divergence when blood stream parameters cause beginning and progression of pathological processes in aorta. Here we designate and list the etiological reasons of disease onset in general and atherosclerosis in particular.

Pathogenetic mechanisms of myocard damage if aorta elasticity is corrupted are established in this research.

We give the definition of “Silent myocardial ischemia”. Its pathophysiological essential is designated.
Angiogenesis modulation in ischemic conditions through hypoxia upregulated ECM-interacting angiopoietin-like 4

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Background

Angiopoietin-like 4 (ANGPTL4) is a member of the Angiopoietin family of secreted proteins, involved in angiogenesis and vessel maintenance.

Methods and Results

By cDNA RDA we identified angptl4 as a gene induced by hypoxia in endothelial cells. We showed the expression of ANGPTL4 in the vessels of hypoxic areas from human critical leg ischemia samples and in a mouse model of femoral artery ligation. In the heart, focal expression in myocytes and vessels in the infarcted areas was evidenced.

We further investigated the protein in vitro and found that in response to hypoxia, endogenous ANGPTL4 accumulates in the subendothelial extracellular matrix (ECM). Although the secreted protein undergoes proteolysis, only full-length ANGPTL4 interacts with the ECM, through its coiled-coil domain (CCD). The strong interaction of ANGPTL4 with the ECM is heparin/heparan sulfate proteoglycan dependent. The angiogenic function of the ECM-bound full-length protein or its CCD alone was investigated using the purified immobilized proteins. Immobilized ANGPTL4 limits the formation of actin stress fibers and focal contacts in the endothelial cells and inhibits their adhesion. Immobilized ANGPTL4 also decreases motility, sprouting of endothelial cells and tube formation. As full-length ANGPTL4, CCD inhibits EC adhesion, motility and tube formation.

Conclusions

ANGPTL4 overexpressed in various ischemic pathologies is able to interact with the endothelial microenvironment where it can modulate angiogenesis through an autocrine pathway. We are currently investigating the role of the protein in vivo in the above mentioned ischemic conditions, using angptl4−/− mice.
**Poster Abstract**

**Obesity as a primary risk factor for sudden cardiac death. Case-control study**

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**Background**

Obesity has become a growing public health problem which is associated with an increased morbidity and mortality, especially in cardiovascular diseases. The aim is to analyze obesity as an independent risk factor for sudden-unexpected death (SUD), mainly of cardiovascular origin, in the province of Seville.

**Methods**

Prospective study of a series of forensic autopsies performed at the Forensic Pathology Service, Institute of Legal Medicine of Seville. Anthropometric data (weight, BMI and waist circumference [WC]), heart weight and left ventricular thickness of the SUD cases (162 m, 26 w) were compared with a control group of 179 suicides and accidental deaths (147 m, 32 w), with no cardiovascular pathology. Median age of SUD group was 52.5 yr [44; 63.7] for men and 56 yr [44.7; 64.7] for women. Median age of controls was 35 yr [27.5; 45] for men and 32.5 yr [24; 52] for women.

**Results**

SUD was of cardiovascular origin in 178 cases (95%). With regard to BMI, 79.5% of men from the SUD group and 58.5% of men from controls had a BMI > 25 kg/m² (p < 0.0005; 95% confidence interval [CI95] 2.6-5.3). In women, 76.8% of cases and 40.6% of controls had a BMI > 25 kg/m² (p = 0.001; CI95 2.9-10.9). According to accepted international criteria (WC > 102/88 cm for men/women), 36.2% of men and 73.1% of women from cases had visceral obesity. These frequencies are almost twice the control rates (men: 14.3%; women: 43.7%) (p < 0.0005; CI95 7.6-13.8 in men and p < 0.0005; CI95 8.9-24.5 for women). Hearts were heavier in cases than in controls, in men 513 g [430; 603.7] vs 363 g [328; 398] (p < 0.0005; CI95 138.7-185) as in women (400 g [341.2; 481.2] vs 258 g [239.7; 302.3]) (p < 0.0005; CI95 89.2-188.9).

**Conclusions**

These results clearly indicate that obesity must be considered as a primary risk factor for sudden cardiac death. Public health campaigns addressed to reduce obesity may contribute to the decrease of sudden cardiac death.

Supported by FIS G078/03 and FIS PI052450. Spanish Ministry of Health.

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**Poster Abstract**

**Fatal pulmonary thromboembolism in an 8 year-old child with nephrotic syndrome and prothrombin 20210 mutation**

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**Background**

The incidence of thromboembolic events in children is very low. However, when diagnosed they are usually associated with an underlying disease, the presence of a risk factor or both.

**Case Report**

We report the case of an 8-year-old child with a corticoid-dependant nephrotic syndrome who was admitted to hospital as a result of bronchopneumonia. He received treatment with diuretics, corticoids and antibiotics with initial improvement of symptoms. However, in the following week he presented dyspnea with tachypnoea and died suddenly in the 14th day of hospital admission. Prophylactic anticoagulation was not performed at any time. The forensic autopsy (post-mortem delay of 6 hours) discovered the presence of massive pulmonary embolism (PE) with hemorrhagic infarction of both lungs and a large thrombus adhered to the right ventricle free wall. Deep veins thrombosis was excluded after careful examination. Hematologic study revealed a heterozygote prothrombin 20210 mutation.

**Conclusion**

Both inherited and acquired conditions contributed to the development of thrombosis and PE in this child. This case outlines the importance of the post-mortem study for the correct diagnosis of the cause and manner of death as well as the genetic familiar counselling.
**Undiagnosed phaeochromocytoma and sudden death due to myocardial ischaemia in a 38 yr old woman**

J Lucena¹, A Rico¹, M Santos¹, A Sanchez², R Gonzalez-Camposa², M Blanco².

**Background**

Pheochromocytomas are rare but possible causes of sudden death. In spite of the serious and potentially lethal cardiovascular complications of these tumours, due to the potent effects of the paroxysmal catecholamine’s release, only a few cases of pheochromocytoma presenting as an acute myocardial infarction have been reported in the literature.

**Case Report**

A 38-year-old woman, with no relevant personal antecedents, complained of vomiting, abdominal pain, palpitations and tachycardia (heart rate of 150 bpm), headache and dizziness that worsened after being treated with Metamizol. She was taken to the emergency department of a hospital, and during her admission, the patient became anxious and dyspnoeic requiring mechanical ventilation. Physical examination revealed a blood pressure of 140/80 mmHg and a regular heart rate of 180 bpm. Laboratory tests demonstrated hyperglycemia and metabolic acidosis. The ECG showed sinus tachycardia with ST segment elevation in leads III, aVF, V2 and V3, and symmetric T wave inversion in leads V4 thru V6. Toxicological analysis in urine was only positive for cannabis. A few hours after the admission, she suffered a cardio respiratory arrest and resuscitation was unsuccessful. Hospital and relatives requested a forensic autopsy with the aim to know the cause and the manner of the death. At necropsy, a pheochromocytoma of the right adrenal gland (4.5 x 3.5 cm, 35 g) was found. Examination of the heart (290 g, left ventricular wall 11 mm) demonstrated an acute myocardial infarction with patent coronary arteries.

**Conclusions**

This case illustrates the importance of including pheochromocytoma in the differential diagnosis of patients with signs and symptoms of an atypical myocardial infarction, especially in the absence of coronary atherosclerosis.

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**Two cases of cardiac arteriovenous malformations complicated by a local angioproliferative process**

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**Introduction**

Vascular malformations of the heart are extremely rare with only two cases of arteriovenous malformations (AVM) reported. We investigated two additional cases.

**Case description**

The first case is a 23-year old boy in whom endomyocardial biopsy revealed a proliferative process on which angiomatosis was initially diagnosed. The patient died three months later of untreatable cardiac failure. At autopsy an AVM composed of large, but dysplastic arteries and veins was found in the perfusion territory of the left descending coronary artery. Amidst the vessels of the malformation we additionally observed large amounts of dilated small vessels, but not the immature capillaries as were seen in the initial biopsy. We considered this highly suggestive for maturation of the angioproliferative process.

The second patient was a 14-year old boy who was known for all his life with a asymmetrical hypertrophy of the left ventricle, with a clinical working diagnosis of hypertrophic cardiomyopathy. He witnessed sudden death due to ventricle fibrillation. At autopsy an asymmetrical hypertrophy of the left ventricle and septum was found, which was histologically composed of large mature vessels of AVM incorporated in a solid growth of immature capillaries. Scarce myocardial disarray was only found in the area affected by AVM, but not elsewhere in the heart.

**Epicrise**

Vascular malformations (VM) are congenital lesions which are present at birth and usually grow very slowly progressive. The cases we present likely became symptomatic due to sudden increase in mass of the AVM lesion leading to fatal electrical and mechanical complications in the respective cases. Such angioproliferative episodes in AVM have also been reported by us to occur in circa 30% of similar AVM lesions in skin and soft tissue. Such angioproliferative reactions are considered to be reactive proliferations and probably relate to local tissue hypoxia.
Poster Abstract

**Presence of a distinct neural component in congenital vascular malformations relates to the histological type and location of the lesion**

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**Aim**
To investigate the presence and extent of an intralesional component of nerve bundles in congenital vascular malformations of soft tissues.

**Methods and results**
Resection specimens of 130 congenital vascular malformations were retrospectively screened for the presence and extent of intralesional mature nerve bundles. Lesions were histologically categorized in arteriovenous malformations (AVM, n=83), pure venous malformations (VM, n=31) or lymphatic-venous malformations (LVM, n=16). For identification of nerves, all sections were immunostained with anti-S100. GLUT-1 immunostaining excluded the presence of infantile hemangiomas in these series. 96 of 130 cases (74%) showed a substantial increase of intralesional nerves in close apposition to the vessels, which appeared to be more extensive in head and neck region compared to other topographic sites. Most cases of AVM showed an increase in nerve elements (87%), which was more than in pure VM (55%), whereas in cases of LVM the areas composed of lymphatic vessels showed an almost complete absence of nerves. Prior surgery in the malformation gave no different nerve pattern compared to de novo cases.

**Conclusion**
The abundant presence of intralesional nerves in the majority of vascular malformations suggests that, at least in a large subset of lesions, neural components are an integral part of the developmental disorder. This is particularly evident in AVM and lesions that arise in the head and neck region of the body.

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Poster Abstract

**Acute thrombosis of coronary arteries and juvenile sudden death: the calcium score does not predict the presence of unstable atherosclerotic plaques.**

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**Background**
The coronary calcium score (CCS) assessed by the multislice computed tomography (MSCT) seems to be an independent predictor of cardiovascular events in addition to the other cardiovascular risk factors. The aim of the present study was to measure the CCS in young patients (< 35 years old) suddenly died from acute coronary thrombosis.

**Material and methods**
Among 77 consecutive cases of juvenile sudden death due to coronary atherosclerosis, 26 cases (34%) aged 22 to 35 years (average 32 ± 2.3, M/F 23/3) showed an acute thrombosis. Formalin-fixed hearts were examined ex-vivo by MSCT 16 slides (LightSpeed Plus, General Electric Company, Milwaukee, WI, USA). 20 consecutive cases of elder victims of coronary sudden death (inclusive age between 44 and 76 years, average 59 ± 12, M/F 17/3) were used as controls. The CCS was measured through Agatston score and volume score. Serial sections of all the principal subepicardic coronary arteries were analyzed and routinely processed with H&E, Heidenhain trichromic and von Kossa staining.

**Results**
Coronary arteries calcification was found by ex-vivo MSCT analyses in 9 (35%) young people and in 13 (65%) controls (p=0.04), with a mean value of CCS of 21 Agatston Equivalent (volume score 21,5) and 269 Agatston Equivalent (volume score 316) respectively. Comparing the morphophatologic results in young vs controls, a multivascular disease was found in 10 (38%) vs 16 (80%) cases (p=0.003); fibrolipidic plaques with abundant lipidic core in 9 (90%) vs 20 (100%) cases, fibrous cap rupture in 8 (31%) vs 20 (100%) cases and endothelial erosion in 18 (69%) vs 0 (all p<0.0001). In the young people a positive CCS was identified in 9 (90%) cases with multivascular disease vs nobody with monovascular disease and in 2 (11%) cases with endothelial erosion vs 7 (87%) with fibrous cap rupture (all p<0.001).

**Conclusions**
In the young people the CCS is a strong predictor of the extension of the coronary arteries pathology but not of the instability of atherosclerotic plaques complicated by acute thrombosis. Moreover a negative CCS does not exclude the presence of coronary atherosclerosis that consists mainly of a monovascular pathology with exuberant intimal fibrocellular proliferation devoid of lipidic core.
Poster Abstract

Alcohol and arrhythmic cardiac death: A prospective and retrospective study of post mortem cases

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Background
Increasing alcohol consumption within the United Kingdom has lead to an increase in alcohol related deaths. Despite the fact that excess alcohol is a known causation of cardiac arrhythmia, which can in turn lead to death, we have observed from experience that this is not a commonly stated cause of death at post mortem. The aim of this study was to assess the prevalence of deaths from a presumed cardiac arrhythmia associated with excess alcohol consumption in post mortem cases.

Methods
Adult post mortems taking place at Southampton General Hospital between October 2007 and March 2008 were observed and post mortems having taken place during January 2006 - February 2007 were assessed retrospectively. Routinely recorded data including past medical history and pathological findings in the heart, lungs and liver were documented. All cardiac deaths with evidence of excess alcohol consumption were reviewed.

Results
1292 post mortems were included. 4 cases were documented to have died from the “classical” scenario of a presumed cardiac arrhythmia associated with evidence of alcohol excess and were certified as such. A further 13 cases were identified in which alcohol associated arrhythmia could have contributed to or caused death. These 17 cases accounted for 1.3% of all deaths surveyed.

Conclusions
Death from a presumed cardiac arrhythmia associated with excess alcohol consumption appears to be an understated cause of death in post mortem cases. This scenario would benefit from becoming a better defined entity and also from improved recognition amongst pathologists.
Sponsorship

The logos of our various sponsors are displayed on the opposite page. We thank the British Heart Foundation and the Pathological Society of Great Britain and Ireland for their generosity. Both have given UK Cardiac Pathology strong support in recent years.

Two patient support organisations have been especially generous and we hope you will visit their stands on the lower ground floor. The Cardiomyopathy Association has sponsored the Thursday Educational day. We are very grateful to Robert Hall and Perry Elliott for organising both this symposium and an education day last November on the Pathology of Sudden Death. A few years ago we could not have imagined just how much help we are receiving from patient support groups.

SADS UK has been involved with pathologists and coroners since the inception of the charity in March 2000. The Founder of the charity, Anne Jolly is on the committee at the Department of Health Pathologist/Coroner Interest Group. The charity responded jointly with other stakeholders on amendments to the draft charter for bereaved people who come into contact with a reformed coroner system, and on proposals for the Coroners and Death Certification Bill. These changes are eagerly awaited by British cardiovascular pathologists. SADS UK regularly attend meetings of the UK Cardiac Pathology Network and we are most grateful for their support.
The cardiac charity SADS UK sponsored the printing of this programme