

THE **Endocrinologist**

Ethics and embryos: raising the debate



PLUS...

**Demystifying
melatonin**

**Imaging and the
posterior pituitary**

**DHEA: separating
hope from hype**

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Deadline for news items for
the Summer 2003 issue: 17 March 2002.
Please send contributions to the above address.

Welcome to this packed issue of *The Endocrinologist*. There's plenty here to suit all interests, and to reflect the huge diversity of subjects that makes up endocrinology.

In fact, it is this diversity that has prompted the Society to look at setting up special interest groups, or SIGs. Through providing members with these fora for the discussion of specialist subjects, the Society would aim to aid communication and strengthen endocrinology as a whole. Would you welcome SIGs? Read page 3 to find out more, and let the Society know your views. Let's hope SIGs might fly!

Pre-implantation genetic diagnosis provides 'PIGD', the second key acronym of the issue. This is a contentious subject which attracts much attention and debate among the academic and clinical population, as well as the media. On page 8, Deborah Bowman seeks to raise the level of the debate and to focus it on the relevant issues.

If you prefer pseudonyms to acronyms, look no further than the touching piece by our creative writer in residence, who goes under the nom de plume of Hotspur! I am sure we can all identify with his plight, recounted on page 9.

Something that has always puzzled me is the origin of the pituitary bright spot. All is made clear on page 10, where Jane Evanson states the case for MR imaging of the posterior pituitary. Restricting this technique to studies of the anterior lobe clearly constitutes a missed opportunity.

Finally, we endocrinologists have often been criticised for ignoring alternative therapies. Two hormones that have been treated as such for years are the 'darkness hormone' melatonin and the 'fountain of youth' DHEA. However, now their real roles and clinical potential are becoming clearer. Read the excellent summaries by Josephine Arendt on melatonin (page 7) and Eleanor Gurnell on DHEA (page 11).

As you open this issue, spring will hopefully be in the air. And as every endocrinologist knows, spring means the BES meeting - so you'd better start packing your bags and heading to Glasgow! If you haven't quite got round to registering, you can find details on the back cover.

Happy reading.

RICHARD ROSS

We're moving!

The Society for Endocrinology and BioScientifica will shortly be moving to new premises at 22 Apex Court, in the same street as the current offices. This will double our current space thus allowing for BioScientifica's continuing expansion. More details in the next issue. Please note, all phone and fax numbers will stay the same.

B R / T / S H
THYROID
FOUNDATION

RESEARCH AWARD 2003 – £10 000

Research must be directly related to thyroid disorders or the basic understanding of thyroid function.

Up to £10 000 is being offered to enable medical researchers to supplement existing projects or to pump-prime new research ideas. Funds will be awarded for consumables, running costs and equipment.

Further information and application forms are available from
Mrs B Nevens, BTF, PO Box 97, Clifford, Wetherby, West Yorkshire LS23 6XD, UK

Closing date for applications: 31 August 2003

WANTED: your views on SIGs!

The Society is evaluating the concept of setting up Special Interest Groups (SIGs). This article outlines the concept and how it might work, and invites your views. We would also at this stage like to hear from you as to which SIGs you would like to see set up.

Aims of SIGs

- To provide a focus for sub-specialities within endocrinology, which would strengthen the discipline overall and provide a framework for different groups to come together in a community and promote interdisciplinary interests within the Society
- To facilitate the organisation of small meetings for focused groups. These could either be stand-alone meetings or could comprise a day of multi-stranded programmes proposed by different groups held on an additional day attached to the Society's annual November meeting
- To increase the profile of endocrinology as a specialty
- To improve communication, and to promote endocrinology as an interdisciplinary subject that interfaces with most biomedical subjects

How would SIGs work?

Members of the Society could belong to as many SIGs as they wish. There are two potential ways of funding this – we could increase the membership fee and include membership of any number of SIGs, or we could give membership of one group free and charge a small extra fee for each additional SIG membership. The disadvantage of the latter option might be that some SIGs might not include all members interested in that topic. Any money raised would be used to cover the costs associated with running SIGs and/or could be used by the SIGs to fund activities.

The SIG members would agree to – set up an informal committee and 'constitution'; initiate and manage communication between members; organise any desired activities on a cost-neutral basis.

The Society would agree to – provide a web page for each SIG; publicise the SIG's aims and activities; give some limited assistance with meetings (eg venue selection, web programme and registration); and provide discussion list facilities if required.

Which SIGs?

There are many options here, from obvious sub-specialities (eg reproductive endocrinology, endocrine physiology, cell biology, growth factors and cytokines, oncology and growth regulation, gene delivery etc) to broad topics, such as diabetes, and to professional sub-groups, such as nurses. Equally, groups could be permanent or could be ephemeral, perhaps to look at a new topic or methodology. The main criteria would be that at least 20 members would join the group, that there would be some enthusiastic leaders to ensure it was active, and that it would not challenge the role of any sister society. Of course, some SIGs might liaise with other societies in the way that the Hormone Group has traditionally worked with the Biochemical Society.

Cross-discipline groups?

There has been discussion about topics where some potential members of an interest group would not be primarily endocrinologists and would not, therefore, be members of the Society. This could pose difficult administrative issues, but we would be interested to hear whether you would be interested in any such groups if the logistics could be managed.

Your views please

Email julie.cragg@endocrinology.org by 31 March 2003 with your suggestions, particularly regarding the following questions:

In principle, do you like the idea of Special Interest Groups?

If no - why?

If yes - which groups would you like to see set up?

How many members do you estimate would be interested in each group?

Would you be prepared to pay a small additional membership fee for each group?

Would you be happy with the level of input from the Society outlined above?

Would you anticipate that non-members of the Society would want to participate in your suggested SIG(s)?

Thank you for your help!

SOCIETY CALENDAR

24-26 March 2003

BES 2003

Glasgow, UK

15 July 2003

Molecular Endocrinology Workshop

Manchester, UK

16-17 July 2003

Advanced Endocrine Course

Manchester, UK

18 July 2003

Clinical Practice Day

Manchester, UK

10-12 September 2003

Endocrine Nurses Training Course: The Pituitary Gland

Durham, UK

3-5 November 2003

194th Meeting of the Society for Endocrinology

London, UK

Members on the move...

W Arlt to Queen Elizabeth Hospital, Birmingham; S M A Bennett to North Tyneside General Hospital, North Shields; A Bickerton to Radcliffe Infirmary, Oxford; C P Burren to St Helier Hospital, Carshalton; L Bradlow to Jurist Institute for Research, Hackensack, NJ, USA; M Cleasby to Garvan Institute of Medical Research, Darlinghurst, Australia; P D Fowler to Ipswich Hospital; P Goulden to Kingston Hospital, Kingston upon Thames; M Haq to St George's Hospital, London; R Jenkins to Pinderfields General Hospital, Wakefield; P M Leung to Covance Clinical Research Unit Ltd, Leeds; G MacColl to University of Edinburgh, Western General Infirmary; F Mahomed to St Mary's Hospital, Isle of Wight; I D Morris to University of York; K Pflieger to Western Australian Institute for Medical Research, Perth; C E Waters to King's College London.

Joseph Chayen

Joseph Chayen was the pioneer of quantitative cytochemistry. He will be remembered for the development of cytochemical bioassays, which allowed the biological activity of circulating hormones to be measured at a time when the early immunoassays were relatively insensitive. It was for this reason that he was awarded the BDH Gold Medal of the Biochemical Society in 1984. However, we should not forget that his early career involved the first demonstration of cytoplasmic DNA. Unfortunately, at that time (1953), this was considered heretical!

Joe obtained his BSc in 1948 at the Royal College of Science (Imperial College London). He entered the MRC Biophysics Research Unit at King's College London, and was sent to Cambridge to learn cytology under the direction of D G Catcheside. There he discovered how to separate plant cells from their matrix, and thereby study individual cells. After his PhD, he continued at King's College, where he pioneered the use of new biophysical techniques, such as interference microscopy and microdensitometry, which allowed him to quantitate observations that had previously been only qualitative. When used with carefully controlled chilling and cryotomy of tissues, these techniques paved the way for the biochemical analysis of cells in their natural environment.

In 1956, he moved to the Royal College of Surgeons, and in 1966 he was appointed Head of the Division of Cellular Biology at the new Kennedy Institute of Rheumatology, a post he held until his formal retirement in 1990. It was during this time that his association with John Daly, myself and 'Jamie' Alaghband-Zadeh gave rise to the development of cytochemical bioassays - the first being that for ACTH. Further assays for TSH, LH, gastrin and PTH brought international recognition in the field of endocrinology. His chief collaborator was Lucille Bitensky, who had moved with him to the Kennedy Institute from the Royal College of Surgeons, and later became his second wife.

The availability of sensitive bioassays attracted the attention of the WHO and, from 1975 to 1988, Joe was a member of the WHO Expert Advisory Panel on Biological Standardisation, and Head of the WHO Collaborating Centre for Cytochemical Bioassays (at the Kennedy Institute).

He continued to work for 11 years after his formal retirement, only ceasing in 2001 through ill-health. His death



Joe Chayen with HRH Princess Margaret, Patron of the Kennedy Institute

was marked by a memorial meeting at the RSM in November last year, attended by colleagues from across Europe and the USA. Jeffrey O'Riordan summed him up as follows: 'He was an impressive scientist, in part classic and in part quite out of the standard pattern. I think he achieved an enormous amount, to some extent not adequately recognised. His partnership with Lucille was extraordinarily productive. My only complaint was his paying me compliments that I did not deserve.'

NIGEL LOVERIDGE



Orchid and Lemons by Saffron Whitehead, St George's Hospital Medical School, London

With regret

We are sorry to announce the deaths of Dr Keith Benson, a previous General Secretary of the Society and a Senior Member, and of Dr Donald Longson, another of our Senior Members. Obituaries will follow shortly.

Meet your Officers

Following last Autumn's AGM, the Society has several new Committee members. Take this opportunity to get to know the officers - and be sure to contact them with your ideas and suggestions!



Steve Bloom becomes the Society's Chairman. Steve has worked for much of his career at the Middlesex Hospital and Royal Postgraduate Medical School. Since 1996, he has been Chairman and Chief of Service for the Directorate of Pathology, Therapy Services and Endocrinology for Hammersmith Hospitals Trust, and from 1997 also Head of the Division of Investigative Science, Imperial College School of Medicine. His endocrine interests centre on neuropeptide regulation of gut hormones and insulin. Amongst many notable roles, Steve has been Chairman of the Bayliss and Starling Society, of the National Institute for Biological Standards Scientific Committee and of the British Diabetic Association Research Committee, as well as Senior Vice President of the Royal College of Physicians. A long-standing Committee member of the Society for Endocrinology, he was previously General Secretary. As Society Chairman, he will chair meetings of the editorial boards of *Journal of Endocrinology*, *Journal of Molecular Endocrinology* and *Endocrine-Related Cancer*. He will sit on the Society's Publications Committee and represent the Society's interests at meetings of the Clinical Endocrinology Trust.



Anne White, the Society's Treasurer, is Professor of Endocrine Sciences at the University of Manchester, and has just been appointed as Associate Dean for Postgraduate Research in the Faculty of Medicine, Dentistry, Nursing and Pharmacy. With Julian Davis, Anne established the Endocrine Sciences Research Group at the University of Manchester. More recently, she held a 2-year Royal Society Industry Fellowship at AstraZeneca, investigating the role of POMC in obesity. Her current research interests include processing of POMC and ACTH, molecular mechanisms of glucocorticoid signalling, and regulation of IGFs in tissue remodelling. Anne has previously served on the Society's Science Committee and as Chair of the BES Programme Organising Committee, as well as being Deputy Chairman of the UK Council for Graduate Education. She took on the roles of Treasurer of the Society and Company Secretary of Bioscientifica in December 2001. As Treasurer, she is also Chairman of the Finance Committee and sits on the Awards, BES Liaison, BES Programme Organising and Publications Committees. Most of her spare time is happily occupied by tasks dreamt up by her teenage children - including frenetic horse riding with her daughter. She and her husband enjoy good food, good wine and good company. Her cooking experiments are the only lab work she is allowed to do these days!



Ann Logan is the Society's new Programme Secretary. She established her own Molecular Neuroscience Group at the University of Birmingham in 1990, and is currently Professor of Molecular Neuroscience in the Division of Medical Sciences, where she heads the Centre for Neurodegeneration and Repair. Her interests focus on the role of growth factors and cytokines in the scarring and regeneration responses of the damaged brain and spinal cord. She was a founder member of the British Growth Factor Group and is now helping to establish the British Society for Gene Therapy. Ann is a Senior Editor for *Journal of Endocrinology*, and is Endocrinology Section Editor for *Current Opinion in Pharmacology*. Within the Society, she has previously been Editor of *The Endocrinologist* and a member of Council. As Programme Secretary, she will chair the Programme Committee for the November meeting, and sit on the BES Liaison and Programme Organising Committees and on the Science Committee. Ann says she keeps her sanity by sailing classic boats and riding classic motor bikes.



John Wass takes on the role of General Secretary. He is Head of the Endocrine Department at the Oxford Centre for Diabetes,

Endocrinology and Metabolism, and Professor of Endocrinology at Oxford University. His work centres around the treatment of pituitary tumours, in particular acromegaly and the study of growth and growth factors. His research interests also include the genetics of osteoporosis and autoimmune thyroid disease, and the development of new pharmacological therapies for pituitary tumours. Before moving to Oxford in 1995, John was a consultant at St Bartholomew's and Professor of Clinical Endocrinology at the University of London. He is the President of the European Federation of Endocrine Societies and UK Representative for the International Society of Endocrinology. He has previously been Chairman of the Society for Endocrinology's Clinical Committee, Editor of *Clinical Endocrinology*, President of the Endocrine Section of the Royal Society of Medicine, and also helped found The Pituitary Foundation. As General Secretary, he will chair meetings of the Publications Committee and sit on the BES Liaison Committee and the Clinical Committee. He will also represent the Society's interests on the *Clinical Endocrinology* Management Board and the Royal College of Physicians Joint Specialist Liaison Committee (Endocrinology and Diabetes). He was recently Editor of the BioScientifica publication *Handbook of Acromegaly*.

Congratulations...

to Barry Furr, who has been awarded an honorary chair at the University of Manchester, and has also been elected a William Pitt Fellow of Pembroke College, Cambridge.

Book token winner

Our thanks and a £50 book token go to Dr M E Symonds from University Hospital, Nottingham, who recruited the most new Society members in the last 3 months of 2002.

Webspinning

Melissa Westwood highlights the best on the web

Trial watch

www.controlled-trials.com

Good or bad, clinical trials always seem to make the news. Now you can keep up with what's happening by using the MetaRegister of Controlled Trials. This is a searchable international database of randomised controlled trials, built by combining the registers held by public, charitable and commercial sponsors. Covering all aspects of healthcare, this site should be useful for practitioners and participants alike. Access is free, though registration is required.

SERVICES: D, L, N; STRONG POINTS: News, drug information;

WEAK POINTS: Nothing significant; RATING: Very good.

Mouse mutaneering

socrates.berkeley.edu/~skarnes/resouce.html

Using gene trap insertion (a tool for simultaneous identification and mutation of mouse genes) Skarnes & Tessier-Lavigne at the University of California have analysed numerous secreted and transmembrane proteins in mice. They use this site to distribute information about the mutations (gene, Genbank link, known phenotype) and details of how to obtain the animals or ES cell lines listed. Could this be the start of a great collaboration?

SERVICES: D, L; STRONG POINTS: Information about mutations;

WEAK POINTS: Some unfinished sections; RATING: Good.

Coping with cytokines

www.copewithcytokines/de/cope.cgi

COPE (Cytokines Online Pathfinder Encyclopaedia) is worth a look even if cytokines aren't your thing, since it actually covers all manner of growth factors, receptors, intracellular signalling molecules, matrix proteins and many other aspects of cell biology. Heroically maintained by Horst Ibelgaufts of the University of Munich, this site is essentially a hypertext dictionary providing mini-reviews (ideal for those just starting out), information on cell lines, and a description of associated terms and useful techniques. You can also 'adopt' your favourite factor and write supplementary entries. This may be a new way to get your work published!

SERVICES: D, L, S, O; STRONG POINTS: Comprehensive;

WEAK POINTS: None; RATING: Excellent.

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.

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

Patient support grants

The Society for Endocrinology and the Clinical Endocrinology Trust are delighted to announce that they have awarded grants totalling around £13 000 to the Anorchidism Support Group, Families with Pituitary Children, the Gender Trust, the Multiple Endocrine Neoplasia Society, the Paget's Disease Association, The Pituitary Foundation, and the Prader-Willi Syndrome Association.

These endocrine patient support groups all successfully submitted proposals that will directly benefit their members. They will each receive up to £2000. The grants will support newsletters, new computers, web site development and patient information leaflets. All projects are to be completed by the end of 2003.

This was the second time that the Trust and the Society have awarded these grants, and all appropriate groups on the Society's database were invited to apply. Further grants will hopefully be available in the future, though this may be a 2-yearly activity, in order to boost the sums available.

The Society's Bristol office maintains a database of endocrine support groups, but most UK patient support groups are listed at www.patient.co.uk/selfhelp.asp.



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

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)

Nature's timekeeper

Melatonin has been lauded as a drug with potentially miraculous properties - even an alleged ability to extend human lifespan. But, at last, careful and rational investigation of its effects seems to be leading to a consensus on its physiological and pathological functions.

Undisputably, melatonin, or N-acetyl-5-methoxytryptamine, is a molecule with remarkable properties, especially a timekeeping function that is conserved across species. It is generated by the central pacemaker or 'clock', found in the suprachiasmatic nucleus (SCN) of the hypothalamus, and is secreted with a robust circadian rhythm. Synchronisation with the 24-hour light-darkness cycle is largely achieved via a pathway from the retina to the SCN. Individuals with no perception of light often show 'free-running' rhythms of slightly longer than 24 hours. Melatonin can be described as the 'hand of the clock', responding to the SCN's signals, and indicating the phase of the cycle. It the marker rhythm of choice for measuring variation of the 'clock' from the norm.

Melatonin is normally produced during the night, so earning it the title of 'darkness hormone'. Light suppresses melatonin via a novel photoreception pathway, with the maximum effect at around 460nm (blue). In many animals, including humans, the duration of secretion extends if nights are longer. This pattern of production serves to cue seasonal rhythms in many photoperiodic species.

Whether melatonin has an essential role in the mammalian circadian timing system has been much debated, and is not entirely resolved. Certainly the evening rise in hormone is associated with increased propensity to sleep, while peak levels correspond to minimum alertness, performance and core body temperature. If melatonin is produced for pathological reasons during daytime, it is strongly associated with sleepiness or naps.

Since its discovery by Aaron Lerner in 1958, it has been known that melatonin induces sleep in the hours after administration. This effect is seen during 'biological day', when endogenous melatonin is minimal. It is accompanied by lowered core body temperature, and the effects are maximised if subjects are recumbent in dim light. It was not until the 1980s, however, that researchers demonstrated entraining and phase-shifting effects of timed pharmacological doses of melatonin on the circadian clocks of rats and humans.

It was these observations that led directly to the current interest in the use of melatonin and its analogues for 'circadian rhythm disorders', such as delayed and advanced sleep phase syndromes, the problems of jet lag and shift work, and the non-24-hour sleep-wake disorder often seen in totally blind people. This last may well be the most important application of melatonin treatment. In most other circumstances, timed exposure to sufficiently bright light can, in theory, re-establish normal rhythms.

It became clear that melatonin could advance or delay circadian rhythms. Treatment before and during the rising phase of the endogenous melatonin rhythm was found to advance the clock, while treatment during and shortly after the declining phase induced delays. Since the human clock tends to delay, it is the advancing properties of melatonin that are most important from a therapeutic point of view. Physiologically speaking, the evening melatonin rise may serve to reinforce both the synchronising effects of light and nocturnal physiological events (such as sleep).

Melatonin can maintain a 24-hour circadian clock in sighted subjects living in very dim light (conditions conducive to 'free run'). In the 'free-running' blind, it has been used to stabilise the sleep-wake cycle to 24 hours, with improvement in sleep and mood variables. Complete synchronisation of more strongly endogenous rhythms, such as melatonin itself, is possible in some, but so far not all, subjects. Success may relate to the precise timing of treatment (to advance the clock in subjects who show a daily delay) and also to the dose (0.5-5.0mg daily). The number of subjects synchronised to date is, however, very small, and the extent to which complete synchronisation is necessary for maximum benefit is not known.



Delayed sleep phase syndrome has been successfully treated using phase-advancing melatonin, but not all trials are consistent. If circadian timing is not measured, subjects may be misdiagnosed. Moreover, the critical importance of the timing of treatment is not always appreciated. Success may also require motivation of the subject to go to bed at a reasonable time. Extreme advanced sleep phase syndrome is a very rare inherited disorder, related to a mutation in casein kinase epsilon, and no reports of treatment with melatonin exist. Advanced sleep phase is common in older people, as is a decline in overall melatonin production. Therapeutic benefits of melatonin in the elderly are currently controversial.

At least twelve trials have studied treatment in jet lag, of which ten have shown therapeutic benefit. Here, again, timing is critical and very difficult when circadian phase is unknown (e.g. after a short stopover or repeated long haul flights). The two unsuccessful studies fell into this category. Another confounding factor is exposure to bright light, which can override melatonin. For example, overnight flights from the USA to the UK expose passengers to bright early morning light that is timed to shift their clocks westwards rather than eastwards.

Resynchronisation by a 16-hour delay rather than an 8-hour advance is clearly undesirable!

Most night-shift workers do not fully adapt their clocks to their working patterns, to avoid conflict with family and social life on rest days. In this situation, melatonin's acute sleepiness-inducing effects could prove useful during the day, combined with the acute alerting effects of light at night. While light is clearly effective, the few published studies on melatonin are not consistent. In theory, treatment could be timed to induce minimal shifts of the clock. Full adaptation is seen in some workers (some oil rig shifts, and in polar regions), which could be hastened by suitable treatment.

The benefits of melatonin are already available to consumers in the USA, with sales reputed to reach \$69m last year. With safety evaluations at last underway, we can hope to see its future registration as a medication in the UK.

JOSEPHINE ARENDT

Ethics and embryos

Pre-implantation genetic diagnosis (PIGD) is highly topical in both the academic literature and the mainstream media. Much discussion centres on the potential ethical and social implications, but sadly fails to address the key issues in a coherent and systematic way.

The main 'stakeholders' in reproductive medicine have acquired the role of lobbyists. Scientists, clinicians, lawyers, ethicists and putative patients appear in the media, making a case that describes a partisan and incomplete analysis of the issues that surround PIGD. Meanwhile, the joint consultation paper on PIGD from the Human Fertilisation and Embryology Authority (HFEA) and Human Genetics Commission attracted only 171 responses. It is time to seek a coherent ethico-legal review of those areas that should be a focus for reflection and discussion, not only for those most involved in the field, but for all members of democratic societies.

To engage with the debate, one needs to divide the issues into:

- (a) principles: should PIGD be permitted at all?
- (b) ethical analysis: how should we regulate the potential and actual consequences of PIGD if it is permitted?

Should PIGD be permitted?

Our understanding of the concept of personhood and the status of the embryo is essential for any ethical analysis of PIGD. If one believes that human life is characterised so as to afford the embryo human status or personhood, it will be difficult, if not impossible, to assume a position that considers PIGD morally acceptable.

The law adopts arbitrary and different definitions of 'human'. For example, for the purposes of research on embryos, day 14 is the limit beyond which research cannot be permitted, the rationale being that neural crests have developed by this stage. It is a legal convenience which has been criticised as 'neuralist' by Peter Saunders, General Secretary of the Christian Medical Fellowship, who notes that 'the development of the nervous system is a continuous process beginning at fertilisation, and choosing an arbitrary point on this continuum discriminates on the basis of neural function'.

The meaning of personhood and the status of the embryo have commonly been understood and discussed in the ethical literature thus:

- Persons are characterised by their rationality or capacity for relationships as opposed to mere sentience
- Embryos have the potential to become a person and should therefore be afforded the status of persons from the moment of fertilisation
- Personhood is a gradual process of development and, accordingly, the status afforded to the embryo, fetus and eventually child will increase incrementally from conception through pregnancy until birth.

Of course, it requires a period of consideration to determine which arguments are most cogent and convincing. This is not easy and can be even more challenging for scientists and clinicians trained in a positivist, evidence-based tradition in which hypotheses are generated to be proven. Ethical theory does not allow for such an approach. However, this does not mean that scientists and clinicians can abrogate their responsibility to engage with the task. Indeed, ethics and law are now an integral part of most medical undergraduate curricula, with a growing interest in their role in scientific training.

Clearly, if one concludes that the embryo is morally equivalent to a person, it is difficult to make a cogent argument for PIGD in any circumstances. To do so would be to ignore the Kantian precept that all persons should be ends in themselves, and never means to ends, no matter how apparently compelling that end may be.

However, even if one rejects the notion of moral equivalence between embryos and people, this does not necessarily render the practical tasks inherent in reproductive medicine comfortable or easy. Dilemmas about the disposition of embryos have proved difficult to resolve for both the couples for whom the embryos were created and the HFEA.

Ethical ends?

If one concludes that the embryo's status is not morally equivalent to a person, the analysis must turn to the morality of 'the intended end' in PIGD. What is a



morally sufficient justification for permitting PIGD?

Many people, both clinicians and lay people, could list a number of conditions that they believe would warrant PIGD. Such 'shopping lists' of justifications for PIGD commonly include conditions like muscular dystrophy, Huntingdon's chorea, haemophilia, fragile X, Turner's syndrome, thalassaemia and sickle cell anaemia. However, there is unlikely to be complete consensus, and there are many 'grey' areas. For example, should PIGD discard carrier embryos? Is the fact that a disease is late-onset rather than congenitally symptomatic relevant?

In some ways, however, it is not the agreement of a list of justifications that should be the subject of ethico-legal attention. Rather, this should focus on the ethical precept of autonomy. In most cases, bioethics requires that the doctor both fosters and respects the competent patient's autonomy. In practice, this finds legal translation in the doctrine of informed consent.

How should patient autonomy be fostered and respected in the context of PIGD? The choice implicit in the concept of informed consent does not equate to a right to demand treatment that is not clinically indicated, so it would be inconsistent if PIGD were available on demand. However, all professionals in reproductive medicine should consider carefully how autonomy is fostered and respected at both an individual and organisational level. All assessments as to whether a particular genetic condition is a sufficient justification for PIGD should be acknowledged to be value judgements to a greater or lesser extent, the result of personal assumptions about the condition in particular and the meaning of 'disability' in general. If that is the case, why should the value judgement of a clinician be considered any more

persuasive than those of the putative parents?

The HFEA recommends that information about clinical conditions and the reality of living with a disability should be available to all patients seeking PIGD. This is admirable and goes some way to acknowledging the difference there is between the biomedical understanding of a particular disease and the social reality of how a disease affects an individual. However, there are multiple realities that cannot ever be comprehensively represented to all patients. For some people, the experience of having a child with fragile X may be represented as a lengthy and lonely struggle, but for others it may be a rewarding and enriching experience in which they feel consistently supported. How can these, and other multiple realities, be realistically discussed with potential parents? This is perhaps one of the greatest ethical challenges facing those working in reproductive medicine.

Whilst the status of the embryo, the morality of the aims of PIGD and the challenge of patient-centred practice pose fundamental ethical questions for the healthcare professional, perhaps the most important stage in considering the ethico-legal issues is to engage with those within and outside the field. Medical students are increasingly afforded such opportunities - but where is the forum for practising doctors and scientific researchers to reflect on the moral challenges that imbue their daily work?

Furthermore, whilst scientists, clinicians, ethicists and lawyers need no second invitation to reflect on the points raised in this paper, how can we engage society at large in discussion of these fundamental questions? Attempts to involve the public in ethical analysis do not have an impressive track record. However, unless and until we manage to become more inclusive, and convince the broader population that these are issues for us all, we will continue to struggle to seek a balance between vociferous but partisan perspectives, and ethical analysis will always be playing 'catch up' with advances in scientific technology.

DEBORAH BOWMAN

Deborah Bowman is Lecturer in Medical Ethics and Law at St George's Hospital Medical School.

Tears on a ward round

Cast your mind back to the old days - when a consultant fulfilled just as many roles but carried fewer labels than today. Though undeniably 'appraiser, assessor, mentor and trainer' for my senior registrar and two senior house officers, I had no such designated titles to cover my keen interest in their welfare and education. Nor was any training organised by the Regional Health Authority to prime me for such undertakings.

It was a wet and unpleasant Tuesday morning, and two senior house officers and I were on a rather easy ward round. We had reached the bedside of a middle-aged man with a benign pituitary adenoma, who had been admitted for some routine endocrine investigations. Suddenly I realised that Alice, the female senior house officer, was quietly sobbing and clearly distressed. Quickly, I took her away from the patient's bay and into the treatment room, where we were alone and could talk quietly. I hastened to reassure her that, in my opinion, the patient was not seriously ill - this was endocrinology after all! I emphasised that the patient's prognosis in terms of life expectancy was excellent and that any endocrine morbidity could be easily dealt with, endocrinology being an excellent speciality for therapeutic options.

She had gradually stopped sobbing and listened silently whilst I spoke. I was feeling quite pleased with how well I had managed the situation, so her first words struck me with the impact of a cold shower: 'I am not crying about the patient - I am upset because I have just finished a love affair and this has made me very unhappy'.

Wow! I felt such a twit, and really quite a helpless twit. After all, I was the senior here, but having never (knowingly) finished a love affair I had less experience than she had - and, of course, no useful advice! Nowadays, there would be an 'away day' for this sort of thing. Furthermore, if Paul Simon is right and there are in fact 50 ways to leave your lover, at very least a 3-month course on 'lover leaving' would be required.

Like all personal tragedies of an emotional nature, the ripples around the main players reach out to affect innocent bystanders. Only after many years did the patient with the benign pituitary adenoma indicate that he believed I was telling him the truth. My constant reassurance that his life expectation was normal and that he did not have aggressive cancer was met by his reply 'then why did that young female doctor weep at my bedside?'. Why indeed?

'HOTSPUR'



The forgotten lobe

Pituitary imaging generally concentrates on abnormalities of the anterior gland. However, the high resolution of MR scanners also allows for assessment of the posterior pituitary, an approach which should not be discounted!

The normal posterior pituitary gland is identified as a focal area of high signal on T1-weighted images, lying in the posterior third of the fossa. This so-called 'posterior pituitary bright spot' (PPBS) must not be confused with the bright signal that is seen in the dorsum sellae, which is due to fatty yellow bone marrow. A fat suppression sequence will remove the signal from the dorsum, leaving the PPBS unaffected.

The absence of this bright spot in patients with central diabetes insipidus indicated that it was caused by neurosecretory granules containing ADH. It is still not certain whether its origin is the vasopressin-neurophysin II complex, the phospholipid membrane or both, but it is accepted that the PPBS reflects ADH storage.

The PPBS has been clearly identified on sagittal T1-weighted

sequences in 52-100% of patients.

With the high resolution MR that is now available, this percentage is likely to be nearer the upper end of the range. However, it is not always possible to definitively identify the PPBS in all normal subjects. This is probably due to partial volume effects, whereby the high signal from the small posterior pituitary gland is 'averaged out' by the lower signal from the much bulkier anterior gland.

Pathologies involving the stalk (e.g. germinoma, Langerhans cell histiocytosis or sarcoidosis) may have abnormal stalk thickening and no PPBS. Identification of the PPBS in an ectopic location is most common in the presence of a macroadenoma. The spot may be seen at the infundibulum, or as a flattened/stretched stalk displaced to one side or stretched over the posterior surface of the adenoma. Larger tumours are more likely to lead to ectopic positioning. It is not known whether an absent or ectopic PPBS pre-operatively is a predictor of long-term diabetes insipidus after surgery.

The illustration shows an ectopic posterior pituitary lobe with the PPBS

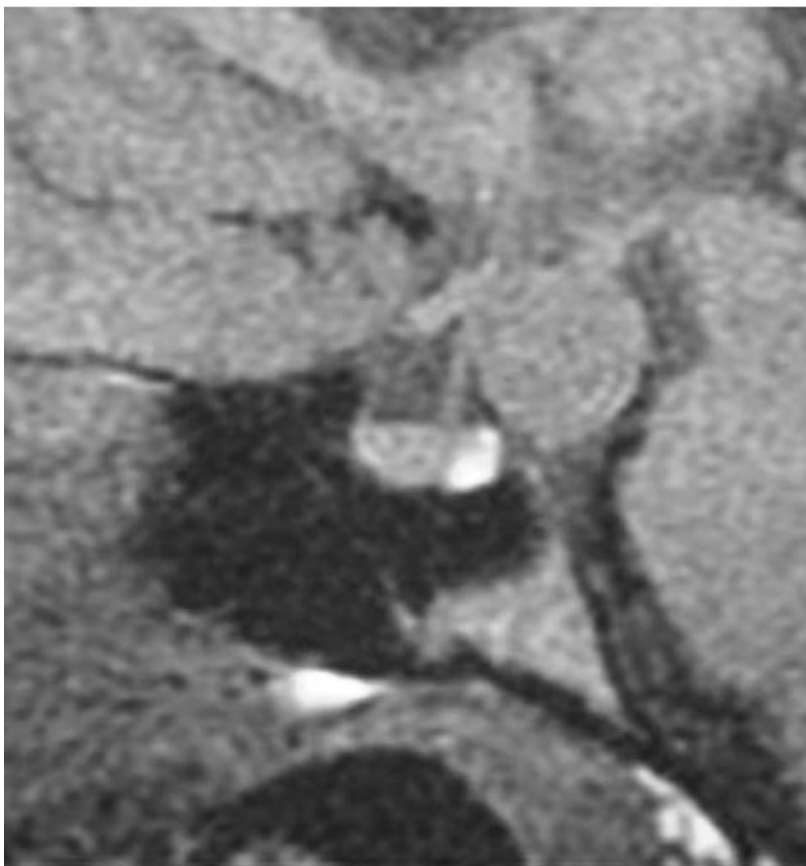
seen at the median eminence on a sagittal image. This abnormality may be found in both GH deficiency and multiple pituitary hormone deficiency. There may be hypoplasia of the anterior lobe and absence of the pituitary stalk. Those patients without a visible stalk are likely to have more severe hormonal deficiency. This condition is now thought most likely to have a genetic cause.

Midline malformations of the brain may also be associated with an ectopic PPBS, e.g. optic nerve hypoplasia, septo-optic dysplasia, absence of the septum pellucidum, agenesis of the corpus callosum and Chiari 1 malformation. These conditions all have a characteristic appearance upon imaging. Coronal sequences through the optic pathways might reveal small hypoplastic optic nerves and absence of the septum pellucidum in septo-optic dysplasia. A sagittal midline sequence will demonstrate absence of the corpus callosum, with the cortical gyri forming the roof of the lateral ventricles.

An association between ectopic PPBS and periventricular heterotopia has recently been observed. This condition is identified as foci of cortical grey matter lying in an aberrant position adjacent to the lateral ventricular margins. It represents a failure of the normal migration of neuronal cells that occurs from 8 weeks of gestation onwards. Although no genetic linkage has been established for this specific abnormality, known genetic mutations are associated with other forms of migrational abnormality.

Imaging of the pituitary gland should include an assessment of the posterior pituitary, with particular attention to the location of the bright spot and the morphology of the stalk. Ectopic positioning of the PPBS in the absence of an intrasellar abnormality should raise the possibility of other midline brain malformations as well as abnormalities of neuronal migration.

JANE EVANSON



A sagittal T1-weighted MR image demonstrates absence of the pituitary stalk with an ectopic posterior pituitary lobe lying at the level of the median eminence.

DHEA: separating hope from hype

Dehydroepiandrosterone (DHEA) is frequently hailed as the holy grail of anti-ageing. But just what is the truth behind this 'fountain of youth'?

Available in the USA as a natural dietary supplement, DHEA and its sulphated derivative DHEAS are actually the most abundant circulating adrenal steroids. Although highly synthesised during fetal development, production falls rapidly postnatally, before increasing again with the onset of adrenarche. Peak levels are achieved by the third decade of life. After this, there is a relentless decline in DHEA production in both sexes, such that, by the age of 80, concentrations are only 10-20% of those in young adults. Meanwhile, adrenal glucocorticoid production is maintained, leading to an alteration in the ratio of circulating cortisol to DHEAS with age.

The physiological role of DHEA is not fully understood. It is clearly a substrate for testosterone and oestradiol biosynthesis in peripheral tissues. The development of axillary and pubic hair which accompanies adrenarche emphasises its role as a sex steroid precursor. When administered in deficiency states in adult women, DHEA's biotransformation leads to a rise in circulating testosterone. However, there is evidence to suggest that it may also exert effects as a neurosteroid. It may be synthesised locally in the CNS, and can enhance or block signalling via the NMDA or GABA receptor pathways respectively. DHEA has also been shown to oppose the action of cortisol, antagonising glucocorticoid-induced thymic involution or corticosterone neurotoxicity in the hippocampus.

However, to date, a specific cell surface or nuclear receptor for DHEA has not been identified. In a study using DNA microarrays, DHEA induced a pattern of gene expression that differs from that of glucocorticoid or testosterone. Furthermore, it modulates cellular MAP kinase signalling independent of sex steroid receptor pathways. Together, these observations suggest that DHEA may have direct actions that are distinct from the effects of its derivative steroids.

The physiology of DHEA in rodents is radically different from that in humans. Lower basal levels of hormone are found neither to rise in adrenarche nor to fall with ageing, suggesting that it is unwise to extrapolate to humans from studies in animal models. Therefore, DHEA therapy has been evaluated in two clinical situations: as a supplement in ageing, and as hormone replacement in adrenal insufficiency.

A large body of epidemiological data in cross-sectional studies has indicated an association between the decline in DHEAS levels and various age-related disorders. Low DHEAS levels correlate with increased cardiovascular disease and mortality in elderly men, and lower bone mineral density and increased breast cancer risk in women. Lower DHEAS levels are associated with depressed mood in older women, while a higher cortisol:DHEA ratio correlates with cognitive decline in both sexes.

However, the lower DHEAS levels may simply be a marker of the ageing process, and so be related to the comorbidities that are associated with ageing, rather than being causally linked to them. To obtain stronger evidence for a causal relationship, several groups have examined the effects of DHEA supplementation in healthy elderly subjects. Yen and colleagues evoked great interest with a placebo-controlled study that described a remarkable increase in physical and psychological well-being following 50mg DHEA supplementation in 30 older men and women. They subsequently reported that a higher dose (100mg) reduced fat mass and enhanced muscle strength in men. In a larger trial with 280 older subjects, Baulieu and co-workers showed an increase in libido, sexual satisfaction and bone mineral density in women, together with enhanced skin hydration and sebum production in both sexes. However, other studies have shown no benefit, with no effect on mood, quality of life or libido.

Adrenal insufficiency (Addison's disease) is associated with very low circulating DHEAS levels. Whilst glucocorticoid and mineralocorticoid deficiencies are treated with oral replacement, the associated failure of adrenal DHEA synthesis is not usually corrected. Indeed, despite optimal conventional steroid replacement therapy, patients with Addison's disease report persistent fatigue and reduced well-

being. Trials of DHEA replacement in Addison's disease might be particularly informative for two reasons. First, they may determine whether DHEA deficiency accounts, at least in part, for the impaired well-being in this disorder. Secondly, correction of the near absolute deficiency of DHEA in a younger patient population might enable a beneficial effect to be discerned more easily than in ageing.

In a randomised, placebo-controlled trial in 24 women with primary and secondary adrenal insufficiency, Arlt and colleagues described a marked increase in sexual interest and satisfaction, together with improved mood and well-being, following 50mg DHEA for 4 months. In a concurrent 3-month study in 39 men and women with Addison's disease, we observed an improvement in mood and fatigue in both sexes. The beneficial response in males, without a change in testosterone levels, suggested a direct effect of DHEA. Most recently, lower dose (25mg) DHEA replacement in women with hypopituitarism was observed by their partners to improve psychological function, and also enhanced sexual interest. We have just completed a longer-term, 12-month trial of 50mg DHEA replacement in 100 patients with Addison's disease. The preliminary results show positive effects on lean body mass, bone mineral density, fatigue and well-being, but with significant androgenic side-effects in older women.

On the basis of current evidence, it is clear that oral DHEA treatment is effective at restoring circulating levels of this steroid in both ageing and adrenally insufficient populations. In both contexts, short-term studies suggest an improvement in well-being, mood and sexual function. However, in the elderly, longer-term studies are required to address whether, as the epidemiological data suggest, DHEA treatment can influence cardiovascular morbidity and mortality, cognitive decline or cancer risk. Likewise, in Addison's disease, longer-term trials will clarify any effects of DHEA on body composition and bone mineral density, and also assess the safety of its prolonged use. If the outcome of such studies is positive, the addition of DHEA to other steroid hormone replacement therapy may enter routine clinical practice.

ELEANOR GURNELL

Hot Topics

Nathalie Gilmore, Jolene Guy and Jane Shepley bring you cutting-edge highlights from the Society's journals.

Phyto-oestrogens suppress cell-mediated immunity

Oestrogen is known to suppress cell-mediated immunity in women and mice. In this study, Yellayi and colleagues have investigated the effects of injected and dietary genistein, a soy phyto-oestrogen, on cell-mediated immunity in ovariectomised mice, and suggest pathways of phyto-oestrogenic action.

Mice were either fed a phyto-oestrogen-free diet prior to a series of genistein injections, or fed set doses of the phyto-oestrogen for 1 month, which produced serum genistein levels comparable with those in humans under various nutritional conditions. Following treatment, the authors evaluated the cell-mediated immune response by measuring the mice's delayed-type hypersensitivity (DTH) response to a hapten.

The authors report a dose-dependent reduction in thymic weight in mice treated by either dietary means or injection. The effects of genistein were reversible, based on the measurement of the DTH response of injected mice that had a period without treatment prior to measurement.

This is the first study to investigate phyto-oestrogen-induced suppression of cell-mediated immunity in mice. As soy-derived products are increasingly consumed by humans, this research will be of great interest to both the scientific community and the general public. JG (See the full article in *Journal of Endocrinology* 176(2), February 2003)

Porosomes under the microscope

In this article, Jena reviews the structure and dynamics of the fusion pore or 'porosome'. This is the specialised area of all secretory cell plasma membranes

where secretory vesicles dock in order to expel their contents from the cell. The existence of these structures was only recently confirmed by atomic force microscopy (AFM), so the reference list is modest, and predominantly from the last decade.

AFM revealed the fusion pore as a pit containing cup-shaped depressions between 100 and 150nm in diameter. The presence of these structures solely at the secretory surfaces of the cell, and their dilation during secretion, indicated their function. Further evidence came from studies using gold-labelled antibodies targeted to specific cellular secretory proteins. Localisation of the label was seen at the porosome following stimulation of secretion.

Jena describes how secretion (or inhibition of secretion) correlates with an increase (or decrease) in the diameter of the depressions. He reviews the current knowledge and hypotheses regarding interactions and dynamics of the porosome machinery with cytoskeletal and membrane proteins.

The detailed morphology of the porosome has now been elucidated using electron microscopy, and its biochemical composition determined. JS (See the full article in *Journal of Endocrinology* 176(2), February 2003)

Role for NGF in uterine development

Oral dosing of newborn mice with tamoxifen is known to cause adult uterine adenomyosis.

The nerve growth factor α (NGF α) gene appears to be affected by tamoxifen during this critical stage of development. Green and co-workers have now investigated NGF and cognate receptor expression in different types of uterine cell in mice, using laser capture microdissection (LCM) and RT-PCR.



Following treatment with tamoxifen and raloxifene, LCM was used to isolate separate subpopulations of luminal epithelial, stromal and myometrial cells from the uterine tissues of both newborn and adult mice. RT-PCR was used to investigate gene expression, while Western blotting enabled the NGF receptors in the different cell types to be examined.

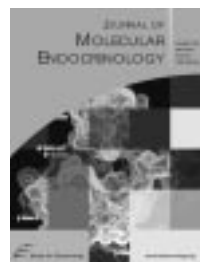
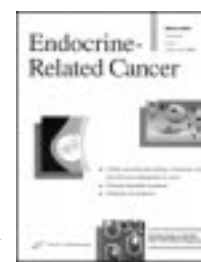
It appears that NGF normally regulates the differentiation of the mesenchyme into uterine myocytes through paracrine mechanisms, and that an early disturbance of this process by tamoxifen plays a key role in the subsequent development of adenomyosis. NG (See the full article in *Journal of Molecular Endocrinology* 30(1), February 2003)

ErbB targeting in carcinoma

ErbB receptors and their ligands are frequently expressed in human tumours. As a result, ErbB has attracted much interest as a potential target for therapy in carcinoma.

Several target-based agents are currently undergoing clinical trials. They have shown acceptable toxicity profiles, and have proved effective in heavily pretreated patients. The mechanisms of action of these compounds, as well as potential therapeutic strategies to improve their efficacy, are discussed in this insightful review by Normanno and colleagues.

The authors conclude that, although clinical trials of anti-erbB-targeting agents have yielded some promising results, further research is needed to identify suitable recipients for this treatment, as patient selection criteria have not yet been established. They also highlight the need for a standardised assay to measure expression of the EGF receptor, and suggest that additional studies are necessary to select markers of response to this therapy. NG (See the full article in *Endocrine-Related Cancer* 10(1), March 2003)



Oxford Handbook of Endocrinology and Diabetes

Eds H E Turner & J A H Wass, Oxford University Press, 2002, 1005 pp, £21.95, ISBN 0 19 263052 0

The editors' aim was to provide us with what they call a readily assimilable 'white coat pocket' guide. This handbook is not only meant for trainees, but also (luckily) for the trained, who 'might have the occasional mental blank'. Considering the number of pages, it is relatively small in size, and so is indeed a handbook.

The chapters cover almost all of clinical endocrinology as it is practised in many centres by many physicians. The index is adequate and, with the use of running titles, you can easily find the appropriate pages of each topic. The use of colours, or notches that separate chapters, might have improved the speed of searching even more, but that is just a matter of taste, and I could easily find my way around.

Having used it for some weeks, I can say that it is a very good handbook, and one which will meet the needs of many clinicians, regardless of their level of training. Readers will find it hard to come up with any patient problems that cannot be addressed by this book. If you do, you should think about writing a case report! The number of references gives adequate opportunities for further reading.

If you decide not to carry this handbook in your white coat pocket for the whole day, make sure you keep it in a safe place - or you may find your colleagues borrow it for longer than you anticipated! The publisher might usefully consider providing this handbook for use with electronic personal digital assistants as well.

AART J VAN DER LELY

Oxford Textbook of Endocrinology and Diabetes

Eds J A H Wass & S M Shalet (Diabetes Section Eds E Gale & S A Amiel), Oxford University Press, 2002, 1925 pp, £245.00, ISBN 0 19 263045 8

While the handbook provides succinct advice on diagnosis and treatment, this textbook addresses both basic science and clinical endocrinology in a very comprehensive way. It has been crafted, according to the editors, with a specific readership in mind, and with the aim of providing a clinical textbook. The result is very successful indeed. This book combines the efforts of scientists from around the world, and the editorial team have succeeded in finding the right balance between basic and clinical science throughout.

The chapters cover almost all of what is considered to be endocrinology at large. I especially liked the large number of 'boxes'. These features enable the reader to screen the context of each topic easily, along with the essential information. This should make it a very handy tool for teachers and students, and for basic scientist and clinicians. Sufficient references are provided with each chapter. These are surprisingly well updated, which must have been a formidable task for the editorial team, considering the size of the publication. The diabetes section is relatively small compared with the rest of the book and with other textbooks on diabetes; however, it still covers the whole range of diabetes quite well in 250 pages.

I agree with the editors that this book will not only be of interest to endocrinologists, but will also be valuable for many other specialists (oncologists, gynaecologists, urologists, etc) who regularly encounter patients with endocrine problems.

AART J VAN DER LELY

PCOS Diet Book

C Harris, Thorsons, 2002, 384 pp, £12.99, ISBN 0007131844

Written for women with PCOS (polycystic ovary syndrome) by a woman with PCOS, this book has an immediate appeal. It is well written, and the general philosophy is very sound: look after yourself and your diet, and you will cope better with your symptoms.

The well-researched background information about PCOS is backed up by references, including many to peer-reviewed papers in the medical literature. The book is punctuated with short and pithy illustrative comments, mainly from women with PCOS, but also from experts in the field.

Much of the advice about healthy eating and dieting is based on the author's own experience of her symptoms of PCOS and finding a healthy diet which made a huge improvement to her daily life. The book is not, however, simply a means of passing on her personal ideas about healthy living. Certainly, she has strong views about the use of dietary supplements and complementary therapies that may not always be supported by unequivocal scientific evidence, but the main principles of her approach to a healthy lifestyle are difficult to fault. These include advice about calorie counting, spacing out meals sensibly, and choosing the right kind of diet in terms of complex carbohydrate and fibre content.

She is perhaps a little too dismissive of endocrine therapies, such as combined oestrogen and progestagen (or anti-androgen) medication for management of the symptoms of PCOS. As every endocrinologist knows, these preparations have an important part to play, and are generally very well tolerated and effective.

On a final positive note, the liberal sprinkling of tempting recipes makes this a very practical and attractive cookbook, as well as an indispensable handbook for women with this highly prevalent and often very distressing condition.

STEVE FRANKS

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/bes2003/).

Warwick University Short Course: an Introduction to Immunology

Coventry, UK, 2-3 April 2003.
 Contact: Steve Hicks, Department of Biological Sciences, University of Warwick, Coventry CV4 7AL, UK (Tel: +44-24-76523540; Fax: +44-24-76523701; Email: s.j.hicks@warwick.ac.uk; Web: www.bio.warwick.ac.uk/shortcourses).

13th International Meeting of the European Society of Gynaecological Oncology (ESGO)

Brussels, Belgium, 6-10 April 2003.
 Contact: ESGO Secretariat, 17 Rue du Cendrier, PO Box 1726, CH-1211 Geneva 1, Switzerland (Tel: +41-22-9080488; Fax: +41-22-7322850; Email: esgo13@esgo.org; Web: www.esgo.org/esgo13/).

46th Journées Internationales d'Endocrinologie Clinique: Endocrinology of Menopause and 'Andropause'

Paris, France, 24-25 April 2003.
 Contact: G Copinschi, Laboratory of Experimental Medicine, Brussels Free University, CP 618, 808 Route de Lennik, B-1070 Brussels, Belgium (Fax: +32-2-5556239; Email: klotz@ulb.ac.be).

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

Bath, UK, 24-27 April 2003.
 Contact: Helen Gregson or Donna Price, BioScientifica Ltd, 16 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-642210; 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, 69001 Lyon, France (Tel: +33-472-985858; Fax: +33-472-985898; Email: info@endocrinology2003.com; Web: www.endocrinology2003.com).

ALDO'03: International Symposium on Aldosterone

London, UK, 27-30 April 2003.
 Contact: Helen Gregson or Donna Price, BioScientifica Ltd, 16 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-642210; Fax: +44-1454-642222; Email: aldo-03@endocrinology.org; Web: www.bioscientifica.com/aldo03).

2nd European Consensus Conference: Menopause - State of the Art Toward Consensus

Athens, Greece, 1-4 May 2003.
 Contact: CFEF/FEMS Executive Organization, 12 rue du Quatre-Septembre, 75002 Paris, France (Tel: +33-1-42865592; Fax: +33-1-42604535; Email: eska@club-internet.fr; Web: www.eska.fr).

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).

International Course on Laboratory Animal Science

Utrecht, The Netherlands, 12-23 May 2003.
 Contact: LFM van Zutphen or Stephen van Meulebrouck, Department of Laboratory Animal Science, Faculty of Veterinary Medicine, PO Box 80.166, 3508 TD Utrecht, The Netherlands (Tel: +31-30-2532033; Fax: +31-30-2537997; Email: pdk@las.vet.uu.nl; Web: las.vet.uu.nl).

1st European Conference of ESF: Functional Genomics and Disease

Prague, Czech Republic, 14-17 May 2003.
 Contact: Tomáš Maxa, Event Production Coordinator, Czech-In, Ostrov Štvanice 38, 170 00 Prague 7, Czech Republic (Tel: +420-2-22317963; Fax: +420-2-22317518; Email: tm@czech-in.cz; Web: www.esffg2003.org).

Frontiers in Reproduction: Molecular and Cellular Concepts and Applications

Woods Hole, MA, USA, 18 May-29 June 2003.
 Contact: Carol Hamel, Admissions Coordinator (Tel: +1-508-2897401; Email: admissions@mbl.edu; Web: courses.mbl.edu).

12th Balkan Congress of Endocrinology and 30th Panhellenic Congress of Endocrinology and Metabolism

Thessaloniki, Greece, 21-25 May 2003.
 Contact: Air Maritime-Erasmus Conferences Ltd, 10 Th. Sofouli Street, 546 46 Thessaloniki, Greece (Tel: +30-31-0426962; Fax: +30-31-0426967; Email: info@airmarit-erasmus.gr; Web: www.airmarit-erasmus.gr).

10th European Federation of Endocrine Societies (EFES) Postgraduate Course in Clinical Endocrinology

Riga, Latvia, 29-31 May 2003.
 Contact: Valdis Pirags, P Stradins University Hospital, Pilsonu Iela 13, LV-1002 Riga, Latvia (Fax: +371-7-069955; Email: pirags@latnet.lv; Web: www.euro-endo.org/latvia.pdf).

2nd World Congress on Fetal Origins of Adult Disease (FOAD 2003)

Brighton, UK, 7-10 June 2003.
 Contact: Hampton Medical Conferences Ltd, 127 High Street, Teddington TW11 8HH, UK (Tel: +44-20-89770011; Fax: +44-20-89770055; Email: foad@hamptonmedical.com; Web: www.FOAD2003.org).

1st European Endoscopic Surgery Week

Glasgow, UK, 16-18 June 2003.
 Contact: BSGE/ESGE, Index Communications Meeting Services, Crown House, 28 Winchester Road, Romsey SO51 8AA, UK (Tel: +44-1794-511331/2; Fax: +44-1794-511455; Email: icms@diap.pipex.com; Web: www.eesw.com) or EAES Office, PO Box 335, 5500 AH Veldhoven, The Netherlands (Tel: +31-40-2525288; Fax: +31-40-2523102; Email: info@eaes-eur.org; Web: www.eaes-eur.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: Tandria Price/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).

8th International Pituitary Congress

New York, USA, 22-25 June 2003.
 Contact: Donna Price, 8th International Pituitary Congress Secretariat, BioScientifica Ltd, 16 The Courtyard, Woodlands, Bradley Stoke, Bristol, BS32 4NQ, UK (Tel: +44-1454-642240; Fax: +44-1454-642222; Email: conferences@endocrinology.org; Web: www.pituitarycongress2003.com).

9th Bath Conference on Osteoporosis

Bath, UK, 23-26 June 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.nos.org.uk).

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: from Membrane to Gene Expression from Structure to Disease

Brussels, Belgium, 4-8 July 2003.
 Contact: V Wouters, ICEO (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: 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: +44-1329-403027; Email: R.E.Hooper@ex.ac.uk).

Fertility 2003: Joint Meeting of the Society for Reproduction and Fertility British Fertility Society and the 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: +44-1454-642219; Fax: +44-1454-642222; Email: fertility2003@endocrinology.org; Web: www.fertility2003.com).

Society for Endocrinology Molecular Endocrinology Workshop

Manchester, UK, 15 July 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).

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 Advanced Endocrine Course

Manchester, UK, 16-17 July 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).

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 Clinical Practice Day

Manchester, UK, 18 July 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).

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).

Oxford Advanced Endocrinology Seminar
Oxford, UK, 15-17 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).

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 (ESPE) 2003

Ljubljana, Slovenia, 18-21 September 2003.
Contact: Ciril Krznisnik, 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.krznisnik@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).

3rd International Symposium on Testosterone: Action Deficiency Substitution

Castle Elmau, Germany, 25-28 September 2003.
Contact: E Nieschlag, Institute of Reproductive Medicine of the University of Münster, Domagkstrasse 11, D-48129 Münster, Germany (Tel: +49-251-8356096; Fax: +49-251-8356093; Email: nieschl@uni-muenster.de or olerink@uni-muenster.de).

11th European Federation of Endocrine Societies (EFES) Postgraduate Course in Clinical Endocrinology

Oxford, UK, 29 September-1 October 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/courses.htm).

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: Helen Gregson, 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).

1st Milan Thyroid Cancer Conference

Milan, Italy, 7-8 November 2003.
Contact: European School of Oncology, Viale Beatrice d'Este 37, Milan, Italy (Tel: +39-02-43359611; Fax: +39-02-43359640; Email: conferences@esoncology.org).

31st Meeting of the British Society for Paediatric Endocrinology and Diabetes 2003

Edinburgh, UK, 20-21 November 2003.
Contact: Helen Gregson, 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.bsped.org.uk).

International Conference on Progress in Bone and Mineral Research 2003

Vienna, Austria, 27-29 November 2003.
Contact: Vienna Academy of Postgraduate Medical Education and Research, Alser Strasse 4, A-1090 Vienna, Austria (Tel: +43-1-40513830; Fax: +43-1-405138323; Email: bone2003@medacad.org).

Joint International Symposium on Calcitonin Gene-Related Peptide, Amylin and Calcitonin, 4th Symposium on Adrenomedullin and Proadrenomedullin N-20 Peptide

Zurich, Switzerland, 18-20 March 2004.
Contact: J A Fischer, Research Laboratory for Calcium Metabolism, University of Zurich, Klinik Balgrist, Forchstrasse 340, CH-8008 Zürich, Switzerland (Tel: +41-1-3861651; Fax: +41-1-3861652; Email: fischerj@balgrist.unizh.ch; Web: www.symposium2004.ch).

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: conferences@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).

20th Annual Meeting of the European Society of Human Reproduction and Embryology

Berlin, Germany, 27-30 June 2004.
Contact: ESHRE Central Office, Van Akenstraat 41, 1850 Grimbergen, Belgium (Email: info@eshre.com; Web: www.eshre.com).

10th International Congress of Auxology: Human Growth in Sickness and in Health

Florence, Italy, 4-7 July 2004.
Contact: Centro Studi Auxologici, Piazza Madonna degli Aldobrandini 1, 50123 Firenze, Italy (Tel: +39-55-290932/212322; Fax: +39-55-290932; Email: congress@auxologia.org; Web: www.auxologia.org).

International Congress of Endocrinology 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; Email: l.h.rees@mms.qmw.ac.uk; Web: www.jingo.com/ise/ice2004.htm).

43rd Annual Meeting of the European Society of Paediatric Endocrinology (ESPE) 2004

Haifa, Israel (alternative venue: Basel, Switzerland), 10-13 September 2004.
Contact: Ze'ev Hochberg, Department of Pediatrics, Rambam Med 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: Gurbuz Erdogan (Email: gurbuz.erdogan@temd.org.tr).

11th World Congress of Gynecological Endocrinology

Florence, Italy, 27-30 September 2004.
Contact: Biomedical Technologies srl, Via Trieste 1, 56126 Pisa, Italy (Tel: +39-050-501934; Fax: +39-050-501239; Email: biomedical@tin.it; Web: www.gynecologicalendocrinology.org).

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).

26th Annual Meeting of the American Society for Bone and Mineral Research (ASBMR)

Seattle, WA, USA, 1-5 October 2004.
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).

6th European Congress of Endocrinology



26-30 April 2003: Lyon, France

Plenary lectures

Biological clocks P Sassone-Corsi (France)

Endocrinology of critical illness G Van de Berghe (Belgium)

Activation mechanisms of glycoprotein hormone receptors T Gudermann (Germany)

Ontogeny of endocrine pancreas O D Madsen (Denmark)

Role of oestrogen receptors: lessons from knock-out mice J A Gustafsson (Sweden)

Regulation of the growth plate by PTHrP H M Kronenberg (USA)

Angiogenesis P Carmeliet (Belgium)

Visit www.endocrinology2003.com, or contact: Congress Agency, Scientific Secretariat, Transit Communications, 18 place Tolozan, 69001 Lyon, France (Tel: +33-4-72985858; Fax: +33-4-72985898; Email: info@endocrinology2003.com).

BES 2003



22ND JOINT MEETING OF THE

British Endocrine Societies

24-26 March 2003

SCOTTISH EXHIBITION AND CONFERENCE CENTRE, GLASGOW, UK

You can't afford to miss this exciting and stimulating programme, as BES 2003 delivers yet another superlative mix of the latest science and clinical practice. Come ready for an action-packed meeting!

High profile plenary lecturers

Keith Parker 'Steroidogenic factor 1: a key mediator of endocrine development'

Ann Klibanski 'The effects of the GH/IGF-I axis on bone density and body composition'

Steve Bloom 'How the brain controls appetite'

Steve Shalet 'Growth hormone outgrows growth'

Nancy Carrasco 'The journey of the sodium/iodide symporter: from its molecular identification to its medical role in thyroid and breast cancer'

Not forgetting an excellent mix of workshops, dedicated Nurse and Young Endocrinologist sessions and the ever-popular 'The Experts' View?'

Wide-ranging symposia

Androgens and prostate cancer

Trophic control of size

Apoptosis/survival signalling

Dominant endocrine cancer syndromes

The adipocyte as an endocrine organ

Prolactin: novel aspects

Radioiodine biology in the 21st century

Hot topics

Glorious Glasgow

Glasgow is Scotland's largest city, and one of the liveliest and most cosmopolitan destinations in Europe. It boasts world famous art collections, superb shopping facilities, and the most vibrant nightlife in Scotland. The Scottish Exhibition and Conference Centre (SECC) will host the BES on their second visit to Glasgow. This is one of Europe's finest integrated conferences and exhibition centres, easily accessible to international and UK visitors. Though located in the heart of the city, the SECC is only 30 minutes from some of the most spectacular Scottish scenery, made famous down the years in verse and song.

Further details from

Tamara Lloyd, BES, 17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK
(Tel: +44 (0)1454-642210; Fax: +44 (0)1454-642222; Email: tamara.lloyd@endocrinology.org;
Web: www.endocrinology.org/sfe/confs.htm)

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