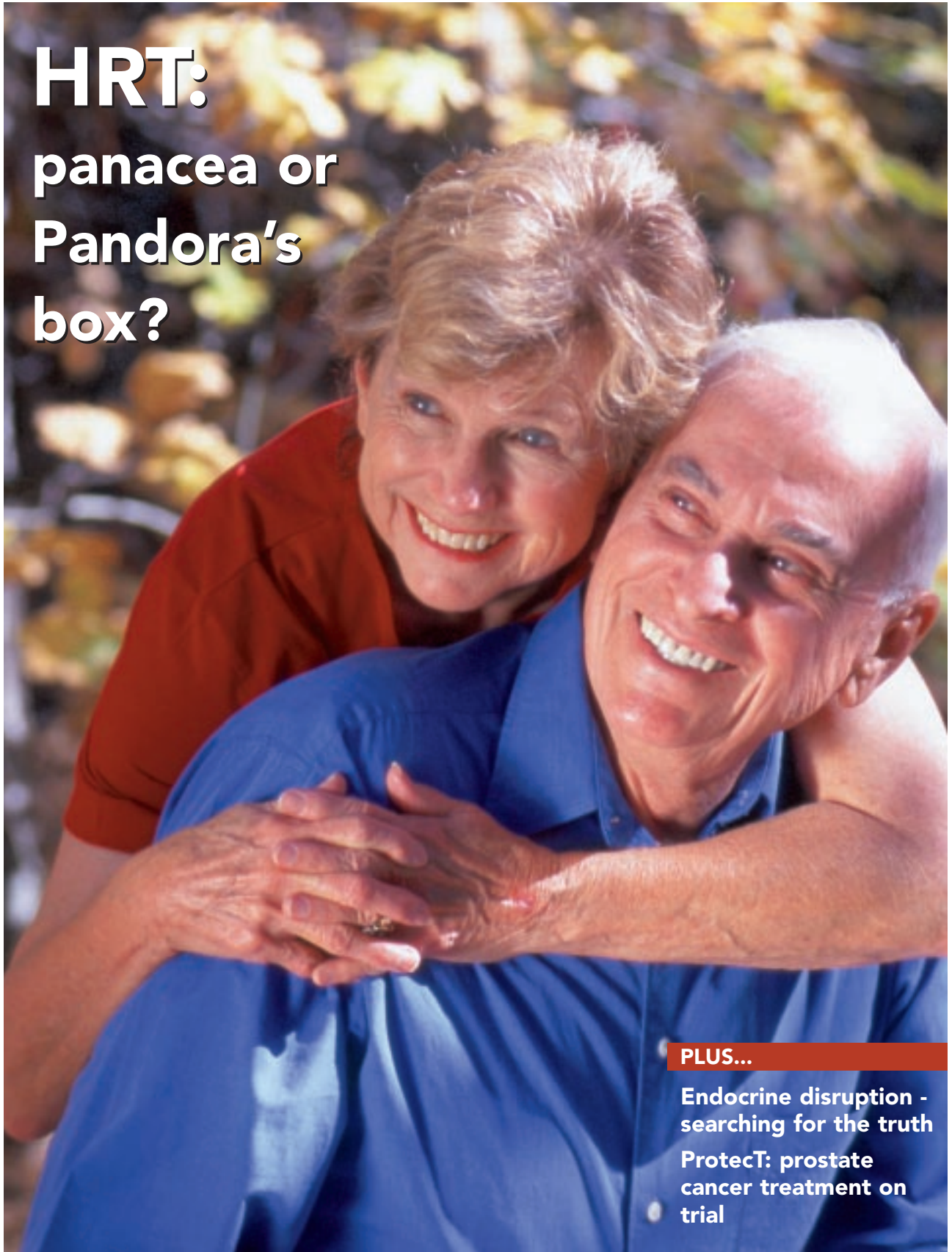


# THE **Endocrinologist**

**HRT:  
panacea or  
Pandora's  
box?**



**PLUS...**

**Endocrine disruption -  
searching for the truth**

**ProtecT: prostate  
cancer treatment on  
trial**

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Company Limited by Guarantee  
Registered in England No. 349408  
Registered Office as above  
Registered Charity No. 266813

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Deadline for news items for  
the Winter 2002 issue: 25 October 2002.  
Please send contributions to the above address.

Promoting the profile of endocrinology is an important role of the Society for Endocrinology and this is reflected in this issue of *The Endocrinologist*. Recent issues of public concern have included HRT in women, endocrine disruptive compounds (EDCs) and prostate cancer, and members of the society have been actively engaged in these public debates.

The termination of the Women's Health Initiative Trial received considerable publicity. In two independent articles, Howard Jacobs and David Purdie, provide different perspectives on this important HRT trial. Endocrine disrupters are commonly discussed in the popular press with little scientific insight. This is corrected in this issue by Richard Sharpe who is Chairman of the Society for Endocrinology's Endocrine Disrupting Panel. His article is an inspiration for those who wish to become scientific detectives. Finally, prostate cancer is the most common cancer in men but, despite this, there is no hard evidence concerning the

effect of screening or aggressive treatment. Freddy Hamdy and his team should be congratulated on the trial that they have established which will answer important questions concerning monitoring and therapy. In his article on page 9, he provides details of the ProtecT study which has received a £13 million investment from the Department of Health and, essentially, will randomise a quarter of a million men to monitoring, surgery or radiotherapy.

If profile means impact then the endocrinology community are succeeding and should be congratulated on the increase in the impact of their journals as discussed on page 3. For me, one of the highest impact sections of *The Endocrinologist* is web-spinning and I am always impressed with Melissa Westwood's ability to find us new and interesting sites. On page 5, you will find out how to play biological karaoke as well as discover how to use the molecular toolbox.

## Are endocrine-active chemicals bad for your health?

Thursday 24 January 2003

THE MØLLER CENTRE, CHURCHILL COLLEGE, CAMBRIDGE



(An Academy of Medical Sciences meeting organised in association with the Society for Endocrinology)

#### Programme includes:

Human male reproductive disorders that may arise during sexual differentiation *Niels Skakkebaek*

Sexual differentiation disorders in wildlife that arise from environmental chemicals *John Sumpter*

Pathways of endocrine disruption during sexual differentiation *Richard Sharpe*

Levels of selected endocrine-active compounds in the US population *Larry L Needham*

Identification of endocrine-active chemicals - strengths and weaknesses of available methods *Andreas Kortenkamp*

A critical look at the evidence for and against human effects of endocrine-active chemicals *Paul Foster*

Please register for this meeting via The Academy of Medical Sciences web site ([www.acmedsci.ac.uk](http://www.acmedsci.ac.uk))

The Academy gratefully acknowledges the support of AstraZeneca plc for this meeting.

AstraZeneca 

# Journals increase impact



You can read the Society's journals online at <http://journals.endocrinology.org> (which includes a link to *Clinical Endocrinology*).

**The recently released impact factors for biomedical publications show huge increases for the Society's journals!**

Both *Endocrine-Related Cancer* and *Journal of Molecular Endocrinology* have reached their highest ever levels, at 3.688 and 3.649 respectively. The value for *Journal of Endocrinology* reached 2.834, continuing the trend which has seen the journal's impact factor increase every year since 1991.

Impact factors are produced annually by the Institute for Scientific Information and the latest values reflect citations in 2001 of articles published in 1999 and 2000. The huge gains illustrate the success of the Society's initiatives to raise the journals' profiles. Work with successive editors and their boards has attracted quality content and maximised the visibility of the electronic versions.

The Society's official clinical journal, *Clinical Endocrinology* (published by Blackwell Publishing), fell slightly to 2.465, but other major clinical journals showed similar decreases.

## Endocrine Nurses News

### Training Course

Our fifth annual Endocrine Nurse Training Course 'Endocrine Nasties – the investigation and treatment options of endocrine malignancies' was held at the Møller Centre in Cambridge, an outstanding venue that will be hard to beat. We were delighted to welcome 63 nurses from across the UK and as far afield as Holland. The initial feedback has been extremely positive so a big thank you to all the nurses who accepted the opportunity to either chair a session or to present for the first time - it was good to see so many people involved.

Following requests for an organised social programme, this year a chauffeured punting trip was arranged on the River Cam. The peace and tranquillity of the river was soon shattered, the wildlife rushed for cover and even those studious souls minding their own business on the riverbank were not safe but, amazingly, no-one fell in!

### Nurses Committee nominations sought

The Nurses Committee is keen to seek a democratic selection of its nurse members. One committee member is due to retire, and all Society members are invited to nominate a new committee member. There is a requirement to maintain the balance of adult and paediatric representation on the Committee and, with this in mind, we would like to invite nominations primarily for a paediatric nurse to join the Committee. The Society would like to make it clear that any endocrine nurse member wishing to stand for election can request a nomination form to be completed by a suitable sponsor. A nomination form can be found on the Society's web site ([www.endocrinology.org/sfe/about.htm](http://www.endocrinology.org/sfe/about.htm)) – click on Committees, and then follow the path to the Nurses Committee and Nomination Form. Forms are also available from Julie Cragg or Ann Lloyd in the Bristol office.

*Nominations should be submitted to the Bristol office (c/o Ann Lloyd) not later than 8 November 2002. If there are more nominations than vacancies, then a ballot will be held within the committee, and this will be announced in the newsletter.*

MAGGIE CARSON, CHAIR, ENDOCRINE NURSE COMMITTEE

### November Meeting

The nurse session is on Monday 4 November and is entitled 'The Impact of Thyroid Eye Disease on Body Image'. We look forward to seeing you there.

### Endocrine Nursing News

December's issue of our new newsletter for nurses will include reports from the September training course and the Nurses session at the November meeting. Endocrine nurses will find this an invaluable way of keeping in touch with one another and with activities arranged by the Nurses Committee on their behalf. Contact Ann Lloyd in the Bristol office ([ann.lloyd@endocrinology.org](mailto:ann.lloyd@endocrinology.org)) if you would like to submit an article for consideration.

## Congratulations

...to **Stephen O'Rahilly** of the University of Cambridge, who has been awarded the 2002 Heinrich Wieland Prize. This prize recognises contributions to the understanding of the chemistry, biochemistry, physiology or clinical science of lipids and fats, and Professor O'Rahilly won the award for his work on the genetics of human obesity and related disorders. He will receive the prize at a ceremony in November at the Institute of Chemistry, University of Munich.

...to **Vance Trudeau** of the University of Ottawa who is the recipient of the University's 2002 Young Researcher of the Year Award. The award is given in recognition of excellence and innovation by a young researcher, and includes a \$10 000 research grant. Professor Trudeau's research includes studies of the effects of sexual hormones on brain development in goldfish, particularly concentrating on gender differences. He is also interested in endocrine-disrupting chemicals.

## SOCIETY CALENDAR

4-6 November 2002

### 193rd Meeting of the Society for Endocrinology

Royal College of Physicians, London, UK  
(see advert on page 16)

26 February 2003

### Clinical Cases Meeting

London, UK

27 February 2003

### Royal College of Radiologists: Imaging in Endocrinology

London, UK

24-26 March 2003

### BES 2003

Glasgow, UK

(see advert on page 12)

**Abstract deadline 15 November 2002!**

15-18 July 2003

### Summer School 2003

(Molecular Endocrinology Workshop, Advanced Endocrine Course and Clinical Practice Day)  
Manchester, UK

10-12 September 2003

### Endocrine Nurses Training Course: The Pituitary Gland

Durham, UK





This issue's illustration is by Dr D R Bangham, and is entitled 'Barga, Italy'. Dr Bangham is author of the Society's publication 'A History of Biological Standardization', which looks at the characterisation and measurement of complex molecules of importance in clinical and research

medicine, in the period from 1900 to 1995. Copies of the book (priced £40.00) are available from Dr Bangham, 4 Crown Close, Mill Hill, London, NW7 4HN, UK

## Basic Science Review Lecturer 2002

Congratulations to Rob Fowkes from Barts and the Royal London, for winning this award with his paper entitled 'Steroidogenic factor-1: a pivotal regulator of gonadotroph gene expression'. He will present his lecture during the Young Endocrinologists session at the Society's meeting in London in November.

## Young Endo Grants

Grants of up to £150 are available to enable young endocrinologist members to attend the Society's meeting on 4-6 November (in addition to the normal annual overseas conference grants). The deadline for applications is 21 October. See [www.endocrinology.org/sfe/grants.htm](http://www.endocrinology.org/sfe/grants.htm), or contact Chris Davis in the Bristol office.

## Science Committee

New members are needed to replace those retiring from the Society's Science Committee. The Committee's role is to speak for the basic science community. It provides input on scientific sessions at the November and BES meetings, as well as to the UK Life Sciences Committee and other bodies. It meets three times a year, usually in London. Nomination forms are available from Julie Cragg ([julie.cragg@endocrinology.org](mailto:julie.cragg@endocrinology.org)), and shortly at [www.endocrinology.org/sfe/commit.htm](http://www.endocrinology.org/sfe/commit.htm).

## Members on the move...

**A Allahabadia** to Northern General Hospital, Sheffield; **F A Antoni** to University of Edinburgh; **S J Assinder** to University of Otago; **A Dixon** to Wolverhampton Diabetes Centre; **M A Elrishi** to Manor Hospital, Walsall; **M Elsheikh** to Royal Berkshire Hospital, Reading; **P Goulden** to St George's Hospital, London; **S J Gregory** to Brigham Women's Hospital, Boston; **B M Harris** to Royal United Hospital, Bath; **C K M Ho** to University of Pennsylvania School of Medicine, Philadelphia; **S Kanumakala** to Royal Alexandra Hospital, Brighton; **D Kapoor** to Barnsley District General Hospital; **J Kisalu** to Royal Free Hospital, London; **S Kouta** to Fairfield Green Hospital, Bury; **F Medici** to Homerton University Hospital, London; **J Muburu** to Indiana University School of Medicine, Indianapolis; **C J Owen** to Institute of Human Genetics, Newcastle upon Tyne; **B Pan** to John Hopkins School of Medicine, Baltimore; **E S Quabius** to University of Aberdeen; **R Sheaves** to Centre for Endocrinology and Diabetes, London; **K A Stokes** to University of Bath; **S Suliman** to Stoke Mandeville Hospital, Aylesbury; **D F Wood** to Barts and the London, Queen Mary's School of Medicine & Dentistry, London.

## OBITUARY



## Mary Pickford 1902-2002

**L**illian Mary Pickford was born in India, but educated in England, and obtained a degree in physiology from Bedford College in 1925.

Because of her gender, her determination to pursue a career in research met with some resistance. However, she was accepted by E B Verney to work at University College London as a part-time research assistant, and was awarded an MSc in 1926. She published her first paper in 1927, and was elected a member of The Physiological Society in 1928.

She completed her medical training at University College Hospital, and practised for a while in Staffordshire. However, her resolve to pursue research remained, and, gaining a Beit Fellowship, she moved to Cambridge (still with Verney), subsequently publishing a seminal paper on central actions of acetylcholine on ADH secretion. She then took a lectureship in the Department of Physiology in the University of Edinburgh, where she remained until her retirement, holding a personal Chair, at the age of 70.

Mary was the first woman to be appointed to a Chair in the Faculty of Medicine at Edinburgh University. She was also the first woman to be elected to the Pharmacological Society. She was an FRS, and an Honorary Member of both The Physiological Society and the Society for Endocrinology.

Mary had stature, in both meanings. She could be a stern critic of her peers, but was kind and encouraging to junior colleagues and students, and forgiving of their failings. She will be fondly remembered by all those who were taught by her, or worked with her. Mary died on 14 August 2002, her 100th birthday.

JOHN A RUSSELL

# Webspinning

## Highlighting the best on the web

### Molecular toolbox

[www.mgb.pitt.edu/moleculartoolbox.htm](http://www.mgb.pitt.edu/moleculartoolbox.htm)

OK, so some of you will have a 'Favourites' file that looks a lot like this web site. However, I'm sure many will appreciate a one-stop shop for all your molecular biology needs. This site provides links to searchable databases, numerous programmes for analysis of DNA (e.g. primer design, restriction mapping, alignments, gene expression) or proteins (post-translational modifications, structure prediction and visualisation, etc), in addition to tutorials, tips and protocols.

SERVICES: T, D, L; STRONG POINTS: Comprehensive, easy to use; WEAK POINTS: None; RATING: Excellent.

### What's the alternative?

[ecvam-sis.jrc.it](http://ecvam-sis.jrc.it)

A web site to keep an eye on. The mission of the ECVAM Scientific Information Service is to establish, maintain and manage a database on advanced alternative procedures to animal experiments. Currently, it's still

at the test stage, and so access to information is limited, even after registration. However, the searchable INVITTOX database does provide information on protocols, test compounds, data analysis, advantages and disadvantages, state of development, validation or regulatory acceptance, and user and/or reference laboratories.

SERVICES: D, L; STRONG POINTS: Concept; WEAK POINTS: Need to register, not particularly easy to navigate; RATING: Good.

### Knock, knock

[n.webring.com/webring?ring=sciencehumor;list](http://n.webring.com/webring?ring=sciencehumor;list)

'Never replicate a successful experiment!' Useful advice indeed - and more pearls of wisdom can be found amongst the collection of jokes, puns, quotes and stories that make up this web ring of science 'humor' (many are American). Find out how to tell if you're a real scientist, uncover the rules for writing a paper, learn the referees'

creed and find out how to be biologically PC. Whatever you do, don't miss out on biology karaoke. Let's hear it for that famous '70s hit 'tRNA'. Of course you know it: remember Village People? remember 'YMCA'? So all together now then - t. R. N. A...

SERVICES: O; WEAK POINTS: Many pages aren't related to biological science; RATING: Good.

Thanks to Kevin Ahern and *Genetic Engineering News*. Don't forget to visit the Society for Endocrinology on the web: [www.endocrinology.org](http://www.endocrinology.org); tell us about your favourite web site: [melissa.westwood@man.ac.uk](mailto:melissa.westwood@man.ac.uk).

#### KEY

**Services** provided at web sites:

- T** Tools - Analytical computing tools
- D** Data - Searchable or downloadable database information
- G** Goods - FTP delivery of useful items (e.g. full package, bug fix or demo software)
- L** Links - Useful links to other sites
- N** News - News of interest
- S** Support - Feedback in response to users' enquiries
- O** Others - e.g. Innovative use of web tools, appearance, editorial point of view

**Ratings:** Excellent, Very Good, Good  
*Nothing below good will be reported here.*

## Grants for BES 2003

The Clinical Endocrinology Trust is offering travel grants to UK-based young endocrinologists (under the age of 35) to attend the BES meeting in Glasgow in March 2003. Forms are available from Chris Davis in the Bristol office ([chris.davis@endocrinology.org](mailto:chris.davis@endocrinology.org)) and will also be available shortly at [www.endocrinology.org/sfe/grants.htm](http://www.endocrinology.org/sfe/grants.htm). The deadline for receipt of completed forms is 10 January 2003.

## 4th National Conference of the Pituitary Foundation



Saturday 23 November 2002

- Plenary sessions - including 'Quality of life for patients' by Professor Ron Akehurst
- 21 workshops on pituitary disorders and lifestyle issues
- Carer issues
- Other endocrine patient support groups

Since 1994, The Pituitary Foundation has provided information and support to patients, their families/carers and the medical profession.

For registration details or further information contact:

The Pituitary Foundation, PO Box 1944, Bristol BS99 2UB, UK  
(Tel/Fax: 0870-7743355; Email: [helpline@pituitary.org.uk](mailto:helpline@pituitary.org.uk);  
Web: [www.pituitary.org.uk](http://www.pituitary.org.uk)). Registered Charity No. 1058968

*'Working to support pituitary patients'*

# HRT: balancing the benefits

Recent long-term studies in the USA and UK have called the safety of postmenopausal hormone replacement therapy into question. This new work makes it difficult for the non-specialist to make an informed decision on the safety and utility of HRT. We asked for the opinions of two prominent endocrinologists who take differing views on the use of HRT.

**The outcomes of two trials of postmenopausal HRT have been reported this year. These prospective randomised controlled trials have yielded data of a far higher quality than were previously available from observational studies, and have important implications for HRT of postmenopausal women.**

The first of these, the heart and estrogen/progestin replacement study (HERS), aimed to discover whether treatment with oestrogen and progestogen prevents further heart attacks in postmenopausal women with coronary heart disease. It comprised 1380 women randomly allocated to continuous combined HRT (details of the preparation are below), compared with 1383 on placebo (average age at entry 67 years). The study's first report was published after an average of 4.1 years of treatment, the second (HERS II) after open label extension of the study to an average of 6.8 years of treatment (JAMA 2002, 288 49-57).

Combined continuous HRT was found not to prevent further heart attacks. Moreover, in the first years of the trial, more heart attacks occurred in the women taking hormones than in those taking placebo. HRT was associated with more venous thromboembolic disease (relative hazard (RH) 2.08, CI 1.28-3.4) and more biliary tract surgery (RH 1.48, CI 1.12-1.95) compared with placebo (JAMA 2002, 288 58-66). There was no overall reduction in mortality in the women on hormone treatment. Compared with women on placebo, those on HRT did have fewer flushing attacks and less vaginal dryness, but they also had more vaginal discharge and unscheduled bleeding. Depressive symptoms were fewer in women on HRT, but this benefit was largely confined to those whose flushing had also improved (JAMA 2002, 287 591-597). There was no advantage of hormone treatment with regard to physical activity and energy.

The second trial was from the Women's Health Initiative (WHI)

(JAMA 2002, 288 321-333). It examined whether treatment with oestrogen and progestogen reduces the risks of heart disease, breast and colon cancer and fractures. It comprised 8506 women randomly allocated to continuous combined HRT (the same

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*'the results provide strong reasons for using non-oestrogen-based methods to prevent heart attacks, osteoporosis and colon cancer'*

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preparation as used in HERS) compared with 8106 on placebo (average age at entry 63 years, range 50-79). More than 90% of the subjects had no evidence of coronary heart disease at entry. The study was designed to run for 8.5 years, but was terminated after just over 5, because the researchers considered that the risks of HRT outweighed the benefits.

Over the course of a year, the following could be attributed to combination HRT (per 10 000 women):

- 7 more coronary disease events
- 8 more strokes
- 8 more pulmonary emboli
- 8 more invasive breast cancers
- 6 fewer colon cancers
- 6 fewer hip fractures

When counting all the adverse events over the 5 years of the study, the excess in the treated women was 100 per 10 000 woman years. So while the risk for any particular woman was 1 in 100, the results showed that combined HRT neither preserved health nor prevented disease. Adverse effects on the heart began to appear in the first 2 years of treatment in both the HERS and WHI studies. The increased risk of breast cancer did not appear for 3 years.

In each study, the HRT preparation was Prempro, which contains Premarin 0.625 mg + medroxyprogesterone acetate (MPA) 2.5 mg. The closest UK

equivalents are Premique (Premarin 0.625 mg + MPA 5.0 mg) and Premique Cycle (Premarin 0.625 mg + MPA 10 mg). MPA is also found in Indivina (oestradiol valerate 1-2 mg + MPA 2.5-5 mg) and Tridestra (oestradiol valerate 2mg + MPA 20 mg). I think the adverse effects are likely to result from treatment with a combination of an oestrogen with a progestogen, and that they are not preparation-specific. However, since this point cannot be considered settled, at the present time it would seem wise for women to avoid these products.

Both studies were well designed and executed, and produced results consistent with other recent reports. They have shown that there is no role for combined continuous HRT in primary (WHI) or secondary (HERS) prevention of coronary heart disease. There are now several non-oestrogenic preventive and therapeutic remedies for osteoporosis that are not associated with the risks of treatment with oestrogen. In my opinion, the results of the HERS and WHI studies provide strong reasons for using non-oestrogen-based methods to prevent heart attacks, osteoporosis and colon cancer in postmenopausal women. On the other hand, I do think it is reasonable to continue to prescribe HRT to reverse the symptoms of oestrogen deficiency. Such treatment will usually be short term.

The results of these studies shed no light on the safety of treatment with oestrogen alone, as used in women who have had a hysterectomy. Information from the WHI on that topic is not scheduled to be published until 2005.

HOWARD JACOBS



**The scientific basis for oestrogen therapy in postmenopausal women centres on the non-reproductive actions of this steroid group. Our knowledge in this area has greatly increased recently, with new techniques to localise oestrogen receptors, and clarification of their physiological roles, tissue by tissue. Among the many systems that include a role for oestrogens, three form the basis for contemporary research and, if appropriate, therapeutic use: the trabecular skeleton, vascular tree and CNS.**

Functional oocyte exhaustion leads not only to infertility but also to elimination of the theca/granulosa cell partnership as a principal source of circulating oestradiol. Ovarian endocrine failure which is obligatory, be it spontaneous or induced medically or surgically, withdraws circulating oestradiol from the now largely redundant hypothalamic-pituitary-ovarian axis. It also, however, withdraws oestradiol from other systems.

The skeleton reacts with a sharply increased rate of turnover, together with a tilt in the bone remodelling cycle in favour of resorption. The ultimate consequence for many women is loss of integrity within the trabecular lattice and, ultimately, vertebral crush and low-trauma peripheral fractures. The oestrogen-deprived cardiovascular (CV) system exhibits an adverse lipid profile and, in *in vitro* and animal studies, progressive atherogenesis. The CNS exhibits oestrogen-sensitive changes in neuronal function, together with alterations in neurotransmitter activity and, *in vitro*, dendrite projection.

HRT is licensed for the treatment of oestrogen-sensitive symptoms and for the prevention and treatment of osteoporosis. There is a wealth of data from randomised controlled trials (RCTs) to support its use for physical symptoms like vasomotor instability, insomnia, tiredness and arthralgia, and psychological symptoms such as loss of short-term memory and concentration span.

With regard to the CV system, *in vitro*, animal and human observational data all suggest that oestrogen replacement can substantially reduce atherogenesis, myocardial infarction

and, to a much lesser degree, stroke. The human studies, although internally consistent, have all suffered from the bane of observational data and the possibility of potential confounders (such as the lifestyles of women who take HRT being less likely to promote CV disease events).

The recent Women's Health Initiative (WHI) study (*JAMA* 2002 **288** 321-333) looked at treatment with 0.625 mg equine oestrogens + continuous 2.5 mg MPA. It found an annual excess of 7 per 10 000 patient years for non-fatal myocardial infarction and 8 per 10 000 patient years for stroke in the treated group. The relevance of these US data to UK practice is severely limited, however, since HRT has never been licensed here for the primary or secondary prevention of CV disease. Indeed, the

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### *oestrogen should still be considered for the prevention and treatment of osteoporosis*

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precise hormone combination used in WHI is not available in the UK. Data from further trials, with CV safety endpoints, that examine oestradiol (natural human oestrogen), and tibolone (synthetic steroid) are required.

With the skeletal system we are on surer ground. Indeed, the 5-year WHI study itself showed a significant reduction in all fractures and, specifically, in hip fracture among the treated women, who were aged 50-79 years at entry. These RCT fracture data now complement the wealth of surrogate end-point data which had indicated that oestrogen restrains bone turnover, rebalances bone resorption/formation and maintains bone mineral density at the key sites of spine, hip and distal radius.

The CNS is an area of intense current enquiry. Several case-control studies and one meta-analysis indicate that oestrogen exposure is associated with a reduction in the risk of Alzheimer's and related dementias (*Neurology* 2001 **57** 2210-2216). These observations complement *in vitro* studies where oestradiol at nanomolar concentrations inhibited the elaboration of beta-amyloid from

its precursor protein. Its phenolic A ring has also been shown to confer antioxidant activity, believed to be central to the protection of neurones and glial cells. However, oestrogen appears to have no role in the treatment of established dementias, and the encouraging observational data have yet to be backed up by RCTs with primary CNS end-points.

The principal adverse events associated with HRT are associated with the engagement of the oestrogen receptor sites in the reproductive tract, and with the vascular tree. Endometrial stimulation, although controlled by discontinuous

progestogen, results in resumption of bleeding and a small increase in the risk of endometrial adenocarcinoma. These effects are annulled by the use of continuous combined oestrogen/progestogen preparations.

Although study results are not consistent, it is generally agreed that there is a small but definite increase in the incidence of breast cancer, compatible with the increased risk associated with delayed menopause. The excess risk amounts to some 2 attributable tumours per 1000 women receiving 5 years of HRT between the ages of 50 and 70 (*Lancet* 1997 **350** 1047-1059). Venous thromboembolic phenomena occur more frequently in patients receiving HRT or raloxifene (*Breast Cancer Research and Treatment* 2001 **65** 125-143), usually within the first 6 months of treatment but, again, the absolute risk is low. Present research is concentrating on the development of tissue-specific oestrogens such as selective estrogen modulators and tibolone which will supply agonism at the required sites, while avoiding the adverse effects of reproductive tissue engagement.

In summary, individual management is paramount. Given careful patient selection for the licensed indications and proper supervision, HRT is generally safe and reliable. Although by no means absolutely safe, oestrogen should still be considered as a primary treatment for menopausal symptoms and for the prevention and treatment of osteoporosis - with the proviso that in the individual case, the physician finds the potential benefits to be greater than the risks.



# Endocrine disruption: separating fact from fiction

**Endocrine disruptive compounds (EDCs) and their effects on humans and wildlife have certainly put endocrinology under the spotlight. The media's use of alarmist terms like 'gender-benders' makes it difficult to present a balanced scientific view in the public domain. Factors that result in altered hormone levels and action are an undoubted hazard, and must be taken seriously. But is the level of human exposure to EDCs sufficient to have a significant effect on our hormone homeostasis?**

It is easiest to split this discussion into three: (1) environmentally persistent chemicals such as DDT and PCBs; (2) more recently identified EDCs that are used ubiquitously, for example bisphenolic and alkylphenolic compounds; (3) chemicals that alter endogenous hormone production, action or metabolism. In all cases, fetal/neonatal exposure is likely to have more far-reaching effects than comparable adult exposure.

It is accepted that the persistent chlorinated environmental chemicals, such as older pesticides (like DDT and PCBs), exerted pronounced adverse effects on some wildlife (e.g. eggshell thinning, immune-suppressive effects). The evidence for effects in humans is less convincing, but this is probably associated with the complex task of ascribing a change to a single chemical exposure. Nevertheless, there is general agreement that environmentally persistent chemicals are likely to exert adverse health effects, and that use of such compounds is therefore no longer acceptable.

In tropical countries with endemic insect-dependent disease transmission, where such pesticides may still be used, the issue of risk-benefits is obviously more complex. Even though adverse effects of persistent chlorinated chemicals undoubtedly occur, to what extent these stem from endocrine disruption is not clear. Many of the so-called EDCs possess activities other than their intrinsic hormonal activity and, in some cases, these may be more important in relation to their biological effects.

Whether more recently identified environmental oestrogenic EDCs, such as bisphenolic and alkylphenolic compounds, pose a health risk via endocrine disruption is more contentious. Integral to this debate are the so-called 'low-dose' ( $\leq 20 \mu\text{g}/\text{kg}$ ) effects of bisphenol A in developing male rodents. These have not been found in all studies, and their relevance to human male reproductive health is also unclear. If the 'low-dose' effects are real, they cannot result from the intrinsically weak oestrogenicity of the compounds, though effects may be the result of some other biological activity.

Exposure to a cocktail of EDCs at low (environmental) doses might result in hormonal effects through summation of their intrinsic hormonal activities, a possibility demonstrated *in vitro* but still to be tested *in vivo*. It will be a Herculean task to evaluate 'real-world' mixtures in animal models in ways that allow reasoned extrapolation to humans or wildlife, and thus enable proper risk assessment. A continuing obstacle to all such assessments in man is the dearth of good human exposure data for the various chemicals.

In the past 3 years, a new and perhaps more worrying dimension has emerged, centred on the ability of some environmental chemicals to alter endogenous hormone production, metabolism, inactivation or excretion. For instance, exposure of rodents *in utero* to certain phthalate esters can drastically lower production of testosterone by the testes in male fetuses, leading to downstream sexual differentiation (cryptorchidism, hypospadias) and other disorders (reduced sperm production/fertility). These disorders are a focus for concern in human males because of a possible increase in their incidence. Furthermore, human exposure to the phthalates in question is high, especially in some women of reproductive age (up to  $160 \mu\text{g}/\text{kg}$  per day), though the levels fall short of those shown to cause a high prevalence of disorders in rodents ( $>250 \text{mg}/\text{kg}$  per day).

More recently, PCBs and a range of environmental polyhalogenated hydrocarbons have been shown to have inhibitory effects on oestrogen sulphotransferase, the primary enzymatic mechanism for oestradiol inactivation prior to its excretion. PCBs have also been shown to affect thyroid hormone action in several different

ways. Some of these effects have been shown at nanomolar or lower concentrations and, as human exposure to all of these compounds is widespread, they raise new possibilities for their relevance to human disease.

Although intriguing, these possibilities are still largely theoretical. However, the worldwide induction of 'imposex' in certain molluscs following exposure to tributyltin (TBT) provides a real example. TBT acts by suppressing aromatase, thereby interfering with conversion of androgens to oestrogens, which results in a build-up of androgens in females (leading to imposex). Its worldwide occurrence emphasises that when endogenous hormonal systems are disturbed the consequences can be dramatic. TBT has no intrinsic hormonal activity, and would not be detected by most *in vitro* screening systems for EDCs. Many environmental chemicals that alter endogenous hormone action do not have intrinsic hormonal activity (PCBs are an exception), so only *in vivo* animal testing at all life stages is likely to detect such compounds.

Human male reproductive disorders associated with altered sex steroid levels and sexual differentiation are increasing in incidence and may represent a syndrome (so-called 'testicular dysgenesis syndrome'). Faced with real wildlife changes that result from 'endocrine disruption' (like the 'coincidence' of imposex in molluscs and intersex in fish), we must consider a possible connection with the increase in human disorders. In doing so, we must adhere rigidly to a scientific approach. Sexual differentiation is hormone-dependent and so inherently susceptible to perturbation - but the cause is not necessarily always the same. We must also recognise that most waste products end up in the aquatic environment. Effects in fish and molluscs may therefore be 'worse case' as they are permanently immersed, and the situation may be completely different for humans. But if there is a link between the wildlife and human changes, then we know that it is environmental, and identification of its cause(s) may allow intervention or prevention, with consequent health benefits.

So how do we move forward? Concentrating on identifying EDCs and evaluating their effects *in vitro* is not the



most efficient approach if our concern is whether such compounds cause health disturbance in humans or wildlife. We should identify situations where health changes consistent with endocrine disruption have occurred, and then seek the cause, recognising that this may be related to genetics, lifestyle and/or environment.

An epidemiological approach is needed, as studies of individuals are of limited value. This poses other problems such as accuracy of the diagnosis. For example, the registry data for hypospadias and cryptorchidism, which may reflect 'endocrine disruption' *in utero*, are unreliable. There are also enormous difficulties in relating occurrence of such disorders to particular environmental exposures during pregnancy. In reality, only carefully designed, prospective studies are likely to provide definitive information. Several such studies of hypospadias and cryptorchidism are in progress, and their results are awaited with interest.

This approach really can work (at least for wildlife), as exemplified by the case of intersex fish in UK rivers. Research has indicated that 'oestrogens' in sewage effluent discharges are the likely cause. The 'culprits' are probably ethinyl oestradiol or endogenous oestradiol, originating from human urine, rather than weaker EDCs such as alkylphenols, which were originally suspected. By focusing on the effect, avoiding the temptation of obvious possibilities and marrying together exposure analyses, laboratory dose-response studies and arduous 'real-world' studies (i.e. river-based fish 'epidemiology'), this scientific detective work nailed the culprit, not the prime suspect. I cannot think of a better guide for all of us working in this area.

RICHARD SHARPE

*Richard Sharpe is Chairman of the Society for Endocrinology's Expert Group on Endocrine Disruptors, which aims to provide a source of referral and expert advice. While hoping not to have misrepresented the views of other members of the group in this article, Dr Sharpe takes responsibility for the emphasis given to certain aspects.*

*A 1-day meeting on 'Endocrine disruption and human male reproductive disorders', organised by the Academy of Medical Sciences in conjunction with the Society for Endocrinology, will take place in Cambridge on 24 January 2003 (see page 2 and [www.acmedsci.ac.uk/ff\\_contact.htm](http://www.acmedsci.ac.uk/ff_contact.htm)).*

## ProtecT: prostate treatment on trial

**Management of prostate cancer remains a popular topic of discussion, presentation, publication and controversy in urology. There is no hard evidence that screening for the disease is beneficial, nor do randomised controlled trials show that aggressive treatment of clinically localised cancers improves survival or quality of life.**

Previous attempts to mount randomised trials of treatment have failed, largely due to methodological problems. Randomised trials of screening are taking place in Europe and the USA. Whilst the results are awaited eagerly, the studies are suffering from increasing contamination issues, related to increasing public awareness of the disease, and the wide availability of testing for prostate specific antigen.

Following failure by the MRC to recruit patients to its treatment study in the early 1990s, a trial of treatment including a 'watchful waiting' arm was deemed impossible. However, the controversy regarding the appropriateness of treatment in early disease persisted. In 1991, approximately 36 radical prostatectomies were performed in the UK. This escalated to some 700 procedures performed by British surgeons in 1999. No recent conclusive evidence has influenced these numbers. Surgeons simply learn how to perform the operation, radiotherapists advocate and deliver radiotherapy (and more recently brachytherapy), and both treatments are offered with confidence to men who are uncertain about the fate of their cancer.

In view of these controversies, and despite the conclusion of the MRC study, a team of researchers from Sheffield, Bristol and Newcastle responded to a call for primary research by the Health Technology Assessment (HTA) panel of the NHS R&D programme in 1997, and submitted a 2-phase proposal known as ProtecT: prostate testing for cancer and treatment.

Phase 1 was to deal with the feasibility of mounting a full-scale randomised trial of treatment effectiveness in clinically localised prostate cancer in the UK. The main aim was to decide whether it would be possible to recruit men to a 3-arm (monitoring, surgery or radiotherapy) or to a 2-arm (surgery versus radiotherapy) trial, following an intensive programme of case-finding and delivery of information. This was accompanied by comprehensive qualitative research, taking into account patients' perspectives. Phase 2 was to mount the main treatment study, based on the findings from the feasibility trial.

Phase 1 was completed in June 2001, showing not only that such a trial is eminently feasible in the UK, but that the majority of men recruited agreed to be randomised to the 3-arm study. Qualitative research, teamwork and scrutinising the attitudes of men and recruiters allowed the previous misconceptions to be rejected.

The Department of Health, through its HTA programme, has agreed to fund the main treatment trial (£13m) involving nine clinical centres in the UK, inviting 230 000 men to be recruited to the trial over the next 5 years. The primary end-point will be survival to 10 years, with many secondary end-points including disease progression, sensitivity/specificity of diagnostic tests, and associated basic science research.


Compared to the £98 000 spent by our Government in 1998 on prostate cancer research, this is a major achievement for the urological community in the UK, and for patients with prostate cancer worldwide. At last, a feasible trial of treatment effectiveness in early prostate cancer is on the horizon.

FREDDIE C HAMDY  
ON BEHALF OF THE ProtecT RESEARCH TEAM

*Principal Investigators in the ProtecT study are Freddie Hamdy (Sheffield), Jenny Donovan (Bristol) and David Neal (Newcastle).*

The Society is pleased to be able to support its members' attendance at meetings through the provision of travel grants. Here are some reports from recent events.

2002  
**SUMMER SCHOOL**  
 Molecular  
 Endocrinology  
 Workshop



Reading, UK, 9 July 2002

About 30 delegates attended this workshop, some travelling a great distance to hear the excellent talks. Attendees could be equally divided among those already undertaking laboratory research, those looking to do so in the near future, and others who were undecided and wanted to learn more about such a career decision.

The day started with informative sessions on steroid receptors and chromatin, and human breast epithelium stem cell biology. The first of these was an excellent introduction to the mechanisms by which the nuclear receptor superfamily influences gene transcription. A subsequent talk entitled 'Imaging of cell signalling and gene expression' described techniques whereby the firefly luciferase gene can be used to yield important genetic information by labelling proteins.

My current area of investigation is childhood obesity and insulin resistance, so I found the discussion on the role of genetics in the development of obesity very interesting. Particular reference was made to the clinical syndromes that result from leptin or melanocortin-4 receptor deficiency. Further talks covered the functional analysis of genetic polymorphisms, and conditional and specific gene targeting, though this latter discussion may have been pitched a little too high for the attendees present.

I would have liked some more general talks on the use of research methods to explain molecular endocrinology, and less of a bias towards genetics. However, the workshop was definitely informative and educational, and I am very pleased that I attended.

M SABIN

## ENDO 2002: 84th Annual Meeting of the Endocrine Society

San Francisco, CA, USA, 19-22 June 2002

The focus of the meeting was 'The impact of the human genome on endocrinology'. The importance and potential of genomics was certainly brought home, as was the promise of other exciting areas, like proteomics and stem cell research. The conference enabled me to bring the literature review for my PhD right up to date, and included posters on the cloning of a second marsupial GnRH receptor, a study using lamprey GnRH, and another on the importance of extracellular loops in binding non-peptide antagonists to the GnRH receptor.

KEVIN PFLEGER

I particularly enjoyed the plenary lectures on 'Genomics, medicine and society' and 'What genomic medicine will mean for you'. They reviewed the latest advances, and also looked at the social implications of genomic screening. The symposium on 'Nutrition and bone' was highly relevant to my work, and included an outstanding presentation on vitamin D by M Holick.

LUCIA MANCINI

The greatest benefit for me was the opportunity to gather feedback on my findings, from both scientists and clinicians. My PhD examines the effects of dietary polyunsaturated fatty acids on reproductive processes in the sheep. Aside from technical queries, I was posed many questions about the clinical relevance of my results in terms of solving everyday fertility problems. This gave me an excellent insight into a clinician's perspective of the sorts of questions we should be trying to answer. It will also help me focus the discussions when writing up my thesis, both in terms of basic science and clinical relevance.

SUSAN KIRKUP

Numerous symposia helped me plan future experiments for my PhD, which addresses neural regulation of the adrenal cortex. I especially enjoyed 'Molecular recognition of the HPA axis', 'Nuclear receptor co-activators', 'Steroid hormone receptors' and 'Orphan nuclear receptors and metabolic signalling'. As well as learning about areas of direct relevance to my project, the conference also increased my general knowledge of endocrinology.

OURANIA KOSTI

This was the perfect opportunity to attend sessions relevant to my interests, including the cross-talk between steroid receptors and cell signalling pathways, and symposia on diabetes and thyroid research. The 'New technology lectures' are always a great favourite of mine, and help to increase my knowledge of cutting-edge research methodology.

PING YE

I attended the 28th International Aldosterone Conference before ENDO 2002. This was an excellent opportunity to meet with specialists in the field. Highlights included Melyssa Bratton's impressive work, showing that the mineralocorticoid receptor can interact directly with cardiac myosin binding protein-c. This means that it may be able to exert effects more rapidly than if it acted through a genomic mechanism, and so may have important implications in cardiac fibrosis.

SCOTT MACKENZIE

# Hot Topics

Highlights from articles in the Society's journals, brought to you by Nathalie Gilmore and Jane Shepley.

## Albumin, evolution and steroid action

The evolution of albumin, steroid hormone action and the origin of vertebrates are inter-related in this fascinating review, which forms part of a special issue entitled 'Beyond carrier proteins'. Here, Baker suggests that an ancestral albumin was present in protochordates and primitive vertebrates. During its evolution into the major human serum protein, it may have played an essential role in steroid hormone signalling.

Albumin's modulation of steroid action would depend on its abundance and differences in affinity for steroid hormones, their metabolites, analogues and receptors. Similarly, it could prevent disruption of endocrine responses by exogenous chemicals. The author also analyses the phylogenetic origins of adrenal and sex steroid receptors, which are believed to originate from genome duplications before or during the Cambrian explosion, over 500 million years ago.

Twelve exciting reviews make up this special issue of *Journal of Endocrinology*, and take a cross-cutting look at the multifunctional and regulatory roles of hormone-binding proteins. They originate from a symposium held at the 2002 Annual Meeting of the Society for Integrative and Comparative Biology. (See the full article in *Journal of Endocrinology* **175(1)**, October 2002 or read it, free of charge, at <http://journals.endocrinology.org>)

## Corticosteroid actions on osteoclasts

Although often prescribed for their anti-inflammatory and immunosuppressive properties, chronic treatment with corticosteroids commonly causes bone loss and osteoporosis. The precise mechanisms

are unclear, but are thought to involve the bone-remodelling unit of osteoblasts and osteoclasts. This study by Hirayama *et al.* analyses the effect of dexamethasone, a synthetic corticosteroid, on the formation and bone-resorbing activity of human osteoclasts *in vitro*.

Dexamethasone had a biphasic effect. It promoted differentiation and proliferation of multi-nucleate cells with osteoclastic markers when added to monocytes in early stages of culture. This agrees with observations of increased osteoclast numbers in bone biopsies from patients with steroid-associated osteoporosis. Delayed treatment with dexamethasone had a less dramatic effect, inhibiting bone-resorption by mature osteoclasts. This may be attributed to increased osteoclast apoptosis.

The authors conclude that the inhibition of osteoclast formation may be an effective basis for therapy of corticosteroid-induced osteoporosis, with the aim of stabilising the bone-remodelling unit.

(See the full article in *Journal of Endocrinology* **175(1)**, October 2002) (Subsequent work (*Journal of Pathology*, In Press) has indicated that steroids specifically inhibit receptor activator of NF- $\kappa$ B ligand-induced, but promote cytokine-induced, osteoclast formation.)

## Model for adipose $\alpha$ 2-ARs

Catecholamines regulate white adipose tissue function and development via adrenergic receptors (ARs). In humans, this tissue mainly expresses  $\alpha$ 2-ARs, with few or no  $\beta$ 3-ARs. Rodents show a predominance of  $\beta$ 3-ARs, which has limited their usefulness in studies of  $\alpha$ 2-ARs in adipose development.

In this paper, Boucher and colleagues report the use of transgenic mice for studies of human hyperplastic obesity. Lines were established that carried the human  $\beta$ 3-AR and  $\alpha$ 2-AR transgenes (including the human gene regulatory elements) on a murine  $\beta$ 3-AR gene knockout background. Analysis showed a 'human-like' pattern of adipocyte  $\alpha$ 2-AR expression. When the mice were fed a high fat diet (unlike controls) they

became obese due to hyperplasia rather than hypertrophy. Interestingly, they did not have elevated glucose and insulin levels and did not suffer from insulin resistance or high blood pressure (as is usually the case for obese mice).

This model will be invaluable in studying factors that affect the regulation of  $\alpha$ 2-AR, such as nutrition and hormones. It will also aid understanding of the interaction between a high fat diet and  $\alpha$ 2-AR in the development of white adipose tissue, and could be used to assess the efficacy of drugs in obesity. (See the full article in *Journal of Molecular Endocrinology* **29(2)**, October 2002)

## Monitoring breast cancer

Comparison of neoadjuvant (pre-surgical) with adjuvant chemotherapy in breast cancer has principally concluded that the neoadjuvant approach leads to a slight reduction in mastectomy, but with a marginally higher risk of local recurrence.

However, neoadjuvant therapy also provides a unique opportunity to study tumour response. In this review, Cleator and co-workers discuss the use of serial biopsies in the course of neoadjuvant chemotherapy. In the absence of a means of predicting response to chemotherapy, these biopsies may yield predictive markers that show a correlation with patient outcome. This could increase understanding of the molecular mechanisms of tumour growth and drug resistance, and help determine optimum modes of treatment.

The authors describe how tumour progression is measured, the most common anti-cancer drugs, and the biological basis of drug resistance in breast cancers. As new data emerges, we may be able to use new technologies such as comparative genomic hybridisation, real-time PCR, expression microarray and proteomics to improve the outcome for breast cancer sufferers.

(See the full article in *Endocrine-Related Cancer* **9(3)**, September 2002)



## Reference Manager 10

ISI ResearchSoft 2002  
([www.adeptstore.com](http://www.adeptstore.com))

**A**n anyone with experience in research, writing papers or theses, will appreciate the amount of work involved in tracking down references, creating databases and generating a bibliography in the appropriate format. Reference Manager aims to ease this task.

The package comprises an online research tool, reference database and a bibliography maker. It provides a simple way of searching online bibliographic databases and can import and store the files in reference databases. When you use Reference Manager to insert citations into your documents, it will generate a bibliography in any format that you need.

Reference Manager 10 has several additional features. These include new fields in each reference page to add links to documents, PDF files, images and articles, and an auto-update feature to download updates to the program and content files via the internet. The 'cite while you write' feature, which allows you to insert references as you write your document, has been upgraded to have an instant formatting function. This generates a formatted bibliography instantly.

The 'travelling library' is one of the best new features. It is created automatically as you cite references in Microsoft Word. Information about the citation is stored in the appropriate field code, which allows your collaborators to insert citations into the document and create a bibliography without having to share databases (i.e. they can use their own).

However, if your collaborators have the same reference in one of their databases as you have in yours, but the record number is different, then the reference will not be recognised as the same citation and will therefore appear twice in the bibliography!

The only inconvenience I found was associated with upgrading from an older version. I had to install the new version and then copy all my old files to it. I found a slight ambiguity in the instructions and had to repeat the process several times. If you have any problems, the technical support via email is excellent.

I think investing in Reference Manager 10 is very worthwhile. Any initial time spent learning how to use the package is more than compensated for by the immense amount of time and effort it saves.

PEAK MANN MH

### BES 2003

22ND JOINT MEETING OF THE

## British Endocrine Societies

24-26 March 2003

Glasgow, UK



#### Symposia

- Androgens and prostate cancer
- Prolactin: novel aspects
- Apoptosis/survival signalling
- Trophic control of size
- The adipocyte as an endocrine organ
- Emerging hot topics
- Dominant endocrine cancer syndromes
- Radio-iodine biology in the 21st century

plus Plenary Lectures, Clinical Management and Molecular Endocrinology Workshops, 'The Expert View', Focussed Science Session, Oral Communications, and Young Endocrinologists and Nurses Sessions

**Abstract deadline: Friday 15 November 2002**

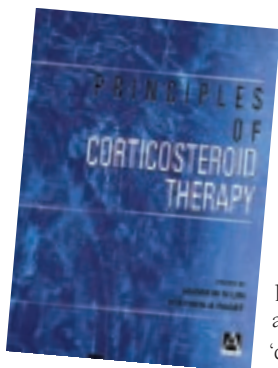
Further details and preliminary programmes from:  
Liz Brookes, BES, 17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ  
(Tel: 01454-642210; Fax: 01454-642222; Email: [conferences@endocrinology.org](mailto:conferences@endocrinology.org); Web: [www.endocrinology.org/sfe/confs.htm](http://www.endocrinology.org/sfe/confs.htm))

## Principles of Corticosteroid Therapy

A N Lin & S A Paget (Eds), Arnold, 2002, 465 pp, £85.00, ISBN 0 340 75934 8

It was back in 1949 that Hench, Kendall, Slocumb and Polley's seminal observations on the use of compound E in rheumatoid arthritis appeared. Perhaps the after effects of the 2002 World Cup have brought out the John Motson in me, but I couldn't help noticing that the editors of this valuable work have assembled an impressive team of 49 contributors from a large range of specialities. I suspect, however, that this symmetry is entirely fortuitous!

This is a comprehensive exposé of the use of corticosteroids in 21st



century medical practice. As expected, the book is bang up to date, and covers the therapeutic potential, as well as the side effect 'dark side', of steroid use. For

those seeking the cosy warmth of Motson-esque statistics, it is divided into 5 sections: 2 introductory chapters, 2 on basic science, 10 addressing systemic effects, 13 on clinical usage, and 6 on special management issues, including medical legal aspects (for readers in the USA).

There is relatively little repetition and I thoroughly enjoyed this book, and certainly revised a lot of general medicine. It is in this aspect that I think that it scores highly - as a quick

and authoritative text on the use of corticosteroids to manage the many and varied inflammatory conditions that we all encounter in the acute medical setting. When 'playing at home', in the chapters on investigation and management of hypo- or hyperadrenalism, I found myself in broad agreement, though, unsurprisingly, could not agree with everything. I am sure that others reading from the perspective of their own specialities will have a similar experience. Overall, however, I was impressed with the clarity of writing and general layout.

This book should certainly be an essential part of any library and, for those involved in general medicine, a personal copy on the office shelf would be highly relevant and most comforting. It is not, nor does it attempt to be, a specialised endocrine text.

JOHN NEWELL-PRICE

## Genetics of Steroid Biosynthesis and Function

Ed J I Mason, Taylor & Francis, 2002, 479 pp, £75.00, ISBN 0 415 27878 3

'Nothing is simple about this pathway ... all aspects are fascinating' conclude Rozman and Waterman in their chapter on sterol biosynthesis. That statement for steroid aficionados applies to the whole book.

The current knowledge of cholesterol dynamics is covered very effectively, and a number of functional and developmental disorders attributable to abnormalities of cholesterol and steroid synthesis are described. Mutations have provided valuable information concerning the structure-function relationships of a number of the enzymes, and will influence the design of new therapeutic agents. There are now few parts of the metabolic pathway yet to be genetically defined. The search for proteins involved in cholesterol trafficking will probably remain a difficult task. Molecular biology has clarified a



number of issues in steroid endocrinology. Lipoid adrenal hyperplasia is caused by defects in steroidogenic acute regulatory (StAR) protein

and not side chain cleavage, as envisaged by biochemical studies. The discovery of StAR may represent one of the most significant advances in steroid research in recent years. Considering the immense interest of British endocrinologists in  $11\beta$ -hydroxysteroid dehydrogenase, the enzymes and genes are given limited coverage in a short chapter on peripheral steroid metabolism. Animal and human models of oestrogen deficiency have revealed unsuspected roles for oestrogens in males and females.

In terms of function, the nuclear receptor family is responsible for the actions of steroids, and is presented primarily in one general chapter on regulation of gene expression. This chapter lacks the clinical scenarios that are featured in most other contributions,

so that some misconceptions are not covered. Hence, pseudohypoaldosteronism is rarely due to disorders of the mineralocorticoid receptor but is usually the consequence of profound renal sodium loss through a defective amiloride-sensitive, epithelial sodium channel. The non-genomic actions of steroids through membrane receptors are sadly only discussed in relation to actions of steroids in the brain. The regulation of the pathways and the enzymes themselves are now under intense investigation for the relevant repressors, co-repressors, co-activators and co-integrators. An outstanding challenge is a full explanation for the independent regulation of the multiple functions of CYP17, although the chapter went some way to clarifying this. New directions of exploration are to be anticipated in relation to steroids in the brain.

The references are in the main from the 15 years up to 2001, usefully reflecting the period of intense activity to define genes and locate the basis of genetic disorders. The book highlights many new and exciting opportunities for future research.

JOHN W HONOUR

**9th European Federation of Endocrine Societies Postgraduate Course in Clinical Endocrinology**

Como, Italy, 17-19 October 2002.  
 Contact: Organising Secretary, Centro Culturale A Volta, Villa Olmo, Via Cantoni 1, 22100 Como, Italy (Tel: +39-03-1579812; Fax: +39-03-1573395; Email: chiara.stefanetti@centrovolta.it).

**Peptides and Non-peptides of Neuroendocrine and Oncologic Relevance**

Como, Italy, 17-19 October 2002.  
 Contact: Eugenio E Müller, Department of Pharmacology, University of Milan, Via Vanvitelli 32, 20129 Milan, Italy (Tel: +39-02-58357010/7012; Fax: +39-02-58357011; Email: eugenio.muller@unimi.it).

**Prader-Willi Syndrome as a Model for Obesity: Symposium in Memory of Andra Prader**

Zürich, Switzerland, 18-19 October 2002.  
 Contact: Dr Urs Eiholzer, for Growth Puberty Adolescence Foundation, Möhrlistrasse 69, 8006 Zürich, Switzerland (Tel: +41-1-3643700; Fax: +41-1-3643701; Email: mail@childgrowth.org; Web: www.childgrowth.org).

**2nd International Conference on Obesity: Obesity - a Woman's Health Problem**

Corfu, Greece, 26 October 2002.  
 Contact: Dr A Michalopoulos (Tel: +30-661-037540; Fax: +30-661-034206; Email: amich@ker.forthnet.gr; Web: www.corfuxenos.gr).

**193rd Meeting of the Society for Endocrinology, including a joint Endocrinology and Diabetes Day in association with Diabetes UK**

London, UK, 4-6 November 2002.  
 Contact: Society for Endocrinology, 17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-642210; Fax: +44-1454-642222; Email: conferences@endocrinology.org; Web: www.endocrinology.org/sfe/conf.htm).

**30th Meeting of the British Society for Paediatric Endocrinology and Diabetes 2002**

Plymouth, UK, 13-15 November 2002.  
 Contact: BioScientifica Ltd, 16 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-642210; Fax: +44-1454-642222; Email: conferences@endocrinology.org; Web: www.bspe.shef.ac.uk).

**Hormones, Body Composition and Physical Performance**

Turin, Italy, 15 November 2002.  
 Contact: Organising Secretariat, Centro Congressi Internazionale srl, Via Cervino 60, 10155 Torino, Italy (Tel: +39-01-12446911; Fax: +39-01-12446900; Email: info@congressiefiere.com; Web: www.congressiefiere.com).

**University of Exeter Advanced Diabetes Course**

Exeter, UK, 20-22 November 2002.  
 Contact: Ruth Hooper, Department of Diabetes and Vascular Medicine, Barrack Road, Exeter EX2 5AX, UK (Tel: +44-1392-403089; Fax: +44-1392-403027; Email: r.e.hooper@ex.ac.uk).

**2nd International Symposium on Progestins, Progesterone Receptor Modulators and Progesterone Antagonists**

Siena, Italy, 20-23 November 2002.  
 Contact: Tzina Lindenberg (Tel: +972-2-6555188; Fax: +972-2-6522018; Email: hormones@netmedia.net.il; Web: www.unisi.it/eventi/progestins).

**Parathyroid Localisation: Utility of Diagnostic Imaging**

London, UK, 22 November 2002.  
 Contact: Daksha Thakrar, BMS Medical Imaging (Fax: +44-20-83617982; Email: daksha.thakrar@bms.com).

**Brain-Immune Interactions in Stress: The Impact of Hormones on Disease**

Bristol, UK, 30 November 2002.  
 Contact: David Jessop, University Research Centre for Neuroendocrinology, University of Bristol, Bristol Royal Infirmary, Marlborough Street, Bristol BS2 8HW, UK (Tel: +44-117-9283402; Fax: +44-117-9283315; Email: david.jessop@bris.ac.uk; Web: www.bris.ac.uk/depts/bing/main.htm).

**Are endocrine active chemicals bad for your health?**

Cambridge, UK, 24 January 2003.  
 Contact: Susan Wicks, The Academy of Medical Sciences, 10 Carlton House Terrace, London SW1Y 5AH, UK (Tel: +44-20-7969-5289; Fax: +44-20-7969-5298; Email: susan.wicks@acmedsci.ac.uk; Web: www.acmedsci.ac.uk).

**7th International Symposium on Graves' Ophthalmopathy,**

Pisa, Italy, 6-8 February 2003.  
 Contact: Tre Emme Congressi srl, Via Risorgimento 4, 56126 Pisa, Italy (Tel: +39-05-044154; Fax: +39-05-0500725; Email: treemme@sirius.pisa.it; Web: www.treemmecongressi.it).

**2nd International Workshop on the Genetics of Bone Metabolism and Disease**

Davos, Switzerland, 15-18 February 2003.  
 Contact: European Calcified Tissue Society, PO Box 4, Dursley GL11 6YL, UK (Tel: +44-1453-549929; Fax: +44-1453-548919; Email: admin@ectsoc.org; Web: www.ectsoc.org).

**Society for Endocrinology Clinical Cases Meeting**

London, UK, 26 February 2003.  
 Contact: Society for Endocrinology, 17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: info@endocrinology.org; Web: www.endocrinology.org/sfe/train.htm).

**Imaging in Endocrinology**

London, UK, 27 February 2003.  
 Contact: Caroline Eason, Royal College of Radiologists, 38 Portland Place, London W1N 4JQ, UK (Tel: +44-207-6364432 ext 124; Email: conf@rcr.ac.uk).

**BES 2003: 22nd Joint Meeting of the British Endocrine Societies**

Glasgow, UK, 24-26 March 2003.  
 Contact: British Endocrine Societies, 17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-642210; Fax: +44-1454-642222; Email: conferences@endocrinology.org; Web: www.endocrinology.org/sfe/conf.htm).

**Serono Foundation for the Advancement of Medical Science: Workshop on Molecular Steroidogenesis**

Bath, UK, 24-27 April 2003.  
 Contact: Helen Gregson or Liz Brookes, BioScientifica Ltd, 16 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-642212; Fax: +44-1454-642222; Email: molster03@endocrinology.org; Web: www.eurosterone.org/serono/index.html).

**6th European Congress of Endocrinology**

Lyon, France, 26-30 April 2003.  
 Contact: Congress Agency Scientific Secretariat, Transit Communications, 18 Place Tolozan, F-69001 Lyon, France (Tel: +33-4-72985858; Fax: +33-4-72985898; Email: info@endocrinology2003.com; Web: www.endocrinology2003.com).

**ALDO'03: International Symposium on Aldosterone**

London, UK, 28-30 April 2003.  
 Contact: Helen Gregson or Liz Brookes, BioScientifica Ltd, 16 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-642212; Fax: +44-1454-642222; Email: aldo-03@endocrinology.org; Web: www.bioscientifica.com/aldo03).

**30th European Symposium on Calcified Tissues**

Rome, Italy, 8-12 May 2003.  
 Contact: Janet Crompton, The Old White Hart, North Nibley, Dursley GL11 6DS, UK (Tel: +44-1453-549929; Fax: +44-1453-548919; Email: admin@ectsoc.org; Web: www.ectsoc.org).

**ENDO 2003: 85th Annual Meeting**

Philadelphia, PA, USA, 19-22 June 2003.  
 Contact: Beverly Glover, Administrative Assistant, Meetings, The Endocrine Society, 4350 East West Highway, Suite 500, Bethesda, MD 20814-4410, USA (Tel: +1-301-9410220; Fax: +1-301-9410259; Email: bglover@endo-society.org; Web: www.endo-society.org).

**4th International Symposium on Hormonal Carcinogenesis**

Valencia, Spain, 21-25 June 2003.  
 Contact: Tandra Price/Dr Jonathan J Li, Department of Pharmacology, Toxicology and Therapeutics, Mail Stop 1018, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160-7417, USA (Tel: +1-913-5884744; Fax: +1-913-5884740; Email: tprice@kumc.edu; Web: www.kumc.edu/hormonecancers).

**National Osteoporosis Society: 9th Bath Conference on Osteoporosis**

Bath, UK, 22-26 June 2003.  
 Contact: Jackie Brown, National Osteoporosis Society, Camerton, Bath BA2 0PJ, UK (Tel: +44-1761-471771; Fax: +44-1761-471104; Email: conferences@nos.org.uk; Web: www.nos.org.uk).



**NOMINATIONS FOR THE ELI LILLY HYPOCCS 2003 AWARD**

The award consists of a certificate and a financial reward of US \$20,000 and will be presented on the occasion of the next annual HypoCCS Symposium in Prague, Czech Republic, 12-15 March 2003. The recipient will be invited to give a lecture and submit a manuscript that will be published in the proceedings of the HypoCCS Symposium

Please contact Pierre Sizonenko (Email: Pierre.C.Sizonenko@hin.ch) for further information

**Nominations must be received by 15th October 2002**



### Serono Foundation for the Advancement of Medical Science: Workshop on Inhibins, Activins and Follistatins

Siena, Italy, 3-4 July 2003.

Contact: Pasquale Florio, Obstetrics and Gynecology, University of Siena, Viale Bracci, 53100 Siena, Italy (Tel/Fax: +39-05-77233454; Email: obgyn@unisi.it; Web: www.unisi.it/eventi/inhibin2003).

### FEBS 2003 Meeting on Signal Transduction: Signal Transduction - from Membrane to Gene Expression, from Structure to Disease

Brussels, Belgium, 4-8 July 2003.

Contact: V Wouters (Tel: +32-2-7795959; Fax: +32-2-7795960; Email: febs@iceo.be; Web: www.febs-signal.be).

### 12th Vitamin D Workshop

Maastricht, The Netherlands, 6-10 July 2003.

Contact: Dr R Bouillon, LEGENDO, Onderwijs en Navorsing (9e Verd), Gasthuisberg, B-3000, Leuven, Belgium (Tel: +32-16-345971; Fax: +32-16-345934; Email: roger.bouillon@medkuleuven.ac.be).

### Bone and Tooth Society Annual Meeting

Sheffield, UK, 9-11 July 2003.

Contact: Janet Crompton, The Old White Hart, North Nibley, Dursley GL11 6DS, UK (Tel: +44-1453-549929; Fax: +44-1453-548919; Email: janetcrompton@compuserve.com; Web: www.batsoc.org.uk).

### University of Exeter Advanced Diabetes Course

Exeter, UK, 9-11 July 2003.

Contact: Ruth Hooper, Department of Diabetes and Vascular Medicine, Barrack Road, Exeter EX2 5AX, UK (Tel: +44-1392-403089; Fax: +44-1392-403027; Email: r.e.hooper@ex.ac.uk).

### Fertility 2003: Joint Meeting of the Society for Reproduction and Fertility, British Fertility Society and British Androgen Society

Aberdeen, UK, 13-17 July 2003.

Contact: Victoria Withy, BioScientifica Ltd, 16 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-642210; Fax: +44-1454-642222; Email: fertility2003@endocrinology.org; Web: www.fertility2003.com).

### Advances in the Molecular Pharmacology and Therapeutics of Bone Disease

Oxford, UK, 15-16 July 2003.

Contact: Janet Crompton, The Old White Hart, North Nibley, Dursley GL11 6DS, UK (Tel: +44-1453-549929; Fax: +44-1453-548919; Email: janetcrompton@compuserve.com; Web: www.paget.org.uk).

### Society for Endocrinology Summer School 2003 (Molecular Endocrinology Workshop, Advanced Endocrine Course and Clinical Practice Day)

Manchester, UK, 15-18 July 2003.

Contact: Ann Lloyd, Society for Endocrinology, 17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: ann.lloyd@endocrinology.org).

### International Symposium on Paget's Disease

Oxford, UK, 16-19 July 2003.

Contact: Janet Crompton, The Old White Hart, North Nibley, Dursley GL11 6DS, UK (Tel: +44-1453-549929; Fax: +44-1453-548919; Email: janetcrompton@compuserve.com; Web: www.paget.org.uk).

### Society for Endocrinology Endocrine Nurses Training Course: The Pituitary Gland

Durham, UK, 10-12 September 2003.

Contact: Ann Lloyd, Society for Endocrinology, 17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: info@endocrinology.org; Web: www.endocrinology.org/sfe/train.htm).

### 75th Annual Meeting of the American Thyroid Association

Palm Beach, FL, USA, 16-21 September 2003.

Contact: ATA, 6066 Leesburg Pike, Suite 650, Falls Church, VA 22041, USA (Email: admin@thyroid.org; Web: www.thyroid.org).

### 42nd Annual Meeting of the European Society of Paediatric Endocrinology

Ljubljana, Slovenia, 18-21 September 2003.

Contact: Dr Ciril Krzisnik, Department of Paediatric Endocrinology, Diabetes and Metabolic Diseases, University Children's Hospital, University Medical Center Ljubljana, Vrazov trg 1, 1000 Ljubljana, Slovenia (Tel: +38-6-12320887; Fax: +38-6-12310246; Email: ciril.krzisnik@mf.uni-lj.si; Web: www.eurospe.org/meetings.jsp).

### 25th Annual Meeting of the American Society for Bone and Mineral Research

Minneapolis, MN, USA, 19-23 September 2003.

Contact: ASBMR, 2025 M Street, NW Suite 800, Washington, DC 20036-3309, USA (Tel: +1-202-3671161; Email: asbmr@dc.sba.com; Web: www.asbmr.org).

### 10th European Federation of Endocrine Societies Postgraduate Course in Clinical Endocrinology

Oxford, UK, 26-28 September 2003.

Contact: Helen Gregson, BioScientifica Ltd, 16 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-642212; Fax: +44-1454-642222; Email: conferences@endocrinology.org; Web: www.euro-endo.org).

### 59th Annual Meeting of the American Society for Reproductive Medicine (ASRM 2003)

San Antonio, TX, USA, 11-16 October 2003.

Contact: ASRM, 1209 Montgomery Highway, Birmingham, AL 35216-2809, USA (Tel: +1-205-9785000; Fax: +1-205-9785018; Email: asrm@asrm.org).

### 194th Meeting of the Society for Endocrinology

London, UK, 3-5 November 2003

Contact: Society for Endocrinology, 17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-642210; Fax: +44-1454-642222; Email: conferences@endocrinology.org; Web: www.endocrinology.org/sfe/confs.htm).

### BES 2004: 23rd Joint Meeting of the British Endocrine Societies in association with EFES

Brighton, UK, 22-24 March 2004.

Contact: British Endocrine Societies, 17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-642210; Fax: +44-1454-642222; Email: info@endocrinology.org; Web: www.endocrinology.org/sfe/confs.htm).

### 31st European Symposium on Calcified Tissues

Nice, France, 5-9 June 2004.

Contact: European Calcified Tissue Society, PO Box 4, Dursley GL11 6YL, UK (Tel: +44-1453-549929; Fax: +44-1453-548919; Email: admin@ectsoc.org; Web: www.ectsoc.org).

### ENDO 2004: 86th Annual Meeting

New Orleans, LA, USA, 16-19 June 2004.

Contact: Beverly Glover, Administrative Assistant, Meetings, The Endocrine Society, 4350 East West Highway, Suite 500, Bethesda, MD 20814-4410, USA (Tel: +1-301-9410220; Fax: +1-301-9410259; Email: bglover@endo-society.org; Web: www.endo-society.org).

### International Society of Endocrinology Congress 2004

Lisbon, Portugal, 1-4 September 2004.

Contact: ISE, Department of Chemical Endocrinology, 51-53 Bartholomew Close, London EC1A 7BE, UK (Tel: +44-20-76064012; Fax: +44-20-77964676).

### 43rd Annual Meeting of the European Society of Paediatric Endocrinology

Haifa, Israel or Basel, Switzerland, 10-13 September 2004.

Contact: Professor Ze'ev Hochberg, Department of Pediatrics, Rambam Medical Center, PO Box 9602, Haifa 31096, Israel (Tel/Fax: +972-4-8542157; Email: z\_hochberg@rambam.health.gov.il; Web: www.eurospe.org/meetings.jsp).

### 30th Annual Meeting of the European Thyroid Association

Istanbul, Turkey, 18-22 September 2004.

Contact: Prof. Gurbuz Erdogan (Email: gurbuz.erdogan@temd.org.tr).

### 76th Annual Meeting of the American Thyroid Association

Vancouver, Canada, 29 September-3 October 2004.

Contact: ATA, 6066 Leesburg Pike, Suite 650, Falls Church, VA 22041, USA (Email: admin@thyroid.org; Web: www.thyroid.org).



## Inhibins, Activins and Follistatins

Siena, Italy

3-4 July 2003

*A workshop covering the following topics:*

Proteins and receptors

Impact on reproduction and development

Cell differentiation and cancer  
Inflammation

**Abstract deadline: 31 January 2003**

SCIENTIFIC COMMITTEE:

N P Groome (UK)

D de Kretser (Australia)

F Petraglia (Italy)

Alan Schneyder (USA)

Wylie Vale (USA)

Contact: P Florio/D D'Antona/S Luisi, Obstetrics and Gynecology, University of Siena, Viale Bracci, 53100 Siena, Italy (Fax +39-0577-233454; Email: obgyn@unisi.it; Web: www.unisi.it/eventi/inhibin2003)

# 193rd Meeting of the Society for Endocrinology



**4-6 November 2002**

Royal College of Physicians, London

**European Medal Lecture** *I Huhtaniemi*

**Asia & Oceania Medal Lecture** *E Simpson*

**Society for Endocrinology Medal Lecture** *ICAF Robinson*

## **Symposia**

Maintenance of pregnancy

Transcriptional control of endocrine development and function

Ageing and cellular senescence

Novel aspects of thyroid disease

plus Debate, Oral Communications, Poster Presentations,  
Young Endocrinologists and Nurses Sessions

## **New for 2002!**

Additional day in association with  Diabetes  
UK

## **Lectures**

PPAR $\gamma$  - *M Gurnell*

Polycystic ovary disease - *S Franks*

PKC inhibitors and glucose toxicity - *P Dodson*

## **Obesity symposium**

Appetite control - *S Bloom*

Human mutations causing obesity - *S O'Rahilly*

Current therapeutics of obesity - *N Finer*

plus SpR posters, Expert Sessions (Impotence, Lumps in the Thyroid) and Workshop

Further information from:

Liz Brookes, Society for Endocrinology,

17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK

(Tel: 01454-642210; Fax: 01454-642222; Email: [conferences@endocrinology.org](mailto:conferences@endocrinology.org);

Web: [www.endocrinology.org](http://www.endocrinology.org))