

# Pharmacology **International**

No. 63 Dec 2004

The half-yearly newsletter from the International Union of Basic and Clinical Pharmacology

## In This Issue

ICSU Grant Front

IUPHAR.org Pg 2

Milestones Pg 3

IUPHAR  
2002 - 2006  
Executive  
Committee, 3rd  
in a 3-part  
series Pg 4

CPT 2004:  
Brisbane,  
Australia Pg 6

Member  
Profile: South  
Africa Pg 8

New IUPHAR  
Compendium Pg 11

Sir John Vane Pg 16

Upcoming  
Events Back

On 7 July this year, IUPHAR learned that the International Council for Science (ICSU) approved our grant application for the year 2005. The IUPHAR proposal entitled 'Consolidation and annotation of knowledge concerning receptors and sites for drug action in the human genome' has been awarded \$100,000.

This award is especially gratifying considering the serious financial cutbacks that ICSU has endured in the last year. That IUPHAR should receive the full amount requested is testament to the hard work and

the top 4 of the 11 chosen. As well, the IUPHAR application was rated A-1 and guaranteed funding. The proposal received a grade of "A" in all areas, including relevance, scientific quality, cost and time effectiveness, and strength of proposers. Comments from the reviewers at ICSU called the proposal "Ambitious, important... Visionary, extremely well planned."

The NC-IUPHAR Receptor Database went live on 30 June 2003. Since then, numerous updates and additions have been made. Eventually, everything in the "IUPHAR

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excellent qualifications of the NC-IUPHAR Database Committee, including NC-IUPHAR chair Prof. Michael Spedding of Institut de Recherches Servier, Prof. Tony Harmor of the University of Edinburgh and Prof. Sir Colin Dollery of Glaxo Wellcome UK.

Compendium of Receptor Characterization and Classification", published in 2002, will be included in the database. Thereafter, information from new research will be added to the database as it becomes available.

Of the 40 applications received, it was reported that the IUPHAR proposal was in



## *Pharmacology International*

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We welcome contributions from member societies.  
Please submit articles and photos to Dr. Sue Piper  
Duckles.

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from each country, regional societies and special  
research interest organizations. If you are an  
individual, please see the Members section on the  
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organization that you can join, or contact us at the  
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## IUPHAR.org has a new look

IUPHAR.org has been updated to make  
its appearance more pleasing and its  
navigation more intuitive, so that you can  
find the information you need.

We have added pages for the IUPHAR  
Section on Bioinformatics (currently  
being formed) and for the IUPHAR  
Working Group on Natural Products,  
chaired by Prof. Ricky Man (Hong  
Kong). The Clinical Division, NC-  
IUPHAR and the IUPHAR Directory  
are now all on the menu bar, and the  
resources area is growing.

We are delighted to report that the  
average number of visitors per day has  
increased three-fold over this time last  
year. IUPHAR.org was accessed by  
users in 91 countries in 2004, up from 63  
countries in 2003. The most-accessed  
pages include the Teaching materials, the  
NC-IUPHAR Receptor Database, the  
IUPHAR Directory, and the new  
"IUPHAR Compendium of Basic  
Principles For Pharmacological  
Research in Humans 2004", which has  
been online since September.

While we do our best to keep all  
member information current, we can  
always use your help. Please send any  
updates and corrections to  
admin@iuphar.org.



## PEOPLE

NC-IUPHAR bids farewell to Prof. **Daniel Hoyer** (France) and Prof. **Steve Watson** (UK), with gratitude for their hard work.

We are delighted to report that Prof. **Philippe Delagrance** of Institut de Recherches Servier (France) has accepted our invitation to join NC-IUPHAR.

Prof. **Donald Birkett** (Australia) was elected to the position of Vice Chair of the IUPHAR

starting on page 6 of this issue for a report on the congress.)

A symposium was sponsored by the **IUPHAR Section on Gastrointestinal Pharmacology** entitled "Advances In Gastrointestinal Pharmacology - From Acid Secretion To Mucosal Protection". The meeting was held in Otsu, Japan on November 20-22, 2004 and was co-sponsored by Kyoto Pharmaceutical University. Former IUPHAR GI Section Chair Koji Takeuchi (Japan) chaired the symposium, and current

# MILESTONES

Division on Clinical Pharmacology by the General Assembly of the Division in Brisbane, Australia during CPT 2004. Prof. **Petra Thuermann** (Germany) was elected to the post of Treasurer of the Division.

As well, IUPHAR welcomes these new councilors for the Division on Clinical Pharmacology: Prof. **Darrell Abernethy** (USA), Prof. **Gilberto Castaneda-Hernandez** (Mexico), Prof. **Wim du Plooy** (South Africa), Prof. **Mohammed Ibrahim A. Ibrahim** (Egypt), Dr. **Hyung-Keun Roh** (Korea), Prof. **David Webb** (UK) and Dr. **Fan-Dian Zeng** (China).

## MEETINGS

The **VIIIth World Congress of Clinical Pharmacology and Therapeutics** was held this past August 01 through 07 in Brisbane, Australia.

The proceedings were published in "Clinical and Experimental Pharmacology and Physiology" Volume 31 Issue s1 Page i-A213, by Blackwell Synergy. (Please see the article

IUPHAR GI Section Chair Prof. dr. Gyula Mózsik (Pécs, Hungary) served on the International Programme Committee.

## MEMBERS

The **New Zealand** Section of the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists has rejoined the Australian society. Within ASCEPT, New Zealand is henceforth represented by Prof. **Tim Maling** of the Capital & Coast District Health Board at Wellington Hospital in New Zealand. ■

**Professor James A Angus, B.Sc. Syd., Ph.D. Syd, FAA** is Dean, Faculty of Medicine, Dentistry & Health Sciences at The University of Melbourne. Previously he held the Chair of Pharmacology and Head of Department of Pharmacology. Prof. Angus has extensive research experience and has published widely

Australian Academy of Science and is a Fellow and member of its Council. Last year he was awarded the Centenary Medal.

In the wider University, Professor Angus has been President of the Academic Board and Pro Vice-Chancellor and currently serves on the

# EXECUTIVE COMMITTEE

## 2002-2006

THIRD IN A 3-PART SERIES



in preclinical pharmacology in relation to cardiovascular and antinociceptive drugs. Building on his strengths in analytical pharmacology with *in vitro* assays, Professor Angus has also published extensively on integrated pharmacology in instrumented conscious animals. Calcium channels, (T,N,L) NO, EDHF, VEGF, Et and cannabinoid receptors with selective agonists and antagonists are ongoing research and development interests. He was awarded the Gottschalk Medal of the

Bio21 Institute Management Committee. He has had numerous contracts with pharmaceutical companies and trained with Sir James Black FRS, OM at University College, London and Wellcome Research Laboratories in Beckenham.

Professor Angus is currently First Vice-President of the International Union of Pharmacology (IUPHAR).

Professor Angus was appointed Dean, Faculty of Medicine, Dentistry & Health Sciences on July 24, 2003. This is the largest Medicine & Allied Health Faculty in Australia and contributes over 50% of the University's research output. It has strong links to major Research Institutes and University Hospitals in Melbourne especially in the medical – biotechnology precinct of Parkville. ■

**Professor LIN Zhi-Bin, Ph.D.** graduated from the Faculty of Medicine, Beijing Medical College in 1961. Following advanced training in the Program in Collaborative Research in the Pharmaceutical Science, University of Illinois at Chicago, USA from 1983 to 1984, he was Vice Director of the Research Institute of Basic Medical Sciences, Beijing Medical University from 1985 to 1989, and Vice Dean, School of Basic Medical Sciences from 1992 to 1993, and Chairman of Department of Pharmacology, Beijing Medical University from 1986 to 1995. He also was Vice President of Beijing Medical

University from 1993 to 1997. Currently as a Professor of Pharmacology and Chairman of Research and Development Center for New Drugs, Peking University Health Science Center, Prof. Lin also has a lot of social and scientific positions, including President, Chinese Pharmacological Society, Member of National Committee, China Association for Science and Technology, Member of National Drug Evaluation Committee, Member of State Pharmacopoeia Committee, and Vice President of Chinese Edible Fungus Association.



Prof. Lin presented a lecture at the XIVth World Congress of Pharmacology in San Francisco, USA in 2002. He has occupied the councilor position of the IUPHAR Executive Committee since 2002. He is President, Organizing Committee of 15th World Congress of Pharmacology (Beijing, 2006).

Prof. Lin has long been researching the pharmacological effect and action mechanism of anti-inflammatory drugs, immunomodulating drugs, endocrine drugs and antitumor drugs, also taking part in the research and development for new drugs. In recent years he has investigated the immunomodulating effect and mechanism of *Ganoderma lucidum*, a traditional Chinese herb, and its active component with modern technological methods. For the first time this research revealed that the immunopotentiating effect of *Ganoderma* polysaccharides related to increasing DNA synthesis of lymphocytes. Further results indicated that this effect related to increasing DNA polymerase- $\alpha$  activity and promoting cytokines such as TNF $\alpha$ , IL-2, IL-6 mRNA

expression and production. Recent study demonstrated that *Ganoderma* polysaccharides can activate macrophages, dendritic cells and lymphocytes, promote TNF $\alpha$ , IFN mRNA expression and production and consequently induce apoptosis of tumor cells. In addition, Prof. Lin has investigated the pharmacology of bee products such as royal jelly, bee pollen and propolis since 1961. For this reason he was President of the Standing Committee on Apitherapy, International Federation of Beekeepers, Associations (APIMONDIA) from 1993 to 1997.

Prof. Lin has received the China Government Special Allowance for Outstanding Achievement since 1992. In 1994, he was conferred the title "Specialist of Young and Middle Age for Outstanding Achievement" by the Ministry of Public Health, China.

The 8th World Conference of Clinical Pharmacology held in Brisbane in August, 2004 was unique because of its focus on global equity of access to safe and efficacious medicines that are selected and used effectively and safely. An expressed goal behind the Australian bid to hold the meeting was to involve clinical pharmacologists from

and financial influences that conspire to take resources away from the people who most need them. He concluded with practical steps clinical pharmacologists could take to alleviate problems of access to medicines.

This theme was reinforced in the Plenary Lecture of Professor Suryawati, Department

## Access to Medicines & High Quality Therapeutics: Global Responsibilities for Clinical Pharmacology

*by Ric Day, Don Birkett, John Miners, Gillian Shenfield, David Henry and Paul Seale*

our region of the world where access to lifesaving medicines and confidence in their quality are matters of most significance. We wanted clinical pharmacologists from the developed and developing world to be aware of and feel some responsibility for the serious global inequities around discovery, development, access to and use of medicines of acceptable quality, safety and efficacy for the major infectious diseases such as TB, malaria and HIV AIDS as well as the emerging lifestyle associated disorders, notably cardiovascular disease.

Dr. Suwit Wibulpolprasert, Senior Advisor on Health Economics, Ministry of Public Health, Thailand, presented an inspirational and challenging plenary lecture on "Philanthropy for the Few - Equity of Access for the Many?" He demonstrated the increasing gap between rich and poor in both developed and developing countries and the many interacting social, political

of Clinical Pharmacology, Gadjah Mada University, Yogyakarta, Indonesia. She challenged all clinical pharmacologists to consider how they might become involved in achieving the three 'As' of medicines use in their own countries, namely Access, Affordability and Appropriate Use. In her talk Prof. Suryawati outlined the roles and contributions of the International Network for Rational Use of Drugs (INRUD) and the International Conferences on Improving the Use of Medicines (ICIUM). Both Dr. Wibulpolprasert and Professor Suryawati exhorted the international umbrella



Prof. Douglas Oliver (South Africa) and Griffith University Ph.D. student Daniel Croker (Australia) at the reception to promote IXth World Conference of Clinical Pharmacology and Therapeutics 2008 in Québec.



organization for clinical pharmacology, the International Union of Basic and Clinical Pharmacologists (IUPHAR), to confirm its support for this new direction in its meetings and activities. At the IUPHAR council meeting coincident with the world conference, this paradigm shift was strongly endorsed.

Dr. Lembit Rago, Clinical Pharmacologist from Lithuania and Director of the WHO's Division of Quality and Safety of Drugs, Geneva, delivered an important and timely plenary review of the status of fixed dose combinations (FDC) of medicines around the globe and the very recent acceptance (2004) of WHO guidance regarding their registration by the World Medical Assembly, highly influential in that it governs and advises WHO. The process has been difficult and lengthy, but there is no doubt that this



Dr. Sue Piper Duckles (USA), Secretary-General of IUPHAR and Dr. Li Xue-Jun (China), Vice Secretary of the Chinese Pharmacological Society and Chair of the Program Committee for the 15th World Congress of Pharmacology in Beijing 2006 in the booth promoting the congress.

## 2004 Young Investigator Awards

47 abstracts were submitted to the Brisbane meeting organizers for consideration for the **2004 Young Investigator Awards**. Five of these were included in the Young Investigators Symposium held on August 5. The following criteria were used in the selection:

- should represent clinical pharmacology in the sense that the research has been done in humans (not in vitro, nor in animals);
- should be original;
- methods should be valid;
- the subject (and results) should be clinically relevant;
- the authors should come from different countries.

A committee assessing the performance including the discussion was selected consisting of Andrew Somogyi (Australia, chairman), Gerd Mikus (Germany) and Rob Moulds (Fiji). Finding it impossible to decide on only 3 winners, ultimately, 4 were chosen with the Bronze award going to 2 authors. Awardees were:

Gold Award, **Shinya Uchida** (Japan) \$1500  
Silver Award, **Malin Lindqvist** (Sweden) \$1000  
Bronze Award, **Jonathan Chan** (Australia) \$500  
**Eleni Aklillu** (Ethiopia) \$500

All winners also received a crystal medallion from IUPHAR to commemorate their participation.

program has very great potential to deliver less expensive yet effective medications for serious conditions such as HIV AIDS worldwide.

A critical and increasing concern is the safety of medicines given the aging population with multiple comorbidities and increasing exposure to multiple, increasingly potent medicines. The way in which pharmacovigilance for new drugs is to be conducted in the future is being shaped by a number of interesting Therapeutic Risk Management initiatives across the world, some of which were presented in a lively Symposium. These initiatives seek to better identify, evaluate and minimize the impact of adverse reactions and to communicate safety risks at all stages of the life cycle of a

*continued on page 12*

## Vision

*The South African Pharmacology Society (SAPS) serves all scientists and health professionals in South Africa (and abroad) interested in pharmacology, regardless of race, religion or gender.*

## Brief History

The South African Pharmacology Society was founded in 1967, with key founders being Profs. Johan Offermeier, Ben Potgieter, Otto Müller, Andries van Zyl, Norman Sapieka, John Reid, Bill Jenkins, Theuns Naude and others. Prof. E.J. Ariëns, one of the pioneers in molecular pharmacology, was the first international

# MEMBER SOUTH

speaker at the 1st annual Congress in 1967, followed by Prof. Arnold Beckett the following year.

Since then, congresses are held annually and distinguished international pharmacologists are



invited to South Africa. In 2003 our current IUPHAR President, Prof. Paul Vanhoutte, was the keynote speaker for our 37<sup>th</sup> Annual Congress. The 38<sup>th</sup> Annual Congress was held

# PROFILES AFRICA

in October 2004 in the centre of South Africa (Bloemfontein, Free State Province), and the upcoming 39<sup>th</sup> Annual Congress is to be held in Cape Town. In addition, South Africa is an exciting tourist destination, and SAPS has held congresses at academic institutions, the



Invited speakers at the 2004 SAPS Congress: (L to R) Dr. Philippe Rasoanaivo (Madagascar), Prof. Ian Hughes (UK), Prof. Olavi Pelkonen (Finland), Prof. Andrew Walubo (Chair of organising committee), Prof. Jarl Wikberg (Sweden) and Prof. Douglas Oliver (SAPS President).

coastline beaches (e.g. Cape Town), game parks (e.g. Kruger National Park) and panoramic mountains (e.g. Drakenberg). SAPS has also helped organise four international congresses during the last nine years. The activities of SAPS encompass both basic and clinical pharmacology and have, over the years, also included regulatory issues of medicine, with respect to efficacy, safety and quality. SAPS members have served on several committees of IUPHAR, past and present. The



SAPS Executive Committee think-tank meeting in Feb '04: (L to R) Ms. Janet Maclachlan (Treasurer), Prof. Ilse Truter and Dr. Elzbieta Osuch.

society has grown, and has currently about 120 members.

### Education

Pharmacology education has been an important aspect of SAPS, in particular the last 10 years. This has resulted in four invitations for the current Chairperson of the IUPHAR Section on Teaching, Prof. Ian Hughes, to present developments in computer aided learning and novel approaches. Our members have also contributed to the programme of the recent satellite education symposium prior to the XIV<sup>th</sup> World Congress of Pharmacology in San Francisco in 2002.

Activities such as the congresses, special symposia and workshops are held every year to form part of continued professional education (life-long learning) for the healthcare professionals in South Africa.

### Research

Areas of research in South Africa developed with the world trends during the last 40 years and national and international collaborations have been established. Typical fields of research include clinical trials, ethnopharmacology, *in vivo* animal studies

### South Africa: Land of Language

South Africa has eleven official languages: Afrikaans, English, Ndebele, Northern Sotho, Southern Sotho, Swati, Tsonga, Tswana, Venda, Xhosa and Zulu.

Eight languages are recognized unofficially: Fanagolo, Lobedu, Northern Ndebele, Phuthi, Sign Language, Khoe, Nama and San.

Additional living languages are: Birwa, Camtho, Gail, Hindi, Korana, Kxoe, N/U, Nama, Oorlams, Ronga, Swahili, Swati, Tshwa, Tsotsitaal, Urdu and Xiri.

As well, the following languages are spoken by a significant number of immigrants and visiting workers: Chinese, German, Greek, Gujarati, Haiom, Portuguese, Tamil, and Eastern Yiddish.

(including behavioural studies), *in vitro* drug dynamics and molecular/signal-transduction pharmacology, drug metabolism and delivery, sports medicine, and pharmacovigilance. Topics for research include the typical wide spectrum seen internationally, such as HIV/AIDS, malaria, tuberculosis, drug discovery in traditional medicine and other topics of particular importance to the African context.



Ms. Ansonette Werkman (SAPS Office Assistant) and Prof. Tiaan Brink (Secretary) at the SAPS Congress.

Several members of SAPS are rated as upcoming, established or internationally recognised/leading researchers by the National Research Foundation of South Africa, which emphasises the leading role our members play in various capacities to foster pharmacological research for the benefit of not only South Africa, but also our continent.

### Technologies & Development

SAPS and its members have embraced both basic and clinical pharmacology since its inception. This was possible because of the balance between basic and clinical research in the academic and industrial worlds in South Africa. In general our laboratories are well-equipped with relevant current technologies and skilled researchers to use them.

SAPS introduced the Young Scientist Award several years ago. This allowed our young

scientists to report on their research for a first post-graduate degree and to compete for several prizes that financially enable them to present their research internationally.

### Future Initiatives and Programs

SAPS has embraced the vision that it does not only play a role in South Africa, but also in Africa and in particular sub-Saharan Africa. In achieving this goal SAPS has initiated, in cooperation with IUPHAR and the International Council for Science (ICSU) regional office for Africa, the initial planning discussions for hosting a workshop in Nairobi, Kenya in 2005/6, entitled:

*"Pharmacology for Africa: Vision for Health through Teaching and Research"*

In questions of  
**SCIENCE**  
the authority of a  
thousand is not worth  
the humble  
**REASONING**  
of a single individual.

Galileo Galilei

# The IUPHAR Compendium of Basic Principles For Pharmacological Research in Humans 2004

"The IUPHAR Compendium of Basic Principles for Pharmacological Research in Humans" is the 4th volume in the highly acclaimed series of research compendia published by the International Union of Basic and Clinical Pharmacology (IUPHAR).

The objective of this compendium is to provide the scientific community interested in human research with an easy-to-use guide on how to design a research protocol with humans aiming to assess the effectiveness of a drug in a determined pathological condition or for drug development.

About the Editors:

**Patrick du Souich**, MD, Ph.D., is a professor and the director of the Department of Pharmacology at the University of Montréal, Canada.

**Sergio Erill**, Ph.D., is the director of the Esteve Group, Spain. He has been Professor and Chairman of the Department of Pharmacology at two different Spanish universities, and President of the Spanish Society for Pharmacology.

**Michael Orme**, Ph.D., is the former Dean of the Faculty of Medicine at the University of Liverpool. He is also Director of Education and Training for the NW Region of England and President of the European Association for Clinical Pharmacology and Therapeutics, which he helped found in 1983.

Contents:

## Section 1 - Introduction

- Chapter 1. Ethical Considerations
- Chapter 2. Good Clinical Practice
- Chapter 3. Assessment of Endpoints: Kinetics and/or Dynamics
- Chapter 4. Pharmacogenetics and Pharmacogenomics
- Chapter 5. Paediatric Drug Research
- Chapter 6. Phase I (Human Pharmacology)
- Chapter 7. Follow-Up of Drugs After Market Entry
- Chapter 8. Bioavailability and Bioequivalence
- Chapter 9. Pharmacoeconomics and Economic Evaluation of Drug Therapies
- Chapter 10. Drug Utilization

## Section 2 - Pharmacological Research in Cardiovascular Disorders

- Chapter 11. Hypertensive Vascular Disease
- Chapter 12. Lipid Lowering Agents
- Chapter 13. Anti-atherosclerotic Drugs
- Chapter 14. Heart Failure
- Chapter 15. Arrhythmias

## Section 3 - Pharmacological Research in Neurologic Disorders

- Chapter 16. Epilepsies and Convulsive Disorders
- Chapter 17. Headache Disorders
- Chapter 18. Alzheimer's Disease and Other Dementias
- Chapter 19. Parkinson's Disease and Other Extrapyrarnidal Disorders
- Chapter 20. Multiple Sclerosis and Other Demyelinating Diseases

## Section 4 - Pharmacological Research in Mental Disorders

- Chapter 21. Mood Disorders
- Chapter 22. Anxiety Disorders
- Chapter 23. Schizophrenic Disorders
- Chapter 24. Alcoholism and Nicotine Addiction

## Section 5 - Pharmacological Research in Joint Disorders

- Chapter 25. Osteoarthritis/arthrosis Short Term Studies
- Chapter 26. Osteoarthritis/arthrosis Long Term Studies
- Chapter 27. Rheumatoid Arthritis

## Section 6 - Pharmacological Research in Other Disorders

- Chapter 28. Neoplastic Diseases
- Chapter 29. Analgesic Drugs for Cancer Pain Management
- Chapter 30. Drugs Used in Osteoporosis

The compendium is available online at the IUPHAR.org website. Hard copies are available for USD65 for members and USD80 for non-members. For information, please email Lindsay Hart at hartl@uci.edu.

PHARMACOLOGY  
International

page

11

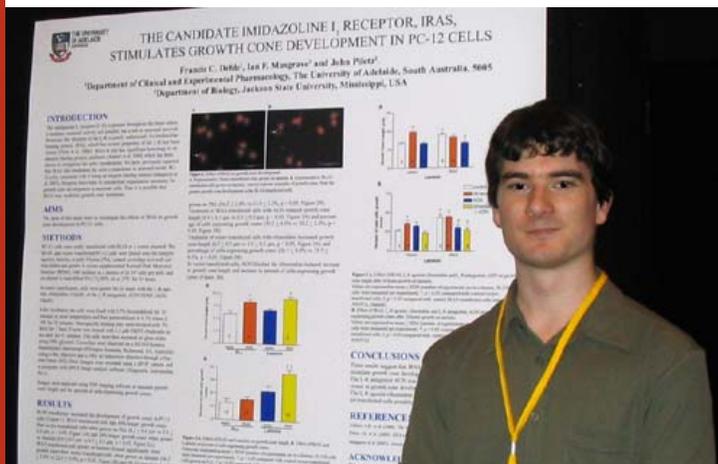


December 2004

*continued from page 7*

drug and, most importantly, to do so proactively according to Dr. Susana Perez-Guttmann, Pfizer Ltd, Barcelona, Spain. The importance of pharmacoepidemiology and employment of advanced information technology to 'mine' large automated health databases have revolutionized the way pharmacovigilance can be undertaken.

The problem of the 'therapeutic orphan' status of children was examined in depth by speakers from Europe, USA and Australia. Incentives to pharmaceutical companies to evaluate already marketed medicines along with mandatory studies in children for new medicines, provided that they are potentially useful in children, has been a successful strategy in the USA since the mid 1990s and is now having a positive impact in Europe. However, the conference heard that political pressure needs to be maintained to overcome this problem for children.



Francis Dehle, a Ph.D. student at the University of Adelaide and a member of the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT), presents a poster on the Imidazoline I<sub>1</sub> receptor.

Attention was given to the rapidly expanding complementary medicines sector. Dr. Charlie Xue, Program Leader, Division of Chinese Medicine, School of Health Sciences RMIT University, Victoria, Australia gave the perspective of WHO on traditional medicine, and provided examples of the role of complementary medicine as a mainstay of

public health systems in Southeast Asia and the Pacific regions. Professor Chu Quoc Truong, Director of The National Hospital of Traditional Medicine, Hanoi, Vietnam explained that in Vietnam the national government has formally integrated traditional medicine with Western conventional medicine, with apparent good effect.

A Symposium on the controversial topic of 'Direct to Consumer Advertising' (DTCA) of prescription pharmaceuticals drew great interest as the situations in Canada, Europe, Thailand, New Zealand and Australia were compared. There were two main themes: first, that regulation is difficult and secondly, that there are many and increasing instances of advertisements that skirt the boundaries of existing laws and regulations in jurisdictions where DTCA is illegal. In developing countries, there is in reality often no distinction between supposed prescription and OTC medicines in terms of access. It is very difficult to control DTCA of so-called prescription drugs when prescription-only status is not upheld at law. However, in countries in which DTCA is currently illegal, there appears to be little appetite for the introduction of DTCA because of concerns around quality of use of advertised medicines, consumer demand leading to distortion beyond the 'reasonable' need for medicines and finally, morbidity and mortality from the adverse effects of medicines whose use was unnecessary. However, it was emphasized that there is continuous and considerable pressure from industry and advertising interests to reverse this attitude.

Juxtaposed with the burning issues of equity and access concerning medicines, a major theme of the Congress was the increasing evidence base and rationale for individualising drug therapy selection and regimens. This theme was developed by Professor Michel Eichelbaum, Director of the Dr. Margarete Fischer-Bosch-Institute for Clinical



Pharmacology, Stuttgart, Germany in his Plenary lecture. Prof. Eichelbaum revealed the impact of genomics on all aspects of drug therapy along with many other speakers in related Symposia. Not only is drug metabolism controlled by gene expression but also drug receptor activity and processes of transport into and out of target organs and cells. The rapid advances in understanding the critical roles and effects of transporters of drugs and influences of genetic variation on these transporters was outlined in a very clear way by Professor Yuichi Sugiyama, Chairman, Department of Biopharmaceutics, Faculty of Pharmaceutical Sciences, University of Tokyo, Japan in his Plenary lecture and in an exciting Symposium that followed. In short, multiple genes and proteins under their control determine all of the critical processes of drug metabolism, disposition and action. Targeting of therapy based on genome wide screens also will be informative regarding prognosis and will increasingly guide therapy.

The discussions on individualising drug therapy extended to dosing regimes and the importance of understanding relationships between pharmacokinetics, quite variable between individuals, and drug effects i.e. pharmacodynamics in drug development and clinical practice. A fascinating new area of attention discussed by Prof. Nick Holford, Auckland, New Zealand, Prof. In-Jin Jang, Clinical Pharmacology, Seoul National University, South Korea and colleagues was the quantitation of the effects of medicines on disease progression as distinct from immediate symptom relief. Parkinson's Disease, hypertension and cardiovascular disease, depression and osteoporosis, prevalent chronic disorders were used to illustrate this important concept.

The impact of the genomic revolution and molecular biology on drug target identification and pharmacological strategies to perturb relevant molecular mechanisms was a major strand running through the meeting. For example, in a Symposium on "Picking the winners and avoiding the losers", Dr. Peter Lord of Johnson & Johnson, USA, discussed

how the use of molecular technologies is enhancing the ability of pharmaceutical companies and regulatory agencies to identify toxicological issues earlier, thereby increasing the rate of success and decreasing time taken from discovery to registration of new drugs. Professor Silviu Itescu (Columbia University USA and The University of Melbourne Australia), provided an excellent overview of the potential that stem cells represent as future therapy, addressing the utility of adult stem cell technology (derived from bone marrow stromal mesenchymal cells) to treat cardiac remodelling following myocardial infarction (heart attack). Silviu's team have obtained remarkable results administering human angioblasts to laboratory animals in which coronary artery ligation has been used to induce infarction. Two weeks after treatment, hearts exhibit new blood vessel formation, and the increased supply of nutrients not only prevents long-term loss (apoptosis) of cardiomyocytes in the peri-infarct area, but actually permits regeneration of cardiac muscle, that is not only viable but is also functional.

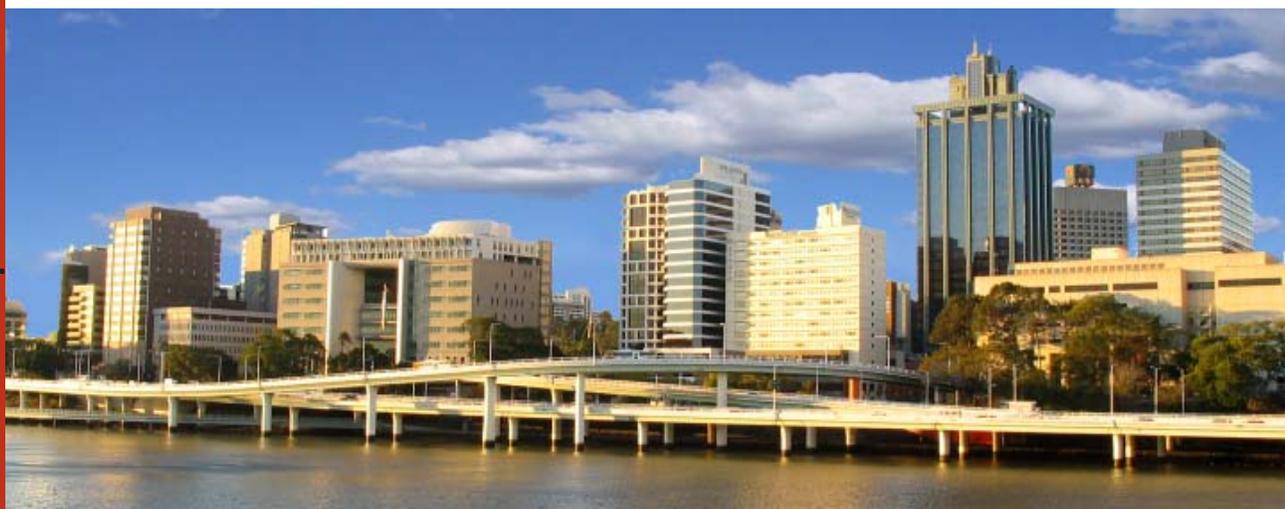
An outstanding smorgasboard of clinical pharmacology and therapeutics was presented in the Therapeutics Horizons stream. An update on relevant pathophysiology preceded exposés of advances in drug therapy in malaria, obesity, osteoporosis, COX-2 selective inhibitors, drug dependence, clinical toxicology and antidotes, cardiac arrhythmias. This series finished on the optimistic topic: "Drugs and Ageing: Can They Deliver Eternal Life?". Artemisinin drugs were found by Dr. Sanjeev Krishna of the Department of Cellular and Molecular Medicine, St. George's Hospital Medical School, London, UK to inhibit a malarial parasite specific ATPase, providing evidence of a direct toxic effect on a vital parasite transport function. Other speakers in the Malaria Symposium including Dr. Tran Tinh Hien of The Hospital for Tropical Diseases, Ho Chi Minh City, Viet Nam, emphasized the importance of using and

*continued on next page*

investigating combinations of antimalarial drugs including artemisinin and combined this approach with earlier diagnosis with robust, simple and fast field tests. A fascinating series of presentations by Dr. Rachel Batterham of the Department of Metabolic Medicine, Hammersmith Hospital, London, UK and Professor Yuji Matsuzawa, Director, Osaka University, Japan dealt with progress in pharmacotherapeutic approaches to obesity, insulin resistance and Type II diabetes and accelerated cardiovascular disease. The complex neurohormonal controls of appetite

has been a major concern in drug development. Prof. Terry Campbell, Sydney, Australia and Professor Naomasa Makita, Cardiovascular Medicine, Hokkaido University Graduate School of Medicine, Sapporo, Japan and colleagues discussed developments in understanding the mechanisms, screening methods and implications for therapeutics.

The breadth of clinical pharmacology, and one of its attractions, was exposed in this meeting with Symposia on Drugs in Sport where Harm



The river city of Brisbane, Queensland, Australia.

and body weight, centred around the arcuate nucleus of the hypothalamus, gut and fat cells, presented an increasing array of targets but also challenges.

Professor Nick Buckley, Canberra, Australia and international speakers shocked delegates in their Symposium that outlined the almost complete lack of any targeted drug development strategies to deal with the millions of poisonings and hundreds of thousands of deaths each year from organophosphate exposure in the Asia-Pacific region.

Drug-induced arrhythmias, increasingly recognised in the last decade, initially focused on antiarrhythmic drugs themselves such as lignocaine and quinidine. More recently, the pro-arrhythmic properties of other drugs by virtue of their effects on cardiac ion channels

Kuipers, Professor of Movement Sciences, Maastricht University, Holland challenged the inclusion of many drugs on the current "prohibited list" as there was little or no evidence that they actually enhance performance. Peter Hemmersbach, Scientific Director Hormone Laboratory and School of Pharmacy, Aker University Hospital, University of Oslo, Norway discussed the difficulties inherent in testing for endogenous compounds such as human growth hormone and touched on future likely developments, including gene transfer technology to enhance sporting performance.

Professor Tom MacDonald, Clinical Pharmacology, Ninewells Hospital & Medical School, Dundee, UK delivered an entertaining Plenary Lecture with the important message that large returns in population health



# IUPHAR Congress Schedule

**2006**

02 - 07 July  
Beijing  
CHINA  
[www.cnphars.org](http://www.cnphars.org)

**2008**

26 - 31 July  
Quebec  
CANADA  
[www.cpt2008.com](http://www.cpt2008.com)

**2010**

17 - 23 July  
Copenhagen  
DENMARK  
[www.iuphar2010.dk](http://www.iuphar2010.dk)

with the networks, products and services in support. The major sponsorship of the world conference by the National Prescribing Service, itself one of the prominent fruits of the QUM movement, effectively emphasised the importance of the QUM in Australia and its potential for the rest of the world.

In his Plenary lecture, Professor Tony Smith, Newcastle, Australia spoke of the unfinished business for clinical pharmacology and world health. He reminded us that clinical pharmacology arose as a discipline largely in developed countries and continues to be vital to the stellar advances in drug discovery. However, many of the needs of developing countries remain unmet, partly because there are only limited numbers of clinical pharmacologists working in these environments. He summarised the tasks they need to be involved in including political advocacy for appropriate drug use, the construction and implementation of national medicines policies and specific issues such as the collaborative development of standard treatment guidelines, essential medicines lists and the promotion of rational prescribing, especially through training programs in medical schools. In his view, our umbrella organization, IUPHAR through its division of clinical pharmacology could begin to address training and educational needs possibly through building links with such organisations as WHO, and the International Network for the Rational Use of Drugs. This commitment from IUPHAR was achieved at the meeting, and our strong impression was that delegates from developed and developing countries left with a similar perspective. ■

outcomes would accrue if we could better implement evidence based guidelines and improve patient adherence to therapy. In the prevalent cardiovascular disorders, lowering blood pressure is the intervention for which there is the best evidence. Despite these proven benefits, BP control is poor worldwide. There are good arguments to support a more aggressive approach to BP management and to treat younger subjects, but, once again, long-term compliance remains sub-optimal. This linked to an important theme running strongly through the meeting namely the concept of "Quality Use of Medicines" or QUM, an acronym developed in Australia in the early 1990s. The conference was an important opportunity for Australia to showcase progress in achieving QUM through our approach and achievements in gathering evidence about what works and then implementing it along

# Sir John Vane

## 1927 - 2004

John Vane became a pharmacologist by accident. His first choice of career, stemming from a childhood hobby, was chemistry and he graduated from the University of Birmingham with a Bachelors degree in that subject in 1946. But John, who was an experimentalist by nature, did not find the actual practice of chemistry as rewarding as he had imagined. Discussing his future with his head of department, he was told that J. H. Burn in Oxford was seeking graduates to be trained in pharmacology. John later wrote “without hesitation I grasped the opportunity and immediately went to the library to find out what pharmacology was all about!” The study of experimental pharmacology turned out to be exactly what he was looking for and he never forgot Burn’s inspirational early influence on his work and thinking.

After qualifying, John spent a short time at Sheffield University before returning to Oxford for postgraduate studies with G. Dawes. In those days it was common for post doctoral scientists to do a stint in the USA and after receiving his D.Phil. John was invited by A. Welch to join the Department of Pharmacology at Yale as an Assistant Professor. These early years were formative ones for John and one may trace the roots of much of his subsequent work back to these early influences and to the friendships he forged at this time.

In 1955 John returned to the UK and embarked upon what might be regarded as the first of his three major creative periods. He joined W. D. M. Paton’s Department of Pharmacology at the Institute of Basic Medical Sciences which was (after some time at Queens Square) located at the Royal College of Surgeons of England in London. John rose quickly through the academic ranks gaining a personal chair himself in 1966. G. V. R. Born, a friend of John from his Oxford days, had

succeeded Paton in 1961 and under the joint influence of Born and Vane, the department at the Royal College provided an astonishingly productive intellectual environment which published much cutting edge science, nurtured many careers and rose to great prominence.

It was during these years that John perfected his signature ‘blood bathed organ cascade’; a combination, and a development along extraordinary lines, of J.H. Gaddum’s parallel bioassay and superfusion techniques of 1953. Blood from animals, or sometimes humans, was passed continuously over a series of isolated tissues chosen for their exquisite sensitivity to, and ability to differentiate between, hormones or other substances under investigation. This technique enabled John to measure instantaneously and with great specificity, the levels of one or more blood hormones. The dynamic nature of this technique suited his temperament for insights and ideas came quickly to him and he was impatient to test them.

When animal blood was used it could be sampled from many different sites in the body and recirculated into the venous return enabling John to pinpoint the organs responsible for the release and removal of hormones such as angiotensin and bradykinin. Working on this problem with S.H. Ferreira, Y.S. Bakhle and others he observed that the pulmonary circulation was a major site for the destruction of bradykinin as well as for the conversion of angiotensin I to angiotensin II. The group speculated that both phenomena were attributable to the same enzyme and deduced that the ‘bradykinin potentiating factor’ from *Bothrops jararaca* venom, which inhibited bradykinin proteolysis, might also block angiotensin I conversion and furthermore, that this strategy could prove a useful therapy for hypertension. John took the idea to Squibb where Welch, John’s mentor from Yale, was by then Research Director. The outcome of this initiative was the development of the revolutionary ACE inhibitors.

A few years later, in 1971, John began what is generally regarded as his finest piece of work.

Aspirin was a drug that had been around since the end of the 19th century, but for all its utility it had defied every attempt to unravel the underlying mechanism that linked together its



distinctive therapeutic and side effects – a pharmacological profile that was also shared by many other ‘non-steroidal anti-inflammatories’. John’s interest in prostaglandins had been kindled some years earlier and over a weekend he conceived the notion that perhaps aspirin worked by inhibiting the generation of these multi-faceted mediators. He turned again to his bio-assay system for the answer and within a few days he had convinced himself and his colleagues that this indeed was the missing mechanism of action. This concept, which he further expanded mainly with Ferreira, S. Moncada and R. J. Flower, profoundly influenced the field including (in the 1990s) the development of Cox-2 inhibitors.

1973 saw a change in John’s circumstances. Born had taken a chair in Cambridge and John

was offered the position of Group Research and Development Director of the (then) Wellcome Foundation, in Beckenham, Kent. In those days ‘The Foundation’ was a unique institution; a pharmaceutical company whose profits were gifted to the charitable Wellcome Trust. Perhaps John was encouraged to accept this post by the thought that Sir Henry Dale, one of his intellectual heroes, was recruited by Henry Wellcome and was crucial to the early development of the company.

The thirteen years that John spent at Wellcome presented him with a new and different set of challenges. He had no more time for lab work as such but continued to exert his influence on research in different ways. John had very definite views about drug discovery believing that if you recruited the most motivated scientists and allowed them to work on problems of their own choice in a well supported environment, then new ideas about disease mechanisms and ultimately new drugs would inevitably ensue. To implement this vision he took Ferreira, Moncada, Flower, G.A. Higgs and others with

him to form a nucleus of his personal research group. In 1976, working mainly through Moncada, R. Gryglewski and S. Bunting, John’s group discovered the potent vasodilator and anti-aggregatory prostaglandin ‘X’. The mystery substance was characterised in collaboration with Upjohn and renamed prostacyclin (PGI<sub>2</sub>). Analogues were later approved for the treatment of pulmonary hypertension and antithrombotic indications. Under John’s management, Wellcome produced several other important drugs including Zovirax, Tracrium and Lamictal.

By now, John’s contributions to his discipline were increasingly recognised. In 1974 he was made a Fellow of the Royal Society, in 1977 he won the Albert Lasker Basic Medical Re-

*continued on next page*

search Award and in 1982 he shared with B. Samuelsson and S. Bergström, the Nobel Prize for Physiology or Medicine for his work on aspirin. In 1984 he was knighted in the New Years Honours list for services to pharmaceutical science. Over fifty other honorary degrees and fellowships followed over the years.

In 1986, aged 59, John left the Wellcome Foundation but the idea that he might simply

retire and enjoy the fruits of a life's work was simply not an option for him. An invitation from St Bartholomew's Hospital Medical School, brokered by another old friend, D Willoughby, coupled with an offer of some start-up funding from Glaxo Group Research, gave John the opportunity to start up a new lab; he accepted this challenge with alacrity thereby initiating the third major phase of his career. As always when starting a fresh venture, John's technique was to surround himself with colleagues that he trusted and respected and to work together with them to build up a critical mass of talented researchers. Groups

headed by E. Änggård, N. Benjamin, I. MacIntyre, D. Tomlinson, B. Whittle and Willoughby, as well as old colleagues Born and Flower, joined with John to promote his vision of free-standing Institute devoted to excellence in inflammation and cardiovascular research. From this confluence of research groups arose The William Harvey Research Institute. Major funding from Ono Pharmaceuticals in Japan enabled his institute rapidly

to expand and it soon became a veritable pharmacological powerhouse with a staff of over 120 people.

John himself, whilst rarely doing lab work, continued to influence the direction of the science focusing again mainly upon hormones influencing the heart and blood vessels as well as on the pharmacology of the Cox-2 inhibitors and even found time to start up (with Änggård) a new company, Vanguard Medica

Ltd. (now Vernalis). He retired as full-time Director of the Institute in 1995 but still maintained his office and continued to influence the course of research and to direct young people. Following the merger of the Institute with the medical school in 2000 John took over the role of Honorary Chairman of the charitable William Harvey Research Foundation.

In getting to know John, there inevitably came a point when one was introduced to his family. John had married Daphne during their Oxford days where their two daughters, Nikki and Miranda had also been born. Although by nature rather a shy

man, John was immensely sociable and together with Daphne and his daughters frequently entertained their friends and colleagues at their home, in restaurants and at scientific meetings around the world. Such parties were legendary and always carried off with enormous panache. Close colleagues were adopted by the Vanes as a sort of extended family which burgeoned as they made many life-long friends. Whenever scientists

Salicylates have been in use since ancient times, when the Egyptians, Greeks and Romans treated pain with willow bark. Aspirin became the "wonder drug" of the 19<sup>th</sup> century for its fever-reducing and anti-inflammatory properties. It was Sir John Vane who discovered how this versatile compound works: by inhibiting the production of prostaglandins.



get together they like to discuss data, experiments and ideas which often make dull listening for others. But if this bothered Daphne, with her background in the liberal arts, she never showed it and always treated John's colleagues with great grace and charm. John was devoted to his 'girls', as he called them, and they provided the strongly supportive base from which he was able to launch his frequent and punishing schedules of work and travel.

Science with its uncompromising regard for facts and evidence rather than beliefs, is one arena where people can truly work together unhindered by considerations of race, colour, creed or gender. Like most scientists John was a committed internationalist in this respect. His labs were full of researchers from around the world and UK scientists usually constituted a minority. Of particular significance was John's relationship with the Polish scientific community which began in the late '60s during the cold war era. John made many trips to Poland during those difficult times often taking hard-to-obtain scientific equipment and reagents with him and offering Polish scientists the opportunity to visit the West and to work in his laboratory. He made many close friends there and visited the country each year, invariably accompanied by Daphne, to attend scientific meetings. In 2003, John was accorded a rare honour in recognition of his contributions to the Anglo-Polish scientific collaboration when he was awarded the Polish Order of Merit at a ceremony in Warsaw.

As in many fields of medical research, John's own studies often depended upon laboratory animals. This drew unwelcome attention from the animal rights extremists who, being humanitarians, pursued a particularly vindictive campaign against him. Hate mail was sent; fire bombs thrown at his house and graffiti daubed on out buildings. These terror tactics did not deter him from his work and he was always an eloquent advocate for the responsible use of animals in scientific research and a source of moral support to others who had suffered in a similar way.

John Vane was heir to the physiological tradition of pharmacology. He watched the molecular biology revolution unfold from the sidelines and his confidence in bioassay as an engine for the generation of new ideas and discoveries remained undiminished throughout his life. He died peacefully in the Princess Royal Hospital in Farnborough on Friday 19th November 2004 of pneumonia but his students, his research style, his extensive publications and his institute are a continuing testimony to his enormous influence as a pharmacologist and as a man.

RJ Flower

*This article is a shortened version of an obituary which first appeared in pA<sub>2</sub>, the Members' magazine of the British Pharmacological Society, and is reproduced here with permission.*

# Upcoming Events

## Symposium on Mechanisms of Vasodilation and EDHF

Antwerp, BELGIUM  
May 31 - June 4, 2005  
[www.mechanisms-antwerp.be](http://www.mechanisms-antwerp.be)

### Committee Chairs:

Arnold G. Herman (Antwerp, Belgium)  
Paul M. Vanhoutte (Hong Kong, China)

- Session 1: "The forgotten controllers: autonomic nerves"
- Session 2: "The endothelium: Nitric Oxide"
- Session 3: "The endothelium: EDHF & EDCF"
- Session 4: "The effector: vascular smooth muscle, contraction and relaxation"
- Session 5: "The effector: vascular smooth muscle growth"
- Session 6: "The vascular wall and disease"

Abstracts submission deadline: March 15, 2005

Contact: [info@mechanisms-antwerp.be](mailto:info@mechanisms-antwerp.be)

## 9th International Congress on Amino Acids and Proteins

Vienna, AUSTRIA  
August 8 - 12, 2005  
[www.proteomics-brainprot.at/icaap/](http://www.proteomics-brainprot.at/icaap/)

Areas include: Amino Acid and Protein-Technology (Proteomics, Analysis, Separation, Synthesis), Biochemistry, Biology, Medicine, Neuroscience, Pharmacology, Nutrition

### Organizers:

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M. Fountoulakis (CH)  
G. Lubec (A)

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## 7th Congress of the European Society for Clinical Pharmacology and Therapeutics (EACPT)

Poznań, POLAND  
June 25 - 29, 2005  
[www.eacpt.pl](http://www.eacpt.pl)

For scientific information and abstracts:  
Polish Society for Clinical Pharmacology and Therapeutics  
ul. Libelta 27  
61 - 707 Poznań  
Tel: +48 61 852 40 03 ext. 31,  
Fax: +48 61 852 74 72,

For general information, registration, hotels, exhibition and tours:  
B.P. Horizon Travel Sp. z o.o.  
ul. Sianowska 37/2  
60 - 431 Poznań, POLAND  
Fax: +48 61 849 98 20

[www.horizon-travel.pl](http://www.horizon-travel.pl)

## XVth World Congress of Pharmacology

Beijing, CHINA  
2 - 7 July 2006  
[www.cnphars.org](http://www.cnphars.org)

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