

The Bulletin

of

The British Society for Cardiovascular Research

Registered Charity Number: 1011141

Vol. 15 No. 2

April 2002

www.kcl.ac.uk/bscr

The BSCR is sponsored by



The Bulletin

The Publication of The British Society for Cardiovascular Research

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Editorial

Welcome to the January 2002 issue of *The Bulletin*. We would like to wish all BSCR members and readers of *The Bulletin* a happy and prosperous new year.

Since the last issue of *The Bulletin* our editor, Dr Helen Maddock has taken up a senior lectureship position at the Department of Applied Human Physiology, Coventry University. We wish Helen much success and happiness in her new post.

This issue features a review article entitled '*Molecular Interactions of Purinoceptor Subtypes found on Blood Platelets*', written by Dr Andrea Townsend-Nicholson of the Department of

Biochemistry and Molecular Biology at University College London.

The new year brings a considerable change to the structure of the BSCR Committee. Dr Barbara McDermott succeeds Dr Gary Baxter as Secretary of the Society and we are pleased to include Barbara's first Column in this issue.

We can look forward to a number of exciting meetings in 2002. These are listed in the Secretary's Column and further details of the BSCR Spring and postponed Autumn meetings are provided towards the back of this issue of *The Bulletin*.

Helen Maddock and Nicola Smart

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Cover design copyright Siân Rees and Anthony Wright, 1997

LABORATORY PROFILE:

by Professor Ken Broadley

Cardiopulmonary Pharmacology Group
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It all started with a fascination for the Langendorff (1895) heart preparation. Berne (1980) had shown that coronary flow was regulated by the oxygen tension of the heart, a process known as coronary autoregulation, and that adenosine was a primary candidate for mediator of the coronary vasodilatation due to hypoxia. There was abundant evidence that adenosine was released from normoxic hearts and increased during periods of hypoxia and by cardiac stimulation by catecholamines and histamine. However, functional demonstration was lacking that adenosine, among the other candidates, was the vasodilator mediator. The inspiration to demonstrate a functional response to adenosine released by the heart was the pioneering experiments of Loewi (1921). He was the first to show the release of a neurotransmitter substance, *vagusstoff*, subsequently identified as acetylcholine. Stimulation of the vago-sympathetic trunk of a frog isolated heart resulted in slowing and reduced force of contraction. When the perfusate was taken to a recipient heart, after stimulation of the donor, this heart was also inhibited. This design was adopted for the Langendorff heart, the effluent arising from the cannulated pulmonary artery of a donor heart being re-oxygenated and taken to supply a recipient heart. The release of a coronary vasodilator substance from the donor heart by catecholamines, pacing and pacing was clearly demonstrated by this technique (Broadley & Rothaul, 1981; Rothaul & Broadley, 1981). These early experiments, however, showed that adenosine was not the mediator and they have not been followed up.

So started the interest in adenosine that has remained a focus of the group's attention to this day, but the move was to its cardiac effects. Look up the cellular mechanism of action of adenosine in slowing the firing rate of the sinu-atrial node and reducing force of contraction of atrial myocardium (adenosine has no direct negative inotropic action on ventricular muscle) in many basic textbooks and it will state that it is due

entirely to stimulation of adenosine A_1 receptors coupled via a G protein to K^+ channels, which are of the same type as linked to muscarinic M_2 receptors ($I_{K_{ach}}$) (Waller, Renwick & Hillier, 2001). This stimulates potassium efflux, which reduces action potential duration and reduces the time available for calcium influx and therefore the force of contraction. We confirmed that adenosine analogues and carbachol indeed enhanced the efflux of ^{86}Rb , an index of K^+ efflux, from isolated atria, and that this was inhibited by the non-selective K^+ channel inhibitor, 4-aminopyridine (Urquhart, Rothaul & Broadley, 1991). However, the negative inotropic responses to adenosine and A_1 receptor agonists were not inhibited by 4-aminopyridine, but the onset of the response is merely slowed (Urquhart, Ford & Broadley, 1993; Ford & Broadley, 1999; Gardner & Broadley, 1999a). Thus, we conclude that there is an additional mechanism for the negative inotropy of atrial muscle not involving $I_{K_{ach}}$ channels. A second line of evidence that supports this hypothesis derives from our studies with purinoceptor antagonists against the cardiac responses. The initial shifts of the dose-response curves for the negative inotropic and chronotropic responses of left and right atria to adenosine agonists by P_1 -receptor antagonists (cyclopentyltheophylline or 8-(*p*-sulfophenyl)theophylline, 8-sPT) is parallel and typical of competitive antagonism and of A_1 receptor involvement. However, as the concentration of antagonist increases, there is no further shift of the curves (Gardner & Broadley, 1999b). In the presence of 4-aminopyridine to block K^+ channels, antagonism of adenosine agonists by 8-sPT was significantly attenuated (Gardner & Broadley, 1999a). Thus, when one of the transduction pathways for the negative inotropic response is blocked (the $I_{K_{ach}}$ channel), the residual response is resistant to A_1 receptor blockade. A likely candidate for the second transduction pathway is through the closure of Ca^{2+} channels. Where there is duality of coupling of a common receptor to more than



The group on the landing of the Welsh School of Pharmacy in front of the 'Old Pharmacy'. Left to right: Dr Tim Martin (Muscagen post doc), Barra Nevin (PhD student), Dr Subas Parija (Wellcome Trust Visiting Fellow), Ken Broadley, Lisa Yates (BHF student), Amar Hamrouni (PhD student), Nicola Smith (BBSRC/gsk student), Sophia Fernandez-Rodriguez (PhD student), Matt Lewis-Lakelin (Post doc), Jill Clark (PhD student), Dr Emma Kidd (Lecturer), Dr Kathryn Baker (BHF post doc).

one transduction pathway has been referred to as receptor-transducer promiscuity. Current studies are underway by Subas Parija, a Wellcome Trust Travel Fellow from India, to examine whether the duality of coupling involves separate G proteins linked to the common A_1 receptor. Alternatively, a common G protein may be involved which cleaves into its G_α and $G_\beta\gamma$ subunits and these may independently be involved in Ca^{2+} channel closure and K^+ channel opening, respectively.

Another aspect of the pharmacology of adenosine that has occupied several members of the group over the past six years has been its cardioprotective activity. The

effects of adenosine agonists on myocardial stunning have been studied in two models of ischaemia. In isolated working hearts exposed to 30 min of ischaemia, followed by reperfusion, myocardial stunning was seen as a reduced recovery of aortic output after reperfusion. The A_{2A} receptor agonist, CGS21680, improved recovery probably by a coronary vasodilator action (Maddock et al 2002). The selective A_3 receptor agonist, IB-MECA also exerted a cardioprotective effect in working hearts by improving the functional recovery, but this effect only occurred when it was introduced at reperfusion and not when added during ischaemia (Maddock et al 1997). The second model uses isolated atria or papillary muscles exposed to

hypoxia or simulated ischaemia (gassing with N₂/CO₂ 95/5 and removing glucose substrate) followed by re-oxygenation, which display a contracture during ischaemia and reduced contractile function on recovery (stunning). The A₃ agonist IB-MECA added at regassing, but not beforehand or during the ischaemia, improves functional recovery of contractility (Gardner & Broadley, 1997). These studies have been and through a studentship to Lisa Yates, are currently being supported by the BHF to examine the underlying mechanisms. That A₃ receptors are involved in the cardioprotection is clear from its prevention by the newly available A₃ receptor antagonists. We are now examining why the protection only occurs when IB-MECA is added at regassing and whether this is due to desensitization of the A₃ receptors when it is added too early. We are attempting to identify the presence of A₃ receptors in the cardiac tissue by radioligand binding to membrane preparations and by autoradiography, using the agonist radioligand, [¹²⁵I]-AB-MECA. Immunohistochemistry is also being applied to tissue slices using a polyclonal antibody against the human A₃ receptor. These studies are being led by Dr Emma Kidd who was appointed to a lectureship and joined the group three years ago. The impressive cardioprotective activity of the A₃ agonist has resulted in a programme to develop a more selective and potent novel A₃ agonist for potential application in myocardial infarction patients. This is one target of a project supported by Muscagen, a Company set up in the Department with venture capital funding, and supports a post doc for the pharmacology (Dr Tim Martin)

In a return to where it all started with the Langendorff preparation, another parallel project supported with a BHF postdoctoral research fellow (Dr Kathryn Baker) is examining the cardiac and coronary vascular effects of two social drugs; cathinone, the active constituent of khat leaves and 'ecstasy'. The khat story was brought to our attention in Cardiff by a cardiologist working in Yemen (Dr Ahmed Al-Motarreb) who was undertaking a PhD in the group. He had noted an increasing incidence of myocardial infarction in Yemen among young men (<50 years) and that this was associated with their khat chewing habit. There was a shift in the circadian rhythm of presentation with MI from the early hours in non-khat chewers to late afternoon and evening in khat chewers, which coincides with the khat chewing session (Al-Motarreb, Al-Kebsi, Al-Adhi and Broadley, 2002).

Cathinone is structurally related to amphetamine and to 'ecstasy' and the incidence of cardiac dysfunction and cardiac failure and death of cardiac origin from their abuse suggested to us that they may all have a common mechanism of cardiac toxicity. Indeed, we have now shown that cathinone and ecstasy are coronary constrictors and the present project is determining the mechanism(s) involved.

The group is due to grow this Autumn with the appointment of Dr Will Ford from the University of Cambridge. He will be continuing the tradition of using Langendorff hearts to further his studies on the cardiac, coronary vascular and cardioprotective effects of cannabinoids.

The photograph of the members of the cardiopulmonary pharmacology group reflects the fact that we work on both the cardiac and respiratory systems. Only the work of the group on the cardiovascular system has been described in this Laboratory Profile, since this has more relevance to the membership of the BSCR. Some of the group are engaged in research on the pulmonary effects of adenosine and related mediators of the asthmatic response; but that is another story!

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Laboratory Profile Articles for *The Bulletin*

Would you like to write a Lab Profile for the BSCR Bulletin? Laboratory Profiles are an opportunity to let BSCR members know about your partiular research area and also provide an insight into your research field. We are keen to hear from anyone in cardiovascular research who would be willing to write for *The Bulletin*.

If you are interested, please contact the Bulletin editors with your ideas:
Helen (h.maddock@coventry.ac.uk) or Nicola (N.Smart@ich.ucl.ac.uk)

Secretary's Column

It does not seem long since my 'introductory' column in January, which brought together news about the new committee membership, new funding and, most importantly, the exciting schedule of forthcoming meetings. This will be brief, by comparison, highlighting new developments in these areas. Firstly, we are delighted to be the recipient of major sponsorship from Aventis, who have indicated that they will continue to fund BSCR activities in 2002. This will ensure a healthy state of finances at least in the immediate future and contribute enormously to our ability to run high quality meetings and symposia.

It is time again when we must think ahead to filling the gaps on the committee which will arise when four of the current members retire from their term of office at the end of this year. Nominations are required for these posts, to be taken up from January 2003, and a form is included for the purpose. Please note that the deadline for nominations is 17 May, so that in the event of a high level of enthusiasm for these positions, details of the nominations can be published and a postal ballot held before the next AGM to be held at the Autumn meeting.

The Autumn meeting, to be held at the University of Bristol is advertised on the back cover of this edition of the Bulletin, and registration and abstract forms are included as inserts. Details of this year's BSCR symposium at the British Cardiac Society Meeting, to be held at the Harrogate International Centre on 15th May 2002, are also included in this issue. Meanwhile, I hope to see many of you at the Spring meeting on 11th-12th April in Reading.

Barbara McDermott



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BRITISH SOCIETY FOR CARDIOVASCULAR RESEARCH

Vacancies on Executive Committee

At the end of 2002 the following members will retire from the Committee, having completed 3 years of service: Dr Adrian Brady, Dr Sarah George, Professor Mike Marber, Dr Lip Bun Tan.

As such, there will be vacancies for 4 new members of the Committee. Nominations are therefore required for these posts, to be taken up from January 2003.

Nominations of both *clinically-qualified investigators* and *basic scientists* are encouraged. If the number of Nominees exceeds the number of vacancies, elections will take place by postal ballot before the AGM. Clause 7b of the Constitution stipulates that “nominations for members of the committee must be made by full members of the Association in writing and must be in the hands of the Secretary at least 60 days before the Annual General Meeting”. This year the AGM will be held at the BSCR Meeting in Bristol, on 6/7 September 2002. To allow time for a postal ballot (if required) to be completed prior to the AGM, nominations must be received by **17 May 2002**.

Please cut out or photocopy the form on the reverse of this page for nominations.

BRITISH SOCIETY FOR CARDIOVASCULAR RESEARCH

Nomination Form for Committee Membership

Name of proposed Committee Member:

Year of first joining the Society:

Please provide brief biographical details and a statement of reasons for wanting to serve on the Committee (please do not exceed the space provided below). In the event that a postal ballot is required, these details will be printed in the Quarterly Bulletin along with a passport-sized photograph (which should be provided with the nomination).

I agree to stand for election to the BSCR Committee

Signature:

Date:

Proposed by:

(BLOCK CAPITALS)

Signature:

Seconded by:

(BLOCK CAPITALS)

Signature:

Please return the completed form by **17 May 2002** to the Secretary:

Dr Barbara McDermott
Department of Therapeutics and Pharmacology, Queen's University Belfast,
Whitla Medical Building, 97 Lisburn Road, Belfast BT9 7BL

Second Announcement

CARDIOVASCULAR DEVELOPMENT

A meeting in association with the
Working Group on Developmental Anatomy & Pathology
European Society of Cardiology

Thursday 4th July - Saturday 6th July 2002

Conference Centre, National Heart & Lung Institute
Imperial College, Faculty of Medicine
London, UK

Organiser: Paul JR Barton

Meeting outline: This meeting will address current concepts in molecular, cellular and anatomical development of the heart and vessels. Topics will include regulation of gene expression, cell cycle, cell migration, regionality and laterality, valve formation and the cardiac conduction system. The meeting will incorporate aspects of normal and abnormal human, rodent, chick and *Xenopus* heart development in naturally occurring and genetically modified models.

Speakers include: Robert Anderson (London), Annalisa Angelini (Padua), Gavin Brooks (Reading), Nigel Brown (London), Gilda Caruso (Bari), Steven Coppen (London), Deborah Henderson (Newcastle), Adrianna Gittenberger de Groot (Leiden), Robert Kelly (Paris), Jorg Manner (Gottingen), Tim Mohun (London), Antoon Moorman (Amsterdam), Andrew Newby (Bristol), Tomas Santalucia (London), Peter Scambler (London), Gaetano Thiene (Padua), Penny Thomas (London), Sandra Webb (London), Arnold Wenink (Leiden), and Siew Yen Ho (London).

Communications: Abstracts on any relevant topics are welcomed for poster presentation, and a number will be selected for oral presentations. Instructions for submitting an abstract are available from the Conference Secretary. Deadline for submission of abstracts **10 May 2002**

Registration: Registration fee £60. Registration forms are available from the Conference Secretary. Deadline for registration **10 May 2002**.

Accommodation: Discount rate hotel accommodation is available through Imperial College Accommodation Office 020 7594 9507/11.

The National Heart & Lung Institute is situated in Chelsea in central London (nearest underground station South Kensington -Circle/District/Piccadilly lines).

Local Organising Committee:

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Nigel J Brand
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CME/CPD approval applied for

BSCR Workshop Report: QT Prolongation and Torsade de Pointes

by Dr Susan Coker (organiser)
3rd May 2001, The University of Liverpool, Foresight Centre

Torsade de pointes is a form of polymorphic ventricular tachycardia that exhibits a characteristic twisting of QRS complexes around the isoelectric axis. Under normal circumstances this arrhythmia is rare, but it can occur when the QT interval of the ECG is prolonged, either as a consequence of a genetic alteration in ion channel behaviour or because of administration of certain drugs. The latter circumstance is of particular concern to the pharmaceutical industry as all new drugs, irrespective of their intended indications, have to be tested for their ability to cause QT prolongation.

A workshop on QT prolongation and torsade de pointes was therefore organised by Dr Susan J Coker (Department of Pharmacology and Therapeutics) and Professor George Hart (Department of Medicine) and held at The University of Liverpool, Foresight Centre in May last year. As the date of the workshop approached, interest grew and eventually the numbers had to be restricted to 40 participants.

After a brief welcome from the organisers, the first session on single cell studies started with an excellent overview from the invited keynote speaker Dr Milou-Daniel Drici (Valbonne, France). Dr Drici focussed on the delayed rectifier K^+ current (I_{Kr}) which is encoded by the human ether-a-go-go gene (HERG). Many drugs that prolong QT intervals block this channel leading to increased action potential duration. He emphasised that I_{Kr} is dependent on extracellular $[K^+]$ and that the blocking effects of drugs like dofetilide are increased when extracellular $[K^+]$ is low. Dr Drici also described studies on the antibiotic, erythromycin, which had shown greater effects on I_{Kr} in cells isolated from female than male rabbits which correlates with clinical observations of QT prolongation and torsade de pointes being much more prevalent in women than in men. In his overview Dr Drici also highlighted the importance of taking careful note of any fainting episodes reported

during phase 3 clinical trials as these could indicate the occurrence of torsade de pointes.

The next presentation featured a double act from Dr Jules Hancox and Dr Harry Witchell (University of Bristol). Dr Hancox described differences in the IC_{50} values for various drugs against HERG current depending on whether HERG was expressed in mammalian cells or oocytes, with lower IC_{50} values being observed in mammalian cells. He focussed on the effects of several drugs with Class I antiarrhythmic action, such as disopyramide, propafenone, flecainide, lignocaine and quinidine and emphasised that their IC_{50} values on HERG current do not necessarily correlate with their propensity to induce arrhythmias. Dr Witchell focussed on the actions of several centrally active drugs used to treat depression. At high concentrations these drugs can block HERG completely and Dr Witchell emphasised that it is relevant to study these high concentrations because these drugs are often prescribed to depressed patients who may overdose. As well as drugs like imipramine, he also showed evidence that selective serotonin reuptake inhibitors (SSRIs) like fluoxetine (ProzacTM) block HERG.

The second session on *in vitro* and *in vivo* models started with a comparison of models by Dr



Goran Duker (AstraZeneca, Molndal, Sweden). He described the “Carlsson” *in vivo* rabbit model in which induction of torsade de pointes by drugs that block I_{Kr} is influenced by alpha-adrenoceptor tone. In conscious rabbits the α -antagonist prazosin prevents torsade de pointes whereas in anaesthetised rabbits an infusion of an α agonist is required to reveal the arrhythmogenic effects of drugs that cause QT prolongation. Dr Duker reported correlation between QT prolongation *in vivo* and the occurrence of torsade de pointes, but less correlation between *in vitro* I_K block and *in vivo* QT prolongation. He then described some characteristics of a dog model where AV block enhanced drug-induced torsade de pointes but the addition of a diuretic to induce hypokalaemia seemed to have less influence. Dr Duker also described recent studies demonstrating that the antihistamine, terfenadine, prolonged monophasic action

potential duration in guinea pigs during constant pacing to maintain heart rate and discussed the effects of a number of drugs in perfused hearts.

In the next talk Dr Susan Coker (University of Liverpool) described some modifications to the “Carlsson” model that allowed a reasonable incidence of torsade de pointes to be seen in pentobarbitone-anaesthetized, open chest, rabbits. This included data from some recent studies which suggest that estrogen increases torsade de pointes. The final presentation in the session was given by Dr Kathy Ryder (Home Office, Dundee). who discussed the current legislative arrangements in the UK and gave potential Project Licence applicants extremely useful guidance. She discussed the balance between the three “Rs”, replacement, refinement and reduction, and emphasised

that it was important to ensure that numbers were adequate for appropriate statistical analysis.

After a buffet lunch there were three presentations on correction of QT intervals for changes in heart rate. Dr Jean-Pierre Valentin (AstraZeneca, Macclesfield) focussed on studies in dogs and showed that at high heart rates Bazett's factor over corrects whereas at low heart rates it under corrects. Problems with other correction factors were highlighted, the influence of anaesthetics on QTc intervals was considered and the need for power calculations in study design was emphasised. The next speaker was Andrew Batey (GlaxoSmithKline, Welwyn) who described variability in QT intervals and heart rate measured by telemetry in freely moving conscious dogs. Bazett's factor did not reduce the variability in QT values and inverted the relationship with heart rate and although Fridericia's factor was better it still did not correct adequately. Beat to beat data revealed the relationships were not linear and a novel method of correcting for changes in heart rate was proposed. The final speaker in this session was Dr Patrick Davey (Northampton General Hospital who discussed clinical data. He firmly expressed the opinion that "Bazett's formula is a dog" and presented evidence supporting the view that Bazett's factor did not correct adequately. He spoke about the influences of left ventricular function and autonomic activity on QT intervals, considered several different correction factors and concluded that it was important to work out appropriate correction factors for individuals.

The final session of the afternoon then returned to the topic of ion channels. Professor George Hart (University of Liverpool) talked about action potential heterogeneity emphasising the differences in action potential durations in various regions of the heart and changes that occur with hypertrophy. He commented that in the preparations used by his group he had never seen "M" cells and that the effects of dofetilide in mid myocardial cells were intermediate between those

observed in epicardial and endocardial cells. The final talk was the second contribution from the keynote speaker Dr Drici, where he focussed on the molecular pharmacology of I_{Kr} and I_{Ks} , the rapidly and slowly activating components of the delayed rectifier current. I_{Ks} knock out mice have a reduced righting reflex, are deaf and have a steeper QT-RR relationship. Dr Drici highlighted the problem of different labs reporting varied IC_{50} values for the effects of drugs on these currents and argued for the inclusion of positive controls in all studies to aid comparability.

As well as having questions after each talk, at the end of each session there was an extended discussion and many of the other participants made very useful contributions during these discussions. The workshop provided the opportunity for a frank exchange of views and many participants left with new information and renewed enthusiasm to tackle some of the many questions that had arisen.

And Finally:

Whilst the workshop itself ran very smoothly, thanks to help from Nichole Byrne, Karen Philp, Phill Roberts and the staff of the Foresight Centre the same cannot be said about previous day. The evening before the workshop turned out to be rather eventful for the organisers and particularly for the keynote speaker, Dr Milou-Daniel Drici. Whilst driving back from Manchester airport after collecting another participant, Dr Coker noticed that traffic around Liverpool airport seemed rather congested and in fact all roads to Liverpool airport were cordoned off by the police. Later it was learned that there was bomb scare at the airport. In the meantime Dr Drici's flight from Nice had landed at Liverpool on time, but was then parked at the end of the runway as far away from the terminal building as possible. After quite some time, during which the bomb squad blew up an elderly lady's misplaced vanity case, the passengers were allowed off the plane from Nice. Dr Drici then found himself in the terminal

building in Liverpool, but with nobody there to meet him, no cash in £ Sterling and he was soon parted with his Visa card by an extremely uncooperative cash machine at the airport. Reluctant to see his American Express card go the same way he persuaded staff at the airport to phone the hotel he was booked into to try to find some way of getting a taxi there. After several confusing mobile telephone calls, some running round the Albert Dock in Liverpool by Dr Coker from restaurant to hotel (she was having dinner with some of the other speakers) one of Dr Coker's PhD students, Karen Philp, was dispatched to the airport to rescue Dr Drici and deliver him to the hotel. After some further drama trying to find a restaurant in Liverpool that would

accept an American Express card Dr Drici eventually managed to get dinner and retire to his hotel to prepare for the workshop the next day. The following day, after his excellent contributions to the workshop Dr Drici was delivered to the airport for his return flight and left still smiling (thank you!) and clutching some emergency rations in case of delays on the return flight.

Dr Susan J Coker, Workshop Organiser
Department of Pharmacology and
Therapeutics, The University of Liverpool

Book reviewer required

The following book has been received for the Book Review feature in *The Bulletin*. If you would like to review this title, please contact the Editors as soon as possible.

- From the *Developments in Cardiovascular Medicine* series: "*Exercise Testing, New Concepts for the New Century*", edited by Myrvin H Ellestad and Ezra A Amsterdam (Kluwer Academic Publishers) ISBN 0-7923-7378-2 September 2001

The reviewer may keep the book after reviewing it.

Submission Deadlines for *The Bulletin*:

<i>Volume</i>	<i>Date</i>	<i>Deadline</i>
<i>15(3)</i>	<i>July 2002</i>	<i>June 1st</i>
<i>15(4)</i>	<i>October 2002</i>	<i>September 1st</i>
<i>16(1)</i>	<i>January 2003</i>	<i>December 1st</i>
<i>16(2)</i>	<i>April 2003</i>	<i>March 1st</i>

Cardiovascular Related Meetings

Cardiovascular Development - Working Group on Developmental Anatomy & Pathology, European Society of Cardiology. Meeting to be held 4th-6th July, 2002 at the Conference Centre, National Heart & Lung Institute, Imperial College, Faculty of Medicine, London, UK. Organiser: Paul JR Barton. For further information, please contact Conference Secretary, Mrs Joanna Harwood, Cardiothoracic Surgery, National Heart & Lung Institute, Imperial College, Faculty of Medicine, Dovehouse Street, London SW3 6LY UK. Tel: +44 (0) 20 7352 8121 x3039; Fax: +44 (0) 20 7376 3442; E-mail: j.harwood@ic.ac.uk

22nd Annual Meeting of the ISHR - European Section, Szeged, Hungary, July 3-6, 2002. For further details, contact Prof. Dr. Ágnes Végh, University of Szeged, Faculty of Medicine, Department of Pharmacology and Pharmacotherapy, Dóm tér 12. H-6720 Szeged, Hungary. Tel: +36-62-545-673 Fax: +36-62-544-565, E-mail: vech@phcol.szote.u-szeged.hu. Web Site: <http://www.cardiovasc.com/ishr2002/>

Translational Approaches to Cardiovascular Disease, the 24th Annual Meeting, ISHR, North American Section, will be held in Madison, Wisconsin, July 24-27, 2002. The abstract deadline is February 1, 2002. Organizer: Richard L. Moss, Ph.D., Director, UW Cardiovascular Research Center, Professor and Chair, Department of Physiology, Telephone: 608-262-1939, Fax: 608-265-5072, email: rlmoss@physiology.wisc.edu

XVIII World Congress of the International Society for Heart Research, August 7-11, 2004, Brisbane, Australia. Enquiries: ISHR 2004 Congress, PO Box 164, Fortitude Valley QLD 4006, Australia. Tel +61 7 3854 1611; Fax +61 7 3854 1507; E-mail: heart2004@ozacomm.com.au; Website: www.baker.edu.au/ISHR

22nd Meeting of the European Society for Microcirculation: 'The Microcirculation and Vascular Biology' will be held at the University of Exeter, Devon, 28th-30th August, 2002. For further information, please contact Hampton Medical Conferences Ltd. (ESM202650), 127 High Street, Teddington, Middlesex TW11 8HH UK Tel: +44 (0) 20 8977 0011; Fax: +44 (0) 20 8977 0055; E-mail: esm@hamptonmedical.com www.hamptonmedical.com; www.medicin.fu-berlin.de/esm Main announcement and Call for Abstracts now available

Congress of the European Society of Cardiology, 31 August - 4 September, 2002, Berlin, Germany. For further information concerning registration, hotels, exhibition, satellite symposia, write to: ESC- The European Heart House 2035, Route des Colles, Les Templiers, BP 179, 06903 Sophia Antipolis Cedex, France. www.escardio.org. General enquiries: +33 -(0)4 92 94 76 00; Fax: +33 -(0)4 92 94 76 01. E-mail: webmaster@escardio.org; Registration: registration@escardio.org; Scientific Programme: scientific@escardio.org; Exhibition: exhibition@escardio.org; Hotels: hotels@escardio.org. On-line registration and abstract submission is available on-line at: www.escardio.org.

Travel Reports for *The Bulletin*

The Bulletin regularly publishes travel reports written by members. These are up to 3 pages in length including photographs, and can be on any conference, course or laboratory visit of interest to other members. If you are planning on travelling to a cardiovascular-related meeting and would like to write a report for the Bulletin, please contact the editors. A bursary of **£100** is available towards the cost of your visit, and this will be provided on receipt of the report. Bon voyage!

BRITISH HEART FOUNDATION GRANTS

Chairs and Programme Grants Committee, November 2001

Programme Grant

Dr I C Zachary & Prof J F Martin, University College London. "Molecular mechanisms of arterial protection mediated by vascular endothelial growth factor in vitro and in vivo" 5 years £750,925

Project grants committee, November 2001 DEFERRED APPLICATIONS AWARDED

Prof R Lewin et al, University of York. "Quality of life in children with congenital heart defects" (2½ years). £136,213

Prof M Malik & Dr V Batchvarov, St George's Hospital Medical School, London. "Drug induced morphological and dynamic changes of ventricular repolarisation" (2½ years). £198,420

Dr A E Canfield et al, University of Manchester. "Role of the calcium sensing receptor (CaR) in vascular smooth muscle cell function and calcification" (3 years). £175,322

Professor M R MacLean, University of Glasgow. "Pulmonary vascular mechanisms underlying genetic susceptibility to pulmonary hypertension in the fawn-hooded rat" (3 years). £100,285

Dr P J Chowienczyk et al, St Thomas' Hospital, London. "Effects of exercise training on oxidative stress, endothelial function and exercise blood pressure in insulin resistant and diabetic subjects" (2 years). £82,806

NEW APPLICATIONS

Dr C Baboonian et al, St George's Hospital Medical School, London. "Antigenic specificity of CD4+CD28 null T cells in unstable angina" (2 years). £71,328

Dr A H Chester et al, Harefield Hospital, London. "Investigations into receptor-mediated mechanisms in the aortic root" (3 years). £126,192

Dr H Farza & Professor H C Watkins, University of Oxford. "Altering cardiac troponin T proteins in mouse: an alternative approach to creating models for hypertrophic and dilated cardiomyopathies" (3 years). £135,350

Professor D J Sheridan & Dr M P Kingsbury St Mary's Hospital, London. "Investigation of aquaporin content and function in lungs adapted to chronic heart failure" (2 years). £45,007

Dr J A Mitchell & Dr P Anning, NHLI, London. "Characterisation of the novel vasodilator properties of ATP in vitro and in vivo" (3 years). £97,299

Professor D I Wilson, University of Southampton. "Investigation chromosome 11q25 for a gene, dysfunction of which causes hypoplastic left heart syndrome" (2 years). £149,332

Dr J Y Jeremy & Professor G D Angelini, Bristol Royal Infirmary. "Angiogenesis and the inhibitory effect of the external stent on porcine vein graft thickening: in vivo and in vitro studies" (2 years). £94,947

Dr P H Scott & Dr A J Peacock, Western Infirmary, Glasgow. "The effect of hypoxia on MAP kinase pathways and gene expression in pulmonary artery fibroblasts: a cell model of vascular remodelling" (3 years). £92,207

Dr A C Cave & Professor A M Shah, King's College London. "Role of NADPH oxidase and oxidant signalling in the development of angiotensin-II induced cardiac myocyte hypertrophy" (3 years). £135,338

Professor R M Wadsworth et al, University of Strathclyde. "Effect of Ras inhibitors on remodelling and intimal hyperplasia in cultured atherosclerotic arteries" (3 years). £75,451

Dr Y Hu & Professor Q Xu, St George's Hospital Medical School, London. "Cell origins in venous bypass graft atherosclerosis" (3 years). £148,406

Professor J R Stradling & Dr R J O Davies, Churchill Hospital, Oxford. "Sleep apnoea and hypertension" (1.5 years). £37,028

Dr R L Williams, University of Cambridge. "Structural studies of NAD(P)H oxidase" (3 years). £144,276

Dr C L Jackson, University of Bristol. "Pharmacological intervention studies in the apolipoprotein E knockout mouse model of atherosclerotic plaque instability" (3 years). £103,871

Professor J C Sparrow et al, University of York. “Functional analysis of mutations in actin that are associated with hypertrophic and dilated cardiomyopathies” (3 years). £141,279

Dr S E Hughes & Professor Q Xu, St George’s Hospital Medical School, London. “Ephrin ligands and eph receptors in the cardiovascular system” (3 years). £161,922

Professor N J Samani et al, Glenfield Hospital, Leicester. “Thrombin generation potential in premature myocardial infarction” (1 year). £35,172

Professor D J Beech & Dr A Sivaprasadarao, University of Leeds. “LTRPCs and cation entry in vascular smooth muscle” (3 years). £128,065

Project grants committee, January 2002

DEFERRED APPLICATIONS AWARDED

Professor R J C Hall & Professor P C Camici, Imperial College, London. “Subendocardial blood flow in myocardial stunning and hibernation” (2 years) £105,651

Dr C P D Wheeler-Jones & Dr T D Carter, Royal Veterinary College, London. “PAR-mediated control of prostanoid synthesis in human endothelium: molecular mechanisms regulating COX-2 expression” (3 years) £144,145

Professor M J Lab & Dr Y E Korchev, Hammersmith Hospital, London. “The role of sarcolemmal K_{ATP} channel localisation in cardiac myocyte function” (3 years). £57,868

Dr J Nourooz-Zadeh et al, Middlesex Hospital, London. “Bioactive nitro(so)prostanes: haemodynamic role in platelet-neutrophil-endothelial interactions” (3 years). £166,815

NEW APPLICATIONS

Dr A K Simonds et al, Royal Brompton Hospital, London. “The causes and consequences of sleep disordered breathing in congestive heart failure” (2 Years). £140,268

Dr S A Jones et al, University of Leeds. “Ageing-dependent deterioration of the cardiac pacemaker, the sinoatrial node” (3 Years). £155,816

Professor D S Latchman et al, Institute of Child Health,

London. “Role of the STAT-1 transcription factor in ischaemia/reperfusion injury in the intact heart” (3 Years). £148,110

Dr N A Turner et al, University of Leeds. “The mechanism of beta-adrenergic receptor-mediated proliferation of human cardiac fibroblasts” (1 Year). £42,498

Dr D P Ramji, Cardiff University. “Interferon- γ -mediated regulation of macrophage lipoprotein lipase gene expression through the transcription factors Sp1 and Sp3: further investigation of the molecular mechanisms” (2 Years). £105,248

Dr A Tinker, University College London. “Elucidating the molecular mechanisms governing the regulation of Kir6.1 + SUR2B; the cloned equivalent of the vascular K_{ATP} channel” (3 Years). £150,808

Professor D J Wheatley et al, Glasgow Royal Infirmary. “Coagulation activation markers and risk of cardiovascular events in patients with prosthetic heart valves” (1 year). £33,114

Dr A Smith & Professor K Burnand, St Thomas’ Hospital, London. “Enhancement of monocyte uPA production to promote venous thrombus resolution” (3 years). £126,239

Professor N D Carter et al, St George’s Hospital Med School, London. “Genome wide-scan and characterisation of a locus for truncus arteriosus in a large consanguineous pedigree” (1 year). £50,182

Professor M J Brown, Addenbrooke’s Hospital, Cambridge. “Spironolactone amiloride thiazide (SALT) study of aldosterone sensitive hypertension” (2 years). £93,551

Dr S E Harding et al, National Heart & Lung Inst., London. “A pilot study on murine embryonic stem cell-derived cardiomyocyte cultures” (1 year). £37,916

Dr S M Harrison & Professor C H Orchard, University of Leeds. “Sodium regulation in normal and hypertrophied cardiac muscle.” (3 years). £123,324

Dr B B Zhang et al, Southampton University Hospital.. “Genealogical, prospective and molecular studies of subarachnoid haemorrhage kindreds.” (1 year). £63,156

Dr M F Scully, Thrombosis Research Institute, London. “Characterisation of heparin binding proteins on the

surface of apoptotic and necrotic cells” (2 years).
£89,140

Dr J M Ames et al. University of Reading. “New electrophoresis methods for quantifying glycated triacylglycerol-rich lipoproteins and their apolipoproteins in diabetic subjects at risk from heart disease” (2 years).
£92,730

Professor MR Boyett et al, University of Leeds. “Atrial arrhythmias- mechanisms underlying the pacemaker activity of the ‘left-sided sinoatrial node’ ” (2 years).
£84,444

Cardiovascular Related Wellcome Trust Grants

November 2001 to January 2002

Wellcome Programme Grant

Professor Paul M Stewart, Department Of Medicine, Queen Elizabeth Hospital, University Of Birmingham. 11beta-Hydroxysteroid Dehydrogenases And Human Disease. 60 Months £943,324

Project Grants

Professor Clive H Orchard, School Of Biomedical Sciences, University Of Leeds. The Role Of The T-Tubules In Determining Ca²⁺ Release In Cardiac Muscle. 36 Months. £239,670

Professor W Martin, Institute Of Biomed And Life Sciences, University Of Glasgow, Scotland. Role Of Edhf In Control Of Vasomotor Tone And Intraocular Pressure In The Eye. 24 Months £88,403

Dr Margaret Thorogood, Department Of Public Health And Policy, Health Promotion Sciences Unit, London School Of Hygiene And Tropical Medicine, London. Southern Africa Stroke Prevention Initiative: The Pilot Stage. 24 Months £185,356

Dr Sikha Saha, Institute For Cardiovascular Studies, Muscle Research Unit, University Of Leeds. Chemical Coding Of Neural Pathways Involved In Cardiovascular Control During Stress And Emotional Responses. 36 Months. £143,655

Professor Charles N Mccollum, Department Of Surgery, University Hospital Of South Manchester, University Of Manchester. Death In Young Adults From Myocardial Infarction And Ischaemic Stroke: The Role Of Patent Foramen Ovale And Thrombophilia. 36 Months. £278,768

Srif

Professor David J Millward, School Of Biomedical And Life Sciences, University Of Surrey, Guildford. A Centre For Nutrition And Food Safety, Integrating Studies Of Human And Bacterial Genotype And Phenotype. £1,150,943

Training Fellowships For Medical & Dental Graduates

Dr Mark Little, Renal Unit Department Of Medicine, Hammersmith Hospital, Imperial College School Of Medicine, London. The Role Of Anti-Neutrophil Cytoplasm Antibodies (Anca) In An Experimental Model Of Systemic Vasculitis. 36 Months. £182,961

Dr Joanna K Lovett, Department Of Clinical Neurology, Radcliffe Infirmary, University Of Oxford. Sex Differences In Stability Of Atheromatous Plaque At The Carotid Bifurcation. 12 Months. £46,064

International Research Fellowships

Dr S A Cook, Cardiovascular Research Centre, Massachusetts General Hospital, Charlestown USA. The Control Of Bad Function By Phosphorylation And The Interaction Of Bad With The 14-3-3 Family Proteins: Implications For Cardiac Myocyte Hypertrophy And Apoptosis. 7 Months. Amount Of Award: £17,226

Symposia

Ms Clare Croft-White, Department Of Health, Skipton House, London. A Contribution Towards A Cardiovascular Research Funders Forum: Workshop On Heart Failure To Be Held At The Royal College Of Physicians On 21 And 22 February 2002. £5,000



BSCR Autumn Meeting 2002

THE DEVELOPING HEART: BIOLOGY AND PROTECTION

Dates: 6th and 7th September, 2002

Venue: The Education Centre, Marlborough Street, Bristol BS2 8AE

Organisers: Saadeh Suleiman and Massimo Caputo

Overall aims:

1. To improve our understanding of the biology of cardiac development.
2. To compare different techniques of myocardial protection in experimental models and during paediatric open heart surgery.

Invited Speakers include: Sir Magdi Yacoub (London), Anton Moorman (Amsterdam), Steven Coppen (London), Sarah George (Bristol), Jürgen Hescheler (Cologne), Michael Artman (New York), Gavin Brooks (Reading), Elinor Griffiths (Bristol), Marianne Thoresen (Bristol), Andrew Parry (Bristol), John Baker (Milwaukee), Mike Shattock (London), Hajime Imura (Tokyo), Pedro del Nido (Boston), Paul Modi (Bristol).

Please visit website www.bris.ac.uk/bhi/meeting.htm

Communications: Part of this meeting will be devoted to the presentation of posters. **Abstract deadline: 6th August 2002.**

Travel & Accommodation: Bristol is ideally situated for travel by car, rail, bus or air. Further details are available on www.bristol.ac.uk/directions.html Accommodation will be available at local hotels. For details contact Jan Wild on address below.

Registration: Free to BSCR members, £50 for non-members. For further information contact: Saadeh Suleiman or Jan Wild, Bristol Heart Institute, University of Bristol, Bristol Royal Infirmary, Bristol BS2 8HW. Tel: 0117 928 3519 or 3582; Fax: 0117 928 3581; Email: M.S.Suleiman@bristol.ac.uk or J.Wild@bristol.ac.uk. Deadline for registration is August 6th, 2002.

Bursaries: The Society will consider awarding travel grants of up to £150 to *bona fide* PhD students. Application forms are available from Dr Barbara McDermott at the address below.

Applications for membership and student bursaries are available from Dr Barbara McDermott, Secretary of the BSCR, Department of Therapeutics and Pharmacology, The Queen's University of Belfast, Whitla Medical Building, 97 Lisburn Road, Belfast BT9 7BL. Tel: 02890-272242/335770; Fax: 02890-438346; E-mail: b.mcdermott@qub.ac.uk