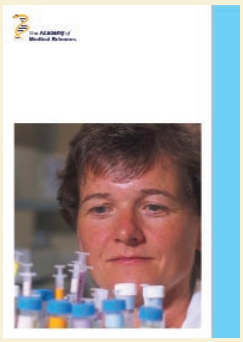
The Academy of Medical Sciences

Fellowship
Newsletter

Availability of Medicines



Review

The Academy's first Review was presented to the Fellowship at the Annual General Meeting on 17 November. The Review summarises the challenges faced, and achievements won, by the Academy in its early years and offers insights into future plans. Articles from Lord Warner, John Bell, Michael Marmot, Fiona Watt, Lorna Marson and the Academy's President, Sir Keith Peters, illustrate the breadth of Academy work and the impact this is making.

The high point of 2004 was the announcement in June of the award of grant-in-aid from the Department of Health of £1.75M over five years. In delivering this most welcome news, Lord Warner praised the Academy for its authoritative and influential reports, for building and sustaining partnerships across sectors, and for undertaking important and innovative work in support of young clinical scientists.

The Academy welcomes feedback from Fellows.
Please email: apollo@acmedsci.ac.uk

The Availability of Medicines: looking 'through a glass darkly'

Professor Trevor M Jones CBE
Former Director General, The Association of the British Pharmaceutical Industry

Modern medicines improve both the quantity and the quality of life allowing patients to lead independent lives and to return to active and productive work to the benefit of themselves, their families and importantly, the economy. But although we treat diseases quite well, we cure very few. Furthermore, the availability of medicines to patients is, to say the least, 'patchy'. Why is this?

Firstly, despite advances in our understanding of the causality of diseases, the scientific obstacles to the discovery of new medicines are still very high. The sequencing of the human genome (and importantly the genomes of pathogens and disease vector organisms) is providing new insights but we still 'look through a glass darkly' at the multiple factors that cause diseases.

The Availability of Medicines: looking 'through a glass darkly' continues on page 2

Continued from the front cover.

For example although the genome of HIV has been known for over a decade, together with the genetic variability of HIV Clades and resistant strains, we still have not found the key to developing an effective vaccine. Whilst thankfully we have an array of antiretroviral medicines which can suppress viraemia and arrest immunological decline, the propensity of the virus to mutate is such that we require the availability of even more of these wonder 'me – too' drugs in our battle against this global enemy.

The second reason for the poor availability of medicines is the massive increase in regulatory requirement that has occurred over the past 10 - 20 years. The regulation of medicines by Governments is necessary to provide society with safeguards in terms of safety quality and efficacy. However, in recent years the balance between 'risk' and 'benefit' has followed precautionary principles that have resulted in a considerable slow down in our ability to provide new medicines. Sir Michael Rawlins has suggested 'Regulation is killing us'!

An example is the requirement of both European and USA regulators that new antiinfective products fulfill the so-called 'Delta 10' requirement (i.e. their clinical efficacy in a phenotypic population shall not be less than 10% of the current product used for treatment.) To achieve such statistical significance, Phase III clinical trials now need to include in excess of 8000 patients! The result has been that many of the pharmaceutical companies who re-entered this field have now transferred their research effort to other therapeutics areas. The development of new anti-infectives has slowed to a snail's pace, whilst our discovery research capability has never been better. All this at a time when the world needs better antimicrobials to combat multi-drug resistant organisms and the emerging biological threats.

A third reason for the lack of availability of medicines, particularly for millions of people in the developing world, is the lack of any financial capacity (or incentives) to pay for the expensive long-term investment that characterizes drug discovery and development. In a world where 2.8 billion of our fellow human beings live on less than $2 per day and where governments either have no money to pay or are in denial over the reality of infectious disease, it is clear why there remain a number of neglected diseases, e.g. leishmaniasis, African trypanosomiasis, Chagas disease, etc. The cost of investment in R&D could not possible be matched by local healthcare budgets. Fortunately, this matter is now the subject of several Public-Private-Partnerships between industry, academia and private charitable foundations but the lack of funding by the international community, particularly by governments, is a genuine threat to the long-term sustainability of such endeavor.

Professor Trevor M Jones CBE
Former Director General, The Association of the British Pharmaceutical Industry

Even when medicines have been developed there are several reasons why they are not available to sectors of the population. For example, where adequate clinical trial data exist (using biomarkers for disease progression), regulatory authorities have been prepared to grant Product Licences for fixed dose combinations of antiretrovirals.

However, due to the rapidly changing pattern of HIV resistance and the number of potential antiretroviral 'cocktail' combinations together with the complexity (especially in sub-Saharan Africa) of obtaining GCP compliant data and, importantly reliable Pharmacovigilance data, very few of such multiple combination products have been approved by the US FDA or the EU EMEA. The situation is particularly acute for children living with HIV for whom the acquisition of data and, particularly formulation issues, are considerably more complex.

Indeed, the availability of Paediatric formulations, with therapeutic claims approved by the Regulatory agencies, presents particular difficulties in the availability of medicines for children. We have long recognised that children are not 'little adults' and that the choice of drug, dose and formulation differs with age and stage of development (e.g. pre-term, neonate, baby, infant, adolescent etc). Entirely new medicines have been the subject of clinical trials in an adult population that is highly selective (usually with at least 30 exclusion criteria). Very rarely will the medicines have been trialed in children.

The originator company bears legal liability for the claims in its Product Licences. In order to obtain such authorization in each of the varied paediatric populations the company has only 10 years of exclusivity before generic competition. It would be unethical and often dangerous to expose children of different ages to new drugs until their safety has been established in a normal and more robust adult population. Even then, the complexity of carrying out such trials (e.g. those that include such procedures as multiple venepuncture to establish pharmacokinetics etc) present considerably further challenges. It is unsurprising, therefore, that most

of the medicines available today and in the foreseeable future will not have been tested in children at the time of launch or even during the period of originator exclusivity. Nevertheless, the industry is prepared to agree a programme of work with the regulatory agencies that, hopefully, can be pursued during the exclusivity period. Frustratingly, the European Directives that would enable such studies are the subject of continuous delay despite a sustained lobby by the industry, by pediatricians and by the British Government.

Finally, perhaps the greatest barrier to the availability of medicines is affordability. Selecting the best medicine for a particular patient is no longer based solely on clinical principles but rather on healthcare budgets, cost effectiveness and political decision relating to priorities. As a nation we can afford the best medicines and the best treatment; we choose not to. It is a sad reflection that the excellence of our clinical and medical R&D is so poorly translated into life-saving and life-prolonging medicines for all. ■

The supply of veterinary medicines in the UK: an industry challenged

Professor Richard Halliwell, FMedSci
Senior Vice-President, Royal College of Veterinary Surgeons

Faced with unremitting bureaucracy, both at national and EU levels, the animal health industry in the UK is facing serious challenges. The national market turnover approximates £400 millions annually and is evenly divided between companion animals and food producing animals. Many of the products employed in companion animal practice were developed initially for human medicine, and then adapted as necessary for animal use. This is less true in the case of food producing animals where greater proportions are biologicals for disease prevention and individual animal treatment is less frequently undertaken. Recent years have seen rationalisation of companies in the arena, with few, larger players remaining. This has had a mixed effect: although there may be greater investment available, products with limited sales potential are not pursued.

The UK laws of prescribing veterinary products require prescribing veterinarians to use the cascade principles, and employ a drug licensed for the condition in the species under treatment. If none exists, then a drug licensed for the condition in another species, or for a different condition in the same species, may be used or failing this, a drug licensed for use in man or an extemporaneous preparation. Although logical and desirable in terms of protecting the investment made in licensing the drug, the clinician's ability to choose the best drug for the circumstances is seriously curtailed. In order to import a drug, a special treatment authorisation must be obtained for the individual case from the Veterinary Medicines Directorate (VMD). Such a system is not appropriate for emergency situations and animal welfare is often compromised.

The impediments to new drug developments exist at UK and European levels. Firstly, an Animal Test Certificate (ATC) must be obtained from the VMD in order to conduct clinical trials. Although some improvements have been made recently, the level of detail required, which is based upon longstanding UK medicines law, is greater than for other EU countries, and the average cost to companies of putting together an application is higher, at some £30-35K. This has resulted in trials moving overseas. The result is that few new drugs are coming onto the market. The impact is greatest, of course, for minor uses and minor species, and although the problem is recognised, the regulatory hurdles still remain.

The market viability in the EU as a whole should be secure. But the regulatory hurdles are still formidable, with member states requiring input under the 'mutual recognition' system, shortly to become the 'decentralised system'. Although central recognition – which all states are obliged to recognise - is an option, the cost (estimated as £100,000), and the volume of material submitted, which can exceed 500,000 pages, are serious disincentives.

In conclusion there are serious concerns regarding the very viability of the animal health industry in the UK and Europe. The reduced bureaucracy that exists in the USA enables veterinary medicine to be practiced at a higher level. Major changes are required in the UK and Europe if we are to catch up. ■

Professor Richard Halliwell, FMedSci

Sir Alan Craft FMedSci
President, Royal College of Paediatrics
and Child Health

Medicines for Children

At long last we are beginning to address the almost scandalous situation regarding medicines for children. This age group are the most vulnerable in society with no voice of their own, yet the vast majority of drugs given to them are untested and unlicensed in this age group. Several initiatives are coming together at this time. Eight years ago the Royal College of Paediatrics recognised this problem and Professor Sir David Hull led a working party funded by the Nuffield Foundation, who produced an excellent book, 'Medicines For Children', which brought together all of the available evidence and expert opinion. It has been widely used by paediatricians and pharmacists. However, very few general practitioners have taken advantage of its wisdom in spite of the huge number of prescriptions that they write for children. The Department of Health in England recently announced that it would purchase a new British National Formulary for children for all of those likely to prescribe for this age group. The BNFC is well on track for publication in the summer of 2005 and will replace 'Medicines for Children' as the authoritative source of advice.

However, most medications will remain unlicensed. In the US, this issue has been addressed by giving the pharmaceutical industry real incentives to test medicines for children and imminent EU legislation should do the same on this side of the Atlantic. But this is only the start. Industry will need skilled professionals and patients on whom to test both old and new drugs. At present there is little capacity in paediatric clinical pharmacology in the UK, and indeed in Europe. Once again the US addressed this issue by establishing 10 academic centres; this has now increased to 14. It is hoped that recent announcements from the DH around clinical trial networks for children will soon be followed by a research capacity building programme.This is an ideal time for pharma and academia to get together for the benefit of children. The legislators are giving both opportunities to both which they must not miss. Children rely on us to make sure they get the maximum benefit and least harm from medicines. ■

Editorial

Sir Alexander Macara FMedSci, Editor

Consider the contemporary scene: newly emerging diseases (SARS), new variants of existing ones (Asian flu) and drug resistant strains of pandemic infections (T.B., MRSA, HIV, sexually transmitted diseases). And that modest list is just the communicable diseases whose historic and constant 'health threats' have been painfully rediscovered in recent years, with the added challenge of a potential terrorist apocalypse. Add to the list the burgeoning burden of chronic disease – physical and mental - as people indulge disordered life-styles ever longer until the inevitable crash occurs and someone has to put the pieces together again.

We cannot be accused of complacency in the contemplation of this gloomy landscape. In the last issue of this newsletter, Derek Wanless set out his strategy of a 'fully-engaged scenario' to mobilise all the resources – economic, physical, societal and structural – required to address this picture by preventing preventable disease in a refreshingly long-term vision and programme. And now the Government in England has published its White Paper on 'Choosing Health', which offers a route map. Simultaneously the Government has shown an awareness of the alarming crisis in science education (*vide*. the vanishing university chemistry departments).

There is an irony at the heart of this encouraging response. All at once it seems, the pharmaceutical industry whose remarkable success, notably in the United Kingdom and at the hands of distinguished Fellows of the Academy, in developing innovative and effective products, has for too long been taken for granted and is consigned to the dog-house. For some critics, it is as though its proud history of life-saving break-throughs and its support of continuing medical education and research, was of little account. Just when it manifestly needs all the understanding and support it can get to meet its problems both in general and in specific fields such as children and animal health so starkly set out in Tom McKillop's 2004 Forum lecture and in the contributions kindly provided by colleagues in this issue, it has become the latest popular whipping-boy following some highly publicised criticisms.

Take heart, Tom *et al*, the medical profession knows what it feels like. As in medical practice, the solution will not be found in yet further regulation.

Sir Alexander Macara FMedSci, Editor

Lastly it is with regret that I note the sad passing of Sir John Vane FRS, a most distinguished Fellow of the Academy and an exceptional Pharmacologist, winner of the Nobel prize for medicine after discovering how aspirin worked.

The UK Clinical Research Collaboration

Grasping the Opportunity

Liam O'Toole
Chief Executive,
UK Clinical Research Collaboration

The Academy of Medical Sciences Report "Strengthening Clinical Research" highlighted the need to revitalise clinical research in the UK. The Research for Patient Benefit Working Party was set up in response to this, and the BIGT Report, which had given out an equally strong message. The Working Party recommended the creation of a new partnership, the UK Clinical Research Collaboration (UKCRC) to establish the UK's place as a global leader in contributions to clinical research.

Creation of the UKCRC offers us an incredible opportunity to reshape the environment in which clinical research is conducted in this country. This is an enormous challenge. Can the UKCRC deliver the changes needed?

The Collaboration has a lot going for it. It brings together many of the major stakeholders: the research funders from Government and charity, industry umbrella groups, the regulatory bodies, NHS, the Royal Colleges, patient groups and of course, the Academy. Between them, these organisations control a large part of the UK clinical research environment, so it is significant that they have come together, and signed up to a shared vision of the future. We also have new resources. The establishment of the UKCRC was backed by a Government commitment to increase funding for medical research and an increase in NHS R&D funding.

We have also inherited a clear set of tasks. The UKCRC partners have agreed on a number of interconnecting workstreams designed to:

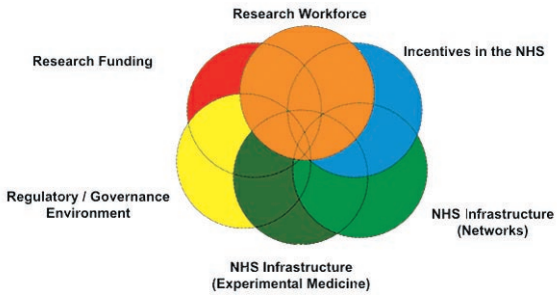
- build up the infrastructure
- co-ordinate clinical research funding
- build up the research workforce
- build incentives for research into the NHS
- streamline the regulatory and governance processes

Currently, work on each of these workstreams is at a different stage of development but they are all important. To improve the environment radically, we will need to impact on all of these areas.

At the moment, for most people, UKCRC means the new DH funded clinical networks (diabetes, medicine for children, stroke and Alzheimer's). These networks have the potential to make a big difference but they need the UKCRC partners to make progress in the other workstreams to have maximum effect. Together with the cancer and mental health networks, they will provide the NHS infrastructure to underpin clinical trials and other well designed studies in a number of topic areas. Linked by a generic co-ordinating centre, these networks will provide a basis for the development of a generic infrastructure to underpin all clinical research. However, these networks are only part of the picture. Building on the Wellcome Trust model for Clinical Research Facilities, negotiations have begun between the major research funders to develop an UKCRC-branded initiative to enhance the experimental medicine infrastructure in the UK.

There is a lot to be optimistic about. However, if we are to have significant impact we must overcome some major challenges. For the UKCRC to be successful it must work as a collaboration rather than as a discrete entity. This means partner organisations taking a lead on specific issues on behalf of the Collaboration as a whole. We will also have to balance the need to move quickly and demonstrate to Government that their new

The UKCRC Workstreams



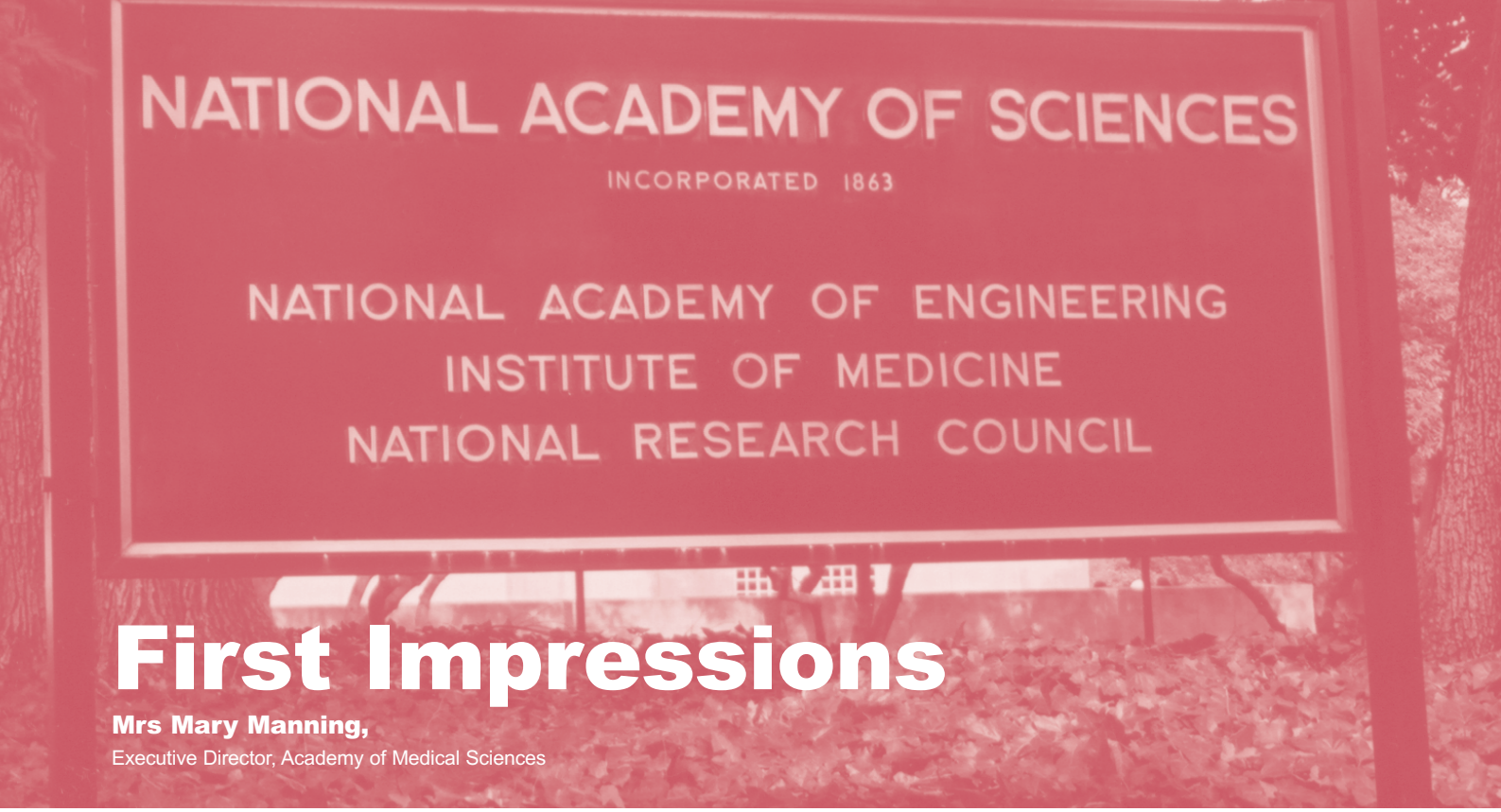
investment is making a difference, with the need to affect sustainable change that results in high quality research. These challenges can only be met through close co-operation from a range of different stakeholders.

There are many groups not on the UKCRC Board that, if we are to move forward, we will need to engage with on specific issues. This must be done without creating a bureaucratic representational structure, so emphasis throughout UKCRC activity will be placed on engagement through consultation and negotiation, rather than formal representation.

It will be equally important to adopt a solutions based approach. Many of the answers to current challenges are already out there. From the start we need to ensure that we use the Collaboration to negotiate, agree and implement collective solutions rather than merely publish further recommendations.

The omens are good. Now we need to harness the power of partnership, grasp this opportunity and make it happen!

www.ukcrc.org



First Impressions

Mrs Mary Manning,
Executive Director, Academy of Medical Sciences

Drop into any office occupied by a member of staff of the Institute of Medicine in Washington DC and the first thing you will be shown is a large pile of reports. Activity is measured in volume inches and with reason: this is an institution that has some 70 study groups and at least two dozen working groups in progress at any one time, produces over 40 publications a year, and can claim that up to 20% of its members are actively involved in Institute projects.

These were my first impressions when I visited the Institute of Medicine in October at the invitation of the Executive Director, Susanne Stoiber. My prime purpose was to attend the annual meeting and admission of new members and to get to know our colleagues in the USA. Based within the headquarters building of the National Academies of Science on Constitution Avenue, the IOM is geographically and culturally at the centre of the Washington political scene.

The Institute of Medicine was established in 1970 by the National Academy of Sciences as a membership body and a policy research organisation to deal with issues of medicine and public health. The majority of studies and activities are requested and funded by the federal government. Private industry, foundations, and state and local governments also initiate studies, as does the IOM itself. The breadth of activity is impressive: looking through the list of publications for the past twelve months I found reports on childhood obesity, diversity in the healthcare workforce, environmental health, SARS, vaccine safety, Gulf War and health, and the review of NASA's longitudinal study of astronaut health – to name but a few.

The production of such an eclectic mix of topical reports is made possible through the broad membership of the IOM: the charter stipulates that at least one quarter of new members be selected from outside the health professions, from such fields as the natural, social and behavioural sciences, as well as law, administration, engineering and the humanities. On the face of it this seems very desirable but, in fact, is not without controversy and there are tensions beneath the surface that might be all too familiar to our own community in the UK.

My visit coincided with the run-up to the presidential election but the hullabaloo surrounding the last minute campaigns of the Presidential candidates hardly registered on the dignified proceedings of the IOM's annual meeting. To quote the IOM's President, Dr Harvey Fineberg: 'A presidential election year tends to accentuate partisan politics in Washington. Word and deed are weighed ever more carefully to sway public opinion…..In this strained atmosphere, the oxygen of objectivity is a precious commodity. In times such as these, an independent, non-partisan, scientific voice like that of the IOM needs to be heard more than ever.'

There is much to admire in the IOM and we could profitably draw upon their experience and knowledge. The warmth of their welcome bodes well for future inter-Academy activity. ■

Mrs Mary Manning with Dr Harvey Fineberg

Academy News

Academy Officers

Council is pleased to announce the appointment of Sir Michael Rutter as Vice-President, in succession to Lord Turnberg who has completed his term of office as founder Vice-President of the Academy.

Academy Council

The election of Ordinary Members of Council took place at the Academy offices on Wednesday 10 November. The following Fellows were elected; their appointment took effect from the AGM on 17 November 2004: -

- Professor Stephen Bloom
- Sir Alan Craft
- Professor Christopher Haslett
- Professor Susan Iversen
- Professor Christopher Kennard
- Professor Stephen O'Rahilly
- Professor Herman Waldmann

Our congratulations and thanks to all who support the Academy in this way.

News and Events

Lord Warner announced on 29 June 2004 that the Department of Health would provide a grant-in-aid of £1.75 million to meet the core running costs of the Academy over the next five years.

Sir Keith Peters, President of the Academy of Medical Sciences, delivered The Harveian Oration, 'Exceptional Matters', before the Fellows of the Royal College of Physicians of London on Tuesday 19 October 2004.

Bursary scheme for young scientists & clinicians:
With generous support from the Foulkes Foundation, the Academy is pleased to announce the launch of a bursary scheme to provide opportunities for young scientists and clinicians to attend Academy meetings and lectures. It is hoped the scheme will enable young people to meet their peers and senior academics, and will foster the development of a life-long network of friends and colleagues from across the spectrum of medical science. The bursaries will cover the cost of the meeting registration fee (where applicable) and contribute to the cost of travel to and from the event. The scheme is open to graduate students and young clinician scientists.

On Monday 29 November the Academy hosted the inaugural Academy of Medical Sciences Lecture on International Health, at Imperial College. The lecture, Understanding Poxviruses: *Jenner genomics and genetic engineering*, was delivered by Professor Bernard Moss, Chief of the Laboratory of Viral Diseases, National Institute of Allergy and Infectious Diseases, USA to an audience of Fellows, guests and students.

Two Fellows focus groups took place in late November, at Imperial College London and at the University of Edinburgh. Fellows took time out to discuss various issues included what the Academy means to them and where the Academy should be heading in the future. Professor Tom Kirkwood FMedSci led the discussion and will report on the outcomes in a future issue.

Awards

Two Academy Fellows received the University of Edinburgh's prestigious Cameron Prize, Professor Ravinder Maini FMedSci and Professor Marc Feldmann FMedSci in November.

Sir David Lane FRS FMedSci was awarded the Royal Society Buchanan Medal in November

New appointments in the Academy office

Ms Jenny Steere, Forum Programme Officer joined the office in November and Ms Liz Holder has taken on the post of Finance Officer.

New Website

Our new website designed to promote careers in academic medicine was launched on 17 November. **www.academicmedicine.ac.uk**

The purpose of the website is to provide information to the public about the need for, and role of, academic medicine and medical science and to encourage young people to consider following a career in medical science and help those who have already embarked on one.

The website includes case studies and interviews with practitioners and has links to medical school and funding body resources as well as explanations of the various medical specialties. It is still a work in progress and will be undergoing further development in the coming months.

Publications and Responses to Government Consultations

Recent publications include:

- October 2004: Response to the House of Lords Select Committee on Science & Technology inquiry into the 'Scientific Aspects of Ageing'
- November 2004: Academy Review

A copy of all the documents can be found on the academy website, **www.acmedsci.ac.uk**

Academy Annual Meeting and Jean Shanks Lecture

The Academy held its 7th Annual meeting at University College London on Wednesday 17 November. Three distinguished Honorary Fellows were admitted to its ranks: Sir William Castell, Sir David Cooksey and The Rt. Revd. Richard Harries, Bishop of Oxford. The meeting concluded with the Jean Shanks Lecture delivered by Sir Philip Cohen FRS FRSE FMedSci, ***Protein kinase inhibitors: the major drug targets of the 21st Century?*** to an enthusiastic audience of Fellows, guests and students.

Image (above)
1: Sir Philip Cohen FRS FRSE FMedSci
2. (left) Sir Keith Peters FRS PMedSci
3. (bottom) Professor Patrick Vallance FMedSci

Images (below)
4: The Annual General Meeting
5. (bottom left) Sir Richard Sykes FRS FMedSci
6. (bottom right) Mrs Mary Manning

Academy Annual Dinner

The Academy held its annual dinner on Wednesday 17 November at the splendid Great Hall at St Bart's. The occasion was enjoyed by over 100 Fellows and distinguished guests.

Images (above)
1: Annual dinner reception at St. Bart's

Images (top right)
2: Dr Jo Harries and the Rt. Revd. Richard Harries HonFMedSci
3: Dr Mike Crumpton CBE FRS FMedSci and Sir William Castell LVO HonFMedSci

Images (below)
4: Professor Peter Openshaw FMedSci, Sir Keith Peters FRS PMedSci and Mrs Maureen Foulkes

Images (above)
5: Professor Robert Souhami CBE FMedSci, Professor Bruce Ponder FRS FMedSci, Mrs Mary Manning and Sir David Cooksey HonFMedSci

Forthcoming Events

Annual Forum Lecture

7th March at 18.00

The Kohn Centre, 6-9 Carlton House Terrace, London SW1Y 5AG

'Cancer research in the UK: areas of optimism and concern' by Professor Alex Markham FMedSci, Chief Executive, Cancer Research UK

To register please email forum@acmedsci.ac.uk or telephone 0207 969 5288

Admission Ceremony for New Fellows

Friday 24th June

Wellcome Trust Lecture Theatre, 6-9 Carlton House Terrace, London SW1Y 5AG
Time to be confirmed.

The independent Academy of Medical Sciences promotes advances in medical science and campaigns to ensure these are translated as quickly as possible into benefits for patients. The Academy's eight hundred Fellows are the United Kingdom's leading medical scientists from hospitals, academia, industry and public service. The Academy's Officers are: Sir Keith Peters, FRS, PMedSci *President*; Sir Michael Rutter CBE FRS FMedSci; Sir John Skehel, FRS, FMedSci *Vice-President*; Sir Colin Dollery, FMedSci *Treasurer* and Professor Patrick Vallance *Registrar*. The Executive Director of the Academy is Mrs Mary Manning.

Editor:
Sir Alexander Macara, FMedSci
Copy-editor:
Ms Roz Morton
Designed and produced by:
www.alt-design.net

Published by:
The Academy of Medical Sciences
10 Carlton House Terrace
London SW1Y 5AH

Phone:
020 7969 5288
Fax:
020 7969 5298
E-mail:
apollo@acmedsci.ac.uk
Web:
www.acmedsci.ac.uk

THE ACADEMY OF MEDICAL SCIENCES IS A COMPANY LIMITED BY GUARANTEE

Registered Charity No.:
1070618
Registered Company No.:
3520281
Registered in England