German World Cup special issue

The Society's first 60 years
Past, present and future for 'the pill'

The great hypothyroidism debate
In this diminishing global village, you can fly as quickly from Manchester to Amsterdam as to London, and more quickly than by Virgin train to Bristol. A flight from Liverpool to Oslo costs less than the price of a beer when you arrive, and your emails reach Estonia as quickly as Edinburgh and are infinitely cheaper than traditional ‘snail-mail’.

The creation of a European Society of Endocrinology represents another step towards overcoming national borders. In that spirit, we celebrate Germany’s hosting of the World Cup with a special issue of The Endocrinologist. After all, in 1974, when Germany last hosted this competition, it was still a nation divided by the Wall, and our recollections of the unlaunched Democratic Republic are still epitomised by the sign in the reception of an East German hotel: ‘If this is your first visit to the DDR you are welcome to it’.

On page 16, Thomas Guderman, President of the German Society of Endocrinology, highlights some major German contributions to the field. He emphasises their Society’s goal of increasing public and academic awareness of endocrinology, aims which bear a striking similarity to the conclusions of our own strategic review. Meanwhile, Wolfgang Oelkers from Berlin reviews the 40 years since the first oral contraceptive became available in the USA (page 15), and looks forward to an even safer generation of transdermal preparations.

It is, as most of you will probably be aware, 60 years since the Society for Endocrinology was formed. A lot has happened in that time and, on page 13, Sue Thorn looks at just a few events in this first chapter of the Society’s history. You only have to compare the £200 required to set up Journal of Endocrinology with the £900 000 budget for this year’s European Congress to appreciate the amount of change our Society has seen over the years.

Julia Buckingham is our Society’s General Secretary. On page 4, she describes the very broad remit of her role, which includes overseeing the Society’s publications, and her ambition to promote endocrinology in a context that will help to attract and retain the brightest of our young clinicians and scientists.

The prescription of thyroxine to patients with normal thyroid function, or the unwillingness of some endocrinologists to do so, is a source of vexation to some patient groups. Helen Jaques from the Society’s publishing staff volunteered to review this controversy. You will find her provoking overview of the ongoing debate on page 8.

Finally and happily, the man who still thinks an Apple Mac is a raincoat for a Granny Smith enters into the World Cup spirit with an amusing stereotype-reinforcing tale of Germanic efficiency (page 17). Perhaps our friend Hotspur should provide prizes for this efficiency?

All in all, the evidence seems to suggest that, fortunately for us, standards in German endocrinology and education are in better shape than their national football team. Meanwhile we Scots can only pin our hopes on Jürgen Clansman.

PETER TRAINER

ECE success!

This year’s very successful European Congress of Endocrinology was held at the Scottish Exhibition and Conference Centre, Glasgow, from 1-5 April 2006. The impressive scientific programme attracted interest from all over the world and in total 2337 delegates attended, representing over 70 different countries.

The plenary sessions covered vitamin D action, statins and rhabdomyolysis, and type 1 diabetes. There were also 17 symposia and 13 very popular ‘Meet the Expert’ sessions.

The social programme proved to be a huge success, with intriguing gizmos and gadgets to entertain guests at the welcome reception held in the Glasgow Science Centre, and traditional dancing and excellent food at the congress banquet and Ceilidh. (See photos from ECE on page 20.)

Special thanks are extended to the programme organising committee and to the European Society of Endocrinology for allowing the UK the chance to hold the ECE.
Council of Management - call for nominations

Professors M Hewison, S Shalet and R Thakker will retire from Council in November 2006. Ordinary members are invited to submit nominations to fill these vacancies. To provide the correct balance of expertise and areas of interest on Council, we particularly seek two basic scientists and one clinician, ideally with experience in metabolic medicine (obesity, diabetes, syndrome X, etc.), basic neuroscience, reproduction or pharmaceutical links.

The form enclosed with this mailing should be returned to the General Secretary at the Bristol office by 28 July 2006. A ballot will be conducted amongst the membership if necessary and the results will be announced at the 2006 AGM during the Society’s annual meeting in London on 6-7 November.

Committees - call for nominations

The Society is seeking new members for the following committees. Full committee remits and nomination forms can be found at www.endocrinology.org/sfe/commit.htm. Forms should be returned to the Bristol office by 28 July 2006. Terms of office will start on 1 January 2007 and run for four years.

Clinical - 2 members plus 1 SpR
Three meetings per year. This committee covers all clinical issues. The elected SpR should also attend meetings of the Young Endocrinologists Steering Group and represent the Society on the RCP Specialty Committee.

Nurses - 1 nurse member
Three meetings per year. Committee responsibilities include the Society’s education programme for endocrine nurses and providing a network for nurses to communicate on relevant issues.

Science - 1 member
Three meetings per year. This committee speaks for the scientific endocrine community and helps define the education and training requirements of scientists working in endocrinology.

Young Endocrinologists - 1 basic science member
One meeting per year. The group looks after the interests of younger endocrinologists up to six years post-doctorate, and works with the Clinical and Science Committees to organise sessions for young endocrinologists at the Society’s conferences.

£2500 to spend as you wish!

Two new Young Endocrinologist prize lectures funded by the Clinical Endocrinology Trust will be launched at the Society’s BES Meeting in March 2007 at the ICC in Birmingham. A call for abstracts will be included in the August mailing.

RE-ELECTION OF OFFICERS

The Society’s officers are required to offer themselves for re-election in the second and subsequent years of their terms of office. If any member wishes to propose an alternative name for any of the posts listed below, please contact Julie Cragg (julie.cragg@endocrinology.org) by 28 July 2006:

John Wass - Chairman
Julia Buckingham - General Secretary
David Ray - Programme Secretary
Anne White’s term as Treasurer ends in November, and Michael Sheppard, who was elected in November 2005, will fill this post.

Senior Membership

If you are retired and have been a member of the Society for 15 years or more, you are entitled to become a Senior Member, for which you pay no membership fees. Please contact Christine Davis in the Society office (christine.davis@endocrinology.org) if you would like to apply.

Members on the move...

SK Attili to Ninewells Hospital and Medical School, Dundee;
F Gibb to Victoria Hospital, Kirkaldy;
GL Hammond to Child and Family Research Institute, Vancouver, Canada;
D Morris to The Ipswich Hospital NHS Trust; R Reynolds to University of Edinburgh.
Meet your General Secretary

The General Secretary’s role is not quite as general as it might sound - there is a very clear job description to keep me on the straight and narrow! As one of the Society’s officers, I am a member of Council and of the officers’ sub-committee and also a Director of BioScientifica, all of which address the development and implementation of strategy, with the goal of promoting endocrinology in its broadest sense. One of my biggest concerns is the recruitment and retention of bright young basic and clinical scientists in endocrinology, and the underlying problems in our educational system which hamper our progress. Consequently, one of my main strategic goals is to see the Society doing more to address these issues both through its own activities and through contribution to the national debate.

Aside from the broad remit of these committees, I have a number of specific duties. A key task is to oversee the organisation of the Bristol office and ensure that it is ‘fit for purpose’. As I am sure you can imagine, with Sue Thorn at the helm in Bristol and John Wass as my predecessor, things are pretty shipshape. Furthermore, the staff are a joy to work with. Mindful of the philosophy ‘if it ain’t broke don’t fix it’, my approach is evolution to meet the Society’s changing needs rather than revolution. Currently, I am working with Sue to ensure that the office can support Council’s decision that the Society should invest last year’s substantial surplus in selected new activities and BioScientifica’s planned expansion.

A second major task is chairing the Publications Committee. This brings together the editors of Journal of Endocrinology, Journal of Molecular Endocrinology, Endocrine-Related Cancer, Clinical Endocrinology and The Endocrinologist, along with Steve Byford and other senior members of the publications team in Bristol. While the editors are responsible for the scientific direction of their respective journals, the committee provides an excellent forum for sharing ideas and best practice. Far from being a talking shop, it is here that the strategy for development is formulated and debated, with topics like content, impact factors, online versus print versions, the peer review process, marketing, pricing and sales featuring regularly.

Current concerns include the impact of open access publishing and, more significantly, of local, national or international ‘repositories’ on the financial viability of the journals and, hence, on the long term sustainability of the peer review system. This is a problem for all scientific publishers, be they charities like us or purely commercial organisations, so we are not tackling it alone but in close association with our sister societies and the Biosciences Federation to find a viable solution.

That aside, the future for our journals looks rosy. They are all highly respected internationally, and I am delighted that Journal of Endocrinology, Journal of Molecular Endocrinology and Endocrine-Related Cancer have all been adopted as official journals of the newly formed European Society of Endocrinology. Developing the opportunities that this will bring for British and European endocrinology will be an important part of the committee’s remit in the next few years.

My other duties as General Secretary are varied. They include deputising when necessary for the Chairman, dealing with special membership applications (e.g. for senior membership) and writing letters of congratulations or, sadly, condolence on behalf of the Society, presenting an annual report to the members and attending the Society’s meetings (but I would do that anyway). Feedback from members about any aspect of the Society’s activities is always welcome. If you have any thoughts, do please contact me at j.buckingham@imperial.ac.uk.

JULIA BUCKINGHAM

Society for Endocrinology

Postgraduate Diploma for SCIENTISTS

FREE TO MEMBERS

Why do I need this diploma?
The Society for Endocrinology has developed an accreditation scheme for basic science postgraduate students to provide a broader education in endocrinology. This will complement the in-depth and focused study of a PhD.

What do I have to do?
To receive a diploma you need to collect ten credits over 3 years. Following the change to one Society BES meeting per year, from 1 January 2007 the criteria over the period of study will be:

1 credit for each Society meeting attended (2 required)
1 credit for attendance at a specific session at that meeting (2 required)
1 credit for presentation (either oral or poster as first author or co-author) at a Society for Endocrinology BES meeting (2 required)
1 credit for each annual 3000-word essay making up an assessed portfolio (3 required)
1 further credit can be gained from any of the above

All students must be members of the Society for Endocrinology in good standing for the duration of their study programme.

Contact Julie Cragg at the Bristol office for an application form (Tel: 01454-642200; Email: julie.cragg@endocrinology.org; Web: www.endocrinology.org)
Council of Management
Council has discussed the Society’s forthcoming strategy (see further details on page 6). They have also approved:
- Premier Corporate Membership for Shire Pharmaceuticals Ltd and Ordinary Corporate Membership for Nycomed UK Ltd
- four applications for Senior Membership
- Honorary Membership for the Chief Executive of the Biosciences Federation, Richard Dyer
- a new format AGM, using maximum publicity to raise the Society’s profile and its future plans and to increase communication with the membership
- a method of electing new members quarterly
- the endorsement policy (see www.endocrinology.org/sfe/soc_position.htm for more details)
- online publication of the handbook as a password-protected searchable database, with no print version
- a change to holding all future ballots electronically, without an accompanying paper ballot

Awards
This committee has been identifying medallists for the BES 2007 and 2008 meetings.

Clinical
The committee has been discussing a proposed autumn clinical update meeting that will replace Summer School from 2007. It will probably take place in early November, outside London, and preferably on the outskirts of a major town, with easy airport access to attract international delegates. By starting at mid-morning on the first day and running until late afternoon on the third, the meeting time will be maximised with fewest overnight stays. The target audience will be predominantly SpRs and junior consultants, as the meeting will be mostly curriculum-based. The maximum number of delegates will be 200. The event will comprise the best training features of the Summer School and regional courses, to build an event containing purely clinical topics. During each update meeting, most areas of endocrinology will be covered.

Committee News
Over 2-3 years, it should cover most areas of the SpR curriculum. The programme will include niche areas of diabetes not covered by other organisations, with an emphasis on metabolic syndromes such as obesity.

Finance
Welcome to Michael Sheppard as the Society’s new Treasurer. He will officially take up his post in November, but will continue to shadow Anne White until then.

Nurses
A period of intensive work has led to the programme for this year’s training course in Southampton, which can be found with the registration form in this mailing. ECE 2006 trialled a pilot scheme for nurses to display their posters during a dedicated nurse coffee break.

Nurse sessions are being developed for BES 2007. They are ‘Helping the patient through different types of thyroid cancer’ and ‘Dealing with MEN.’ The committee has also discussed setting up a mentoring scheme to put nurse members who are new to the speciality in touch with more experienced nurse members. Further details will follow.

Programme
Invitations have been sent to speakers for the 197th Meeting of the Society, and the preliminary programme is included with this mailing. The abstract deadline is 31 July 2006. It will be held at Kensington Town Hall, London, on 6-7 November. This year is the Society’s Diamond Jubilee, and we envisage a lively programme with an increase in prizes for abstracts and presentations, together with some limited edition give-aways!

The structure of the committee has changed to reflect the move to one Society premier data meeting per year. It now incorporates members of both the original Programme Committee and the BES Committee. Areas of therapeutic interest are now represented rather than specific organisations.

The committee has finalised much of the programme for the Society for Endocrinology BES 2007 meeting at the ICC in Birmingham on 5-8 March 2007. Invitations have been sent to speakers and chairs. A standard programme template has been produced for use at subsequent meetings, though this is open to modification if required.

Science
Three full members have joined the committee: Karen Chapman, Chris McCabe and Melissa Westwood. Joy Hinson will remain on the committee as the education representative. Rob Fowkes has become Programme Advisor, following Martin Hewison’s move to the USA. Many of the committee’s suggestions have been incorporated into the programme for BES 2007; development of suggestions for BES 2008 will begin shortly.

Young Endocrinologists
This steering group normally corresponds by email, but met formally in early February. Alison Mostyn’s term of office as Chair finishes shortly and we are pleased to announce that Kim Jonas from the Royal Veterinary College in London has agreed to take on this role. We thank Alison for her expertise over the past few years and for her time and commitment in establishing the group and arranging sessions at conferences.
**Strategy update**

- Council has used the discussion document from last autumn’s strategy awayday to draft an implementation plan, which is outlined below. This identifies several focal areas for the Society over the next few years. Each area has a lead Council member to head the various projects, working closely with Society staff.

**Attracting and retaining good young scientists, doctors and nurses in endocrinology**. Proposed actions include providing more grants and prizes, developing a mentoring scheme and young endocrinologist training, and increasing interaction between younger and more established endocrinologists.

**Lobbying and influencing government, universities, NHS and others**. This could be achieved by developing the Society’s links with our sister societies (like the Biochemical Society, the British Pharmacological Society and the Physiological Society), supporting the Biosciences Federation and the RCP, and collaborating with them on issues such as career structures, research funding, public awareness of science, patient care and best practice.

**Enhancing public and patient information**. Suggestions include hosting a public web site providing access to patient sites, educational materials, advice to GPs and a new dedicated press area.

**Education**. This might include the collation of all Society educational material, as well as sourcing additional educational resources.

The discussion document has also led Council to add a further item to the Society’s objectives, which are now as follows:

- to advance education and research in endocrinology for the public benefit
- to be the voice of endocrinology in the UK
- to be a major focus of endocrinology outside the USA
- to support endocrinologists worldwide and to foster a sense of community
- to raise the profile of endocrinology
- to attract good young scientists, doctors and nurses into endocrinology and to retain them.

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**Michael Harbuz**

- The loss of Mick Harbuz has left a great hole at the heart of the University of Bristol and in the world of neuroendocrinology. He was simply one of those people, who, without apparent effort, ensured that everything he touched proceeded smoothly and to the highest standard.

I first met him when he was a final year postgraduate in the Department of Physiology and Biochemistry at the University of Reading. He was working on a British Egg Marketing Board Research and Education Trust Scholarship of £2700 per annum! At that time he was studying chickens; he told me his real interest was in the biochemistry of the brain and its relationship with disease.

Inviting Mick to join us at the Westminster Hospital was one of the best decisions of my life. He was a fantastic postdoctoral fellow: always enthusiastic, a meticulous experimental scientist and determined to maintain friendship and solidarity within the group. He soon developed his own independent research programme in neuroendocrinology. He was especially interested in the mechanisms underlying susceptibility to, and severity of, inflammatory disease. His initial studies helped establish the roles of hypothalamic CRF and vasopressin in mediating the HPA responses to acute and chronic stress.

Together with David Jessop, he developed the model of adjuvant arthritis to investigate the neuroimmuno-endocrinological effects of chronic inflammatory disorders. This led to interesting studies on the role of cytokines in modulating HPA activity and in the protective role of sex steroids. Mick also made major contributions to our understanding of susceptibility to inflammatory disease and, in particular, showed the long-term protective effects of a single immune challenge. He noted the importance of behavioural responses in determining susceptibility to disease. These studies suggested that the individual’s response to a stressful situation could influence the severity of the inflammation. Again with David Jessop, Mick was the first to identify the endomorphins in immune tissues and to demonstrate their potential as anti-inflammatory agents.

Mick also had a particular interest in complementary medicine. He worked with music therapist Professor Lesley Bunt at the Bristol Cancer Help Centre to assess the impact of music therapy on people affected by cancer. He used his neuroendocrinology to identify and link the physiological aspects to the psychological aspects of this therapy, in the hope that it would help us better understand the impact of music therapy in the Bristol approach to cancer care.

Mick had many roles within the University of Bristol. He was Dean of Graduate Studies in the Faculty of Medicine and Dentistry from 2003 to 2005. Since September 2004 he had been Faculty Education Director, responsible for all the faculty’s postgraduate programmes, and as such was a member of the University’s Education Committee. He was instrumental in drawing up the faculty’s education strategy and in ensuring that this was consistent with the overall university strategy. He was held in high esteem by colleagues at faculty and university level for his professionalism and integrity, as well as his great sense of humour and joie de vivre. Mick was indeed one of those people who creates a happy working environment - a good example of positive neuroendocrinology!

He was Secretary and a committee member of the Brain, Immune Network Group from 1994 to 1998, and then Chairman from 1998 to 2004. He was a committee member of the British Neuroendocrine Group, and then Membership Secretary and Treasurer of the British Society of Neuroendocrinology from 1998 to 2004.

His passing at the age of 47 has deprived us of the ideal colleague. He was an excellent scientist, a loyal friend and, above all, a fantastic team player. The neuroendocrinology community and all his colleagues at the University of Bristol will miss him greatly.

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With regret

We are also very sorry to announce the deaths of Professor B Mawer (Manchester), Professor I H Mills (Cambridge) and Dr V Petrow (North Carolina, USA), who were members of the Society.
NICE guideline on GH in adults

NICE (the National Institute for Health and Clinical Excellence) will take evidence in July on whether their current guideline on GH in adults should be updated. If any member wants to express an opinion to the Society’s Clinical Committee, please email julie.cragg@endocrinology.org by 1 June.

Evelyn Ashley Smith Endocrine Nurse Award

The British Thyroid Foundation (BTF) is offering an award of £500 to enable an endocrine nurse to provide improved care to patients with thyroid disorders. This award was made possible by the late Evelyn Ashley Smith, who was a BTF member for many years.

Applications are invited from endocrine nurses within the UK and Ireland. The award will be offered to (a) support training needs including conference attendance, (b) support a specific project lasting one year, (c) reward a piece of work already completed, but not yet published. Applicants must demonstrate that the activity supported by the award is aimed at enhancing care of patients with thyroid disorders.

Application forms are available from www.btf-thyroid.org or from BTF, Endocrine Nurse Award, PO Box 97, Clifford, Wetherby LS23 6XD. The closing date for their receipt is 1 July 2006.

Science in a Soundbite

When scientific controversies hit the headlines, the Science Media Centre encourages scientists to tell their side of the story, and offers them support. This support includes popular ‘Science in a Soundbite’ guides on communicating how science works. These crib sheets are compiled with the help of scientists who have experience of dealing successfully with the media, and national news journalists. Guides so far cover risk, peer review and animal research, and one is due soon on scientific uncertainty. A further leaflet supports academic scientists who find they have to defend research that has been funded by industry, with a perceived conflict of interest. For further information or to download Science in a Soundbite leaflets go to www.scienzemediacentre.org.
Hypothyroidism: the debate rages on

The long-running debate on the prescription of thyroid hormone to patients with symptoms compatible with hypothyroidism, but in whom thyroid function tests (TFTs) are normal, has recently resurfaced. This has prompted discussion among clinicians and vitriolic responses from patient groups.

At the beginning of 2006, the Society received a petition of over 2000 signatures registering ‘a formal complaint against the clinical practice of the majority of the medical profession with regard to the diagnosis and management of hypothyroidism’. The signatories accuse the medical profession, specifically the General Medical Council, of ‘over-reliance on blood tests’, ‘emotional abuse and blatant disregard...over the suffering experienced by untreated/incorrectly treated thyroid patients’ and ‘ongoing reluctance to encourage debate or further research on hypothyroidism’.

Professor Tony Weetman, President of the British Thyroid Association (BTA), responded to these accusations in an editorial in the March issue of Clinical Endocrinology, countering that clinicians have ‘robust assays to diagnose the condition and an effective replacement in the form of synthetic thyroxine’. His so-called ‘derogatory, anti-patient editorial’ has prompted dozens of emails from angry patient groups, as well as various allegations of ‘medical condescension’.

At the heart of the dispute is the use of TFTs to diagnose an undertactive thyroid in a patient, and the prescription of synthetic thyroid hormones, such as thyroxine, for patients with ‘normal’ free thyroid hormone levels. As Professor Michael Sheppard, Chair of the Society’s Clinical Committee, points out, ‘the symptoms of thyroid disorders are diffuse and difficult to link to the thyroid, especially as many people in their 50s and 60s may well experience fatigue, weakness and weight gain’. Consequently, TFTs have proved invaluable in diagnosing hypothyroidism.

Approximately 10 million blood serum TFTs are carried out in the UK each year at an estimated cost of £30 million, and are used to measure circulating thyroid-stimulating hormone (TSH), free thyroxine (FT4) or free triiodothyronine. Hypothyroidism is associated with an increase in serum TSH concentration followed by a decrease in FT4 levels, at which point symptoms typically appear and the patients will benefit from treatment by thyroid hormone replacement. Patients with TSH levels over 10mU/L but FT4 levels within the reference range are considered to be suffering from subclinical hypothyroidism and will likewise receive thyroxine treatment to normalise their hormone levels.

The present debate concerns patients whose TSH levels are within the reference range and who therefore have no biochemical evidence of thyroid dysfunction and are considered normal. The reference range is based on a normal bell-shaped graph, with serum levels of TSH and FT4 outside the 95% reference interval described as pathological.

The BTA recommends no treatment for thyroid disease if TFTs are within the normal laboratory reference range, and their sister patient support group, the British Thyroid Foundation (BTF), confirms that hypothyroidism should be confirmed biochemically. Michael Sheppard agrees unreservedly with these guidelines: ‘the increased sophistication of TFTs means that if all three tests are within the reference range, a clinician can conclude without any doubt that a patient’s symptoms are not due to thyroid disease’.

However, this has not dissuaded some practitioners. In 2000, BBC News highlighted the trend in clinicians prescribing thyroid hormone to people with normal thyroid hormone levels who were just feeling run down, and many private practices continue to profit from providing thyroxine to anxious patients. This does seem to be a particular issue for hypothyroidism, as Professor Sheppard acknowledges, ‘if a patient was suffering from headaches, dizziness and other symptoms of hypertension, they would visit their GP for a blood pressure test and be satisfied with the conclusion provided’.

Prescription of synthetic thyroid hormone to patients with normal hormone levels can prove dangerous, increasing the risk of atrial fibrillation by two- to threefold over a 10-year period in patients over 50 years old, the key risk demographic for hypothyroidism. Excess hormone can also accelerate bone loss, though there is no definitive evidence of an increase in fractures in such cases. Rather than the adverse physical effects of excess thyroid hormone, what most concerns practitioners is that by colluding with the patient and treating them for a disease that they do not have, a clinician could overlook a genuine and more serious diagnosis.

Ultimately, it is doctors who are best positioned to counter this misunderstanding. ‘Doctors need to be honest and tell patients that there isn’t a problem they can identify rather than dismissing them by saying that there isn’t a problem at all’ says Tony Weetman.

Professional bodies also recognise their role in dispelling the uncertainty surrounding TFTs. The BTA, in conjunction with the Association for Clinical Biochemistry and the BTF, is amending its guidelines for TFTs to establish a national benchmark for thyroid function testing. Likewise, the Society’s Clinical Committee has published a statement of principles on TFTs, highlighting the conscientious work of UK researchers and clinicians in their response to thyroid disease, and stating emphatically that the Committee supports the use of blood tests to construct precise diagnoses (see www.endocrinology.org/sfe/thyroid-statement.pdf).

Scientists are unanimous that TFTs are suitable to confirm hypothyroidism. The focus must shift to reassuring anxious patients that other diagnoses are being considered and to highlighting to borderline cases that their family history and antibody tests are being taken into account. Only by listening to patient fears, and not dismissing without discussion an insistence on a diagnosis of hypothyroidism, can clinicians hope to quell the current hysteria. 

HELEN JAQUES
ARDANA BIOSCIENCE LTD

Ardana is a pharmaceutical company focused on improving human reproductive health. The company was listed on the London Stock Exchange in March 2005. It was founded in 2000 to commercialise the pioneering research undertaken by the Medical Research Council’s Human Reproductive Science Unit (HRSU) in Edinburgh, UK.

Since its foundation, Edinburgh-based Ardana has built a broad portfolio of products and actively pursues product and technology in-licensing and out-licensing to maintain a robust pipeline.

Ardana’s products include a testosterone replacement therapy that has already been launched by Ardana as a treatment for men with hypogonadism. Products in clinical development cover a range of conditions including a further compound for male hypogonadism, growth hormone deficiency, prostate cancer, benign prostatic hyperplasia, erectile dysfunction and endometriosis. In addition, Ardana has a strong portfolio of follow-on products in development.

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With approximately 60 000 employees, AstraZeneca’s headquarters are in London while R&D management is based in Sweden. Worldwide, AstraZeneca has six major research and development sites, four discovery facilities and a clinical research site. In total, AstraZeneca’s R&D organisation employs approximately 12 000 people located in seven countries: Canada, France, India, Japan, Sweden, the UK and the USA. AstraZeneca has manufacturing activities in more than 20 countries.

Scientists at AstraZeneca have discovered and developed many of today’s leading prescription medicines. AstraZeneca, a global leader in the development of cancer therapies, is committed to continuing the fight against cancer, through early detection and awareness programmes and through fundamental medical advances. AstraZeneca scientists are focused on developing a broad portfolio of anticancer products to extend and improve the quality of patients’ lives. Over the past 30 years, AstraZeneca has developed effective cancer medicines for patients with breast and prostate cancer. AstraZeneca produces Casodex (bicalutamide), the world’s leading antiandrogen, and Zoladex (goserelin acetate), the second largest-selling LHRH agonist in the world, Nolvadex, the first antiestrogen used in breast cancer and the pure antioestrogen, Faslodex. Recently, we have also introduced a highly effective and well tolerated third generation aromatase inhibitor, Arimidex, that has shown superior efficacy to the previous gold standard hormonal treatment for breast cancer, Tamoxifen. Current R&D focuses on developing treatment options across the prostate and breast cancer continuum, and specifically on novel biologically targeted approaches such as EGFR-TK inhibition, VEGFR-TK inhibition and vascular targeting.

AstraZeneca has a major interest in two other areas where there is a major endocrine component: diabetes and obesity, and stress-related disorders. In these conditions AstraZeneca is looking for novel therapies that are a significant improvement on current treatments.

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Current projects include:

- European Journal of Endocrinology, published in print and online with HighWire Press for the European Society of Endocrinology
- Reproduction, published in print and online with HighWire Press for the Society for Reproduction and Fertility
- A range of books including, Zuckerman: Scientist Extraordinary, Handbook of Acromegaly, also available as a CD-ROM, Molecular Pathology and Therapy of Pituitary Disease, and Pituitary and Periphery: Communication In and Out

Reduced rate subscriptions to journals and discounts on books are available to some groups. BioScientifica is owned by the Society for Endocrinology.

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Ferring Pharmaceuticals Ltd, The Courtyard, Waterside Drive, Langley SL3 6EZ, UK (Tel: 01753-214800; Web: www.ferring.co.uk)

GENZYME THERAPEUTICS

Founded in 1981, Genzyme is now one of the world’s largest and most established biotechnology companies. With more than 25 major products and services marketed in over 60 countries, Genzyme is a global leader in the effort to develop and apply the most advanced capabilities in biotechnology, in order to address a range of unmet medical needs. With corporate headquarters in Cambridge, Massachusetts, USA, Genzyme has approximately 4600 employees working in 40 countries throughout the world.

The European headquarters are in Naarden, The Netherlands, and the UK headquarters covering the whole of the British Isles are now based in Oxford. Genzyme-sponsored R&D has led to the introduction of new treatments for many serious health problems, from rare and debilitating genetic diseases to renal disease, orthopaedic injuries and thyroid cancer.

One of Genzyme’s most significant successes is Thyrogen (thyrotropin alfa), which contains a highly purified recombinant form of human thyroid-stimulating hormone. It can be used to eliminate the devastating and painful symptoms of thyroid hormone withdrawal that patients may experience when they are tested for a recurrence of thyroid cancer. Thyrogen will also lead to more accurate thyroglobulin measurements on thyroid hormone suppression. Genzyme has a commitment to improving the lives of patients and supporting the work of doctors and other healthcare providers.

Genzyme Therapeutics, 17 Hollands Road, Haverhill CB9 8PU, UK (Tel: 01440-716443; Web: www.genzyme.com)

IPSEN LTD

Ipsen Ltd is the UK subsidiary of Ipsen, a European pharmaceutical group with over 20 products on the market and a total worldwide staff of nearly 4000.

Ipsen Ltd’s Endocrinology and Oncology Business Unit is responsible for a portfolio of products with sophisticated sustained release delivery systems. The portfolio includes products which both lower and increase growth hormone, i.e. Somatuline (lanreotide) and NutropinAq (somatropin), and products which both lower and increase testosterone, i.e. Decapeptyl (triptorelin) and Testim Gel (testosterone).

Ipsen’s development strategy is based on a combination of products in targeted therapeutic areas: oncology, endocrinology and neuromuscular disorders, which are growth drivers, and primary care products, which contribute significantly to its research financing. This strategy is also supported by an active policy of partnerships.

Its R&D programme is based on four technological platforms; peptide engineering, protein engineering, medicinal chemistry and advanced drug delivery. The location of its four R&D centres (Paris, Boston, Barcelona, London) gives the Group a competitive edge in gaining access to leading university research teams and highly qualified personnel. Nearly 700 people in R&D are dedicated to the discovery and development of innovative drugs for patient care.

Ipsen Ltd, 190 Bath Road, Slough SL1 3XE, UK (Tel: 01753-627777; Fax: 01753-627778; Web: www.ipsen.co.uk)

NOVARTIS PHARMACEUTICALS UK LTD

Novartis is a Swiss, research-based company which currently operates in over 140 countries worldwide, employing 78 500 people including over 3000 people at 11 sites in the UK. In 2004, the company spent approximately $3.5 billion on R&D. This is equivalent to almost 19% of all pharmaceutical sales being reinvested in R&D.

Novartis Oncology has a strong heritage in cancer care. Indeed, over the past 25 years, pioneering research has repeatedly resulted in new and innovative products. From the development of the first aromatase inhibitors for breast cancer, through advances in bisphosphonate therapy, to the cutting edge of rationally designed molecularly targeted compounds, we continue to build and expand our heritage through focused research programmes across a broad spectrum of cancer care.

Novartis Pharmaceuticals UK Ltd, Frimley Business Park, Frimley, Camberley GU16 7SR, UK (Tel: 01276-692255; Fax: 01276-698605; Web: www.novartis.com)

NOVO NORDISK LTD

Novo Nordisk Ltd is a focused healthcare company with a leading position in areas such as diabetes, growth hormone therapy, haemostasis management and hormone replacement therapy. With the broadest diabetes product portfolio in the industry, including advanced products within the area of insulin delivery systems, Novo Nordisk is the world leader in diabetes care.

Within the area of growth hormone therapy, Novo Nordisk has always been at the forefront of research into the use of human growth hormone (hGH). The company launched its first growth hormone product in 1966. Since then, Novo Nordisk has
made a series of significant breakthroughs in the development of indications and convenient delivery systems for HGH. In 1999, Novo Nordisk launched the first ready-to-use liquid growth hormone, Norditropin® SimpleXx®. This is supplied in a pen system that was developed utilising existing diabetes experience, to ensure that people who use growth hormone can simply, comfortably and accurately administer their dose. Novo Nordisk also provides patients with the support of a homecare service and the convenience of home delivery.

Novo Nordisk manufactures and markets pharmaceutical products and services that make a significant difference to patients, the medical profession and society. With headquarters in Denmark, Novo Nordisk employs approximately 18,700 people in 68 countries and markets its products in 179 countries. Novo Nordisk Ltd, Broadfield Park, Brighton Road, Crawley RH11 9RT, UK (Tel: 01293-762000; Web: www.novonordisk.com)

NYCOMED UK

Nycomed is a pharmaceutical company dedicated to meeting medical needs in Europe. The company provides specialist hospital products throughout the UK and Ireland. Its core disease areas are currently in the cardiovascular, osteoporosis, pain management and surgical arenas.

New products are sourced through licensing agreements with research companies. Here, Nycomed provides late-stage clinical development, registration and marketing. Nycomed employs about 3300 people throughout Europe and Russia-CIS.

Nycomed UK, The Magdalene Centre, Oxford Science Centre, Oxford OX4 4GA, UK (Tel: 01865-784500; Fax: 01865-784501; Web: www.nycomed.co.uk)

ORGANON

Organon Laboratories Ltd, Cambridge Science Park, Cambridge CB4 0FL, UK (Tel: 01223-432700; Web: www.organon.co.uk)

PFIZER LTD

Pfizer, with its UK business headquarters in Surrey and global headquarters in New York, is a research-based global pharmaceutical company. Pfizer discovers, develops, manufactures and markets leading prescription medicines for humans and animals, and many of the world’s best-known consumer products.

Since 1998 Pfizer has made a capital investment of more than £1 billion in the UK and, following its acquisition of Pharmacia in April 2003, is the largest supplier of medicines to the NHS. It is estimated that on any given day, 40 million people around the world are treated with a Pfizer medicine. Pfizer is excited to add the Pharmacia endocrine care portfolio of Genotropin (somatropin recombinant) and Somavert (pegvisomant powder and solvent for solution for injection) to the organisation. Pfizer is highly committed to these important products and to continued investment in this key therapeutic category. Pfizer wishes to continue to help enhance patient care today while refining therapy for future generations. Pfizer will be using its resources and capabilities to help provide the greatest value to patients.

Pfizer Ltd, Walton Oaks, Dorking Road, Tadworth KT20 7NS, UK (Tel: 01304-616161; Web: www.pfizer.co.uk)

PROSTRAKAN

ProStrakan, Buckholm Mill, Galashiels TD1 2HB, UK (Tel: 01896-668060; Web: www.strakan.com/unitedkingdom.html)

SANDOZ INTERNATIONAL GMBH

Sandoz, a division of the Novartis group, is a world leader in high-quality generics and biopharmaceutical medicinal products. Sandoz develops and markets a wide variety of active ingredients and finished products, having a portfolio of more than 600 active substances in over 5000 forms. Novartis is the only major pharmaceutical company to have leadership positions in both patented prescription drugs and generic pharmaceuticals. In 2005, Hexal AG, Germany and EonLabs Inc., US became part of Sandoz and the business employed about 20 000 people worldwide. It sold its products in more than 110 countries and posted sales of US$4.7 billion.

Sandoz’s recombinant human growth hormone Omnitrope received a positive opinion by the European Medicines Agency’s Committee on Medicinal Products for Human Use (CHMP) in January 2006. In Australia, Omnitrope was launched in November 2005.

Biosimilar medicines made by Sandoz:

• fully adhere to the new and rigorous European standards for biosimilar medicinal products
• guarantee a high-quality production process as Sandoz ranks among the world’s largest and most experienced manufacturers of biotechnological products
• ensure patient care and safety through appropriate pre-clinical development, clinical trials and post-marketing surveillance including a state of the art pharmacovigilance system
• help reduce the burden on health care systems by providing the public with safe and effective medicines at competitive prices.

Sandoz International GmbH, Industriestrasse 25, 83607 Holzkirchen, Germany (Tel: +49-8024-4762591; Fax: +49-8024-4762599; Web: www.sandoz.com)

SCHERING HEALTH CARE LTD

Schering is the UK subsidiary of Schering AG, a research-based pharmaceutical company based in Berlin. We focus on four strategic business areas: gynaecology and andrology, oncology, diagnostic imaging and specialised therapeutics.

Our andrology portfolio consists of Nebido* (testosterone undecanoate) and Testogel* (testosterone) licensed for the treatment of hypogonadism in men. As a successful pharmaceutical company, we are investing in the future of medicine, developing drugs of high medical value so as to continuously improve the quality of life.

Making the most of knowledge, we use interdisciplinary networks to build bridges to academic researchers around the world, as well as to highly specialised biotech pioneers and partners in the pharmaceutical industry. We combine our own long-standing medical and pharmaceutical expertise with the latest discoveries from genomic research. Throughout, our research focuses on a meaningful combination of early diagnosis, prevention, treatment and therapy control.

Schering Health Care Ltd, The Brow, Burgess Hill RH15 9NE, UK (Tel: 01444-232323; Fax: 01444-246613; Web: www.schering.co.uk)
Shire’s strategic goal is to become the leading specialty pharmaceutical company that focuses on meeting the needs of the specialist physician. Shire focuses its business on the central nervous system, gastrointestinal tract, general products and human genetic therapies - all being areas in which Shire has a commercial presence. The structure is sufficiently flexible to allow Shire to target new therapeutic areas to the extent opportunities arise through acquisitions. Shire believes that a carefully selected portfolio of products with strategically aligned and relatively small-scale sales forces will deliver strong results. The company’s strategy is to develop and market products for specialty physicians. Shire’s in-licensing and merger and acquisition efforts are focused on products in niche markets with strong intellectual property protection either in the USA or Europe.

Shire Pharmaceuticals Ltd, Hampshire International Business Park, Chineham, Basingstoke RG24 8EPF (Tel: 01256-894000; Web: www.shire.com)
The first 60 years

The Society for Endocrinology’s first 60 years have been eventful, to say the least. The Society and its publications, always inextricably linked, have seen many challenges, from the advent of World War II less than two months after publication of the first issue of Journal of Endocrinology, to the current pressures on scientists, clinicians and nurses caused by uncertain career structures, proliferating administrative and bureaucratic burdens, and the scepticism of some parts of the public towards scientists and doctors.

I have not attempted a comprehensive history of the Society in this article. That would certainly take more than a few pages of The Endocrinologist! I have instead looked anecdotally at one or two aspects of the Society and how it has changed over the years. There are two very good sources that I have particularly drawn on for this. One is Lord Zuckerman’s article on the founding of Journal of Endocrinology and the Society for Endocrinology (Journal of Endocrinology (1984) 100 1-6; see www.endocrinology.org/sfe/JOEv100p1_6.pdf). Bernard Donovan adds some interesting insights in his recent book on the life of Solly Zuckerman (Zuckerman: Scientist Extraordinary (2005) BioScientifica, Bristol; see also review on page 19).

The Society’s origins

The Society was actually preceded by Journal of Endocrinology by seven years. Zuckerman places the initial discussion on a bus to Croydon Airport in 1937, when he, Sir Charles Dodds FRS, Sir Alan Parkes FRS and Sir Frank Young FRS were on their way to Paris for a symposium on the physiology of reproduction. A committee was set up that went on to become the Council of Management of the Journal of Endocrinology Ltd, a non-profit company set up to run the journal. There were ten initial members of the ‘Council of Management’, and it is notable that nine of them were fellows of the Royal Society. Each of these ten provided ‘Council of Management’ and it is notable that nine of them were fellows of the Royal Society. Each of these ten provided a guarantee of £40 towards the running of the journal.

The initial committee set three rules that proved particularly far-sighted: that the scientists involved would be responsible for the finances; that it should be owned by a society, not a group of individuals; and that there should be sufficient financial backing to ensure it was viable. It is fortunate that these ground rules were in place, because there were several approaches from major publishers who offered good financial deals in return for ownership of the journal. The BMA was particularly forceful, and some of the committee were in favour of this, as it removed their financial liability. If such a deal had been struck, it is unlikely that the Society for Endocrinology would have been started, as the journal was an integral factor, both financially and in terms of providing the membership base.

By the time the first issue was published on 1 July 1939, there were already 250 subscribers - most publishers would salivate at such a prospect these days. However, by the time the second issue was published, the war had already begun. Several volumes appeared during the war, albeit sporadically, the first five volumes taking nine years altogether.

Despite his research work and his substantial war work, the indefatigable Zuckerman had submitted a proposal in 1944 that symposia should be held, and by January 1946 contributors to Journal of Endocrinology were invited to discuss setting up the Society for Endocrinology. The Society was quickly formed and the first AGM, in July 1946, elected Sir Alan Parkes as Chairman. It took some time to knit the two organisations (the Society for Endocrinology and the Journal of Endocrinology Ltd) together, but by 1948 it was agreed that all members would be members of both organisations.

It is amusing to note that one of the (unnamed) objectors to the establishment of Journal of Endocrinology gave as his reason that there were only about six researchers in the UK with any interest in endocrinology. I imagine Zuckerman could be an overpowering person at times, but he did have the courage of his convictions and pushed the journal and the Society into existence because he believed strongly in the need for them. And here we are now with a total of almost 1900 members.

The structure of the Society

Once the Society for Endocrinology was set up, there were in fact two parallel organisations, the Society for Endocrinology and the Journal of Endocrinology Ltd (the Journal). There was no legal link between these two, but being elected a member of the Society automatically gave membership of the Journal of Endocrinology Ltd, and the governing bodies (the Society’s Committee and the Journal’s Council of Management) had common membership.

This became problematic for several reasons. First, although the Journal was a limited company - and became a charity from 1961 - the Society was an unincorporated association with no protection for its committee. This mattered less in the early years when its activities were fairly limited, financial risks were much lower, and the world was less litigious. However, as time went on, the committee members were left more exposed and, as the Society had no money and charged no registration fee for the November meeting, the Journal had to subsidise it each year by means of a subvention. You have only to consider that the recently hosted European Congress of Endocrinology in Glasgow had a budget of £900 000 to realise that this would have been a heart-stopping level of risk for the elected ‘twelve good (wo)men and true’ if the structure had not been changed.

Nonetheless, at the time of the merger of the two organisations in 1998, one of the main reasons was to remove the identity confusion caused by the two companies and compounded by the advent of the British Endocrine Societies (BES). The BES was a federation formed in 1982 to host a combined annual meeting, and had its own governing committee and programme organising committee. In addition, the Journal had all the money that people thought of as belonging to the
The first 60 years continued from page 13

Society, and all the grants that people thought of as ‘Society for Endocrinology’ grants were actually from the Journal. Even the staff and Council members were frequently confused as to who was responsible for any particular activity, so the members - and the public and other societies - had no chance.

The prospect of merging the two organisations, which involved using the Literary and Scientific Institutions Act of 1854 and getting permission from the Charity Commission, was quite daunting, but in the event proceeded smoothly and took only about a year.

The recent decision to hold only one annual data conference and to have a single programme committee has hopefully completed a process of simplification that means all our activities take place under one name and governed by one council.

Publishing activities
Publications have always been an integral part of the Society’s activities. A few anecdotes will show how things have changed, though! The ten initial committee members committed £40 each to the new Journal of Endocrinology. In the event, they were only called upon to contribute £20 each, and they got this sum back in 1948. The last time I carried out a costing exercise for a new journal (many years ago) the total investment was estimated at around £750,000.

In his 1984 article in Journal of Endocrinology, Zuckerman gave one of the reasons for starting a new journal in 1939 as ‘frustration ... with the delays in the publication of papers’. Sound familiar? He tells us that, in the immediate post-war years, it took about two years to get a paper published. When I joined the Society in 1991, it was still taking about 33 weeks from submission to publication, and this was in line with most other journals. It has taken substantial investment to get that time down, but we have now halved the time to around 35 days from submission to first decision, and around 11 weeks from acceptance to publication. Changes in 2006, including the imminent introduction of ScholarOne’s ManuscriptCentral peer review system and the recent move of editing and typesetting services to India, are expected to make a further noticeable reduction in peer review and publication times.

The Society for Endocrinology is unusual for a small society in that we publish for ourselves, rather than contracting one of the large commercial publishers to do this for us. This has been quite a challenge, as journal publishing became more complex during the 1990s. The main reasons for our continuing success are that we were lucky enough to recruit senior publications staff who are both experienced and strategically clear-sighted, and also that the advent of BioScientifica means we now have five journals to share investment costs, salaries and overheads.

I was interested to note that, in 1956, the Society for the Study of Fertility (SSF; now the Society for Reproduction and Fertility) had proposed that Journal of Endocrinology be changed to Journal of Endocrinology and Reproduction and become the official journal of both societies. However, opinions were too divided and the SSF started its own journal, originally called Journal of Reproduction and now renamed Reproduction. But life has come full circle as it has a tendency to do, and Reproduction is now published by BioScientifica in a symbiotic collaboration that allows the journals to retain their separate identities while developing in parallel and sharing experience.

The journals published by the Society and BioScientifica are still absolutely core to the Society’s academic and financial well-being. They are facing challenges as never before. Whether these are opportunities or threats remains to be seen. There are difficulties with staying ahead of the game as a small publisher in such a fast-moving and technological era, but we have the advantage of being close to our authors, editors and readers, and being able to take the decisions we think are right for us, especially as regards using the online journals to increase our profile. The proof of the pudding is in the eating, and at present our journals’ impact factors stand at their highest ever. All four official journals have values over three, with increases of 25-250% in the last four years.

Money talks
When the Journal and Society were set up, the £200 used to start the journal was no doubt a considerable investment by the individuals concerned, but it was possible for a group of scientists to fund such a venture. Nowadays, running the Society and BioScientifica is a big business. The combined income for the year May 2005 to April 2006 is estimated to have been not far short of £4 million. This is managed and administered at the Society’s three-storey office in Bristol, which houses almost 40 staff.

In addition to running its journals, conferences and courses, the money is used to award grants. This was a minor item of expenditure in the early 1990s, running at about £15,000-30,000 per year. It has increased in recent years to a maximum of almost £200,000 in one year. There was a degree of temporary cutback in 2003-2005, in order to ensure that the fall in the value of the Society’s shares did not prejudice our long-term survival, but we have now got over that blip and Council are making plans to increase grant spending again.

The next 60 years
The Society’s and BioScientifica’s performance in the year 2004-2005 means that we have around £500,000 to...
A short history of oral contraception

In 1960, the first combined hormonal oral contraceptive, containing 150µg mestranol (a methylether of ethinyl-oestradiol (EE)) and 9.8mg norethynodrel (Enovid®) was approved by the US FDA. Pincus and his associates had developed ‘the pill’, but they, like other famous endocrine therapists, were standing on the shoulders of inventive chemists and biochemists.

It was Inhoffen and Hohlweg in 1938 who synthesised the extremely potent EE that largely escaped the hepatic metabolism of 17β-oestradiol, and Djerassi in 1954 who developed ethinylated derivatives of 19-nortestosterone (among them norethynodrel) as highly potent orally active progestogens. In 1921, Haberlandt and colleagues in Innsbruck had shown that transplantation of ovaries of pregnant rabbits into fertile female rabbits suppressed their ovulation and fertility. The effective hormone was progesterone, which was demonstrated in 1944.

Oestrogens alone also suppress ovulation at high dosage, but in the pill it is mainly the progestogen that inhibits ovulation, while the oestrogen serves to imitate regular menstrual bleedings. This is the basic premise of hormonal contraception, except for low-dose contraception using progestogens alone (the mini-pill). This seems to act mainly by changing the properties of uterine cervical mucus such that its penetration by spermatozoa is inhibited.

The effectiveness of the combined oral contraceptives in women who took the pill regularly was unrivalled by any other method. It changed sexual and social life and the demographic development of the modern world, though not always in a desirable direction.

When I spent a sabbatical year (1970-1971) at the MRC Blood Pressure Unit in Glasgow, the effect of oral contraceptives on blood pressure was an important topic of research. Several alarming cases of malignant hypertension in women taking the pill, some of them leading to irreversible renal failure or death, had focused interest on its non-reproductive side-effects. It was found that EE greatly stimulated the synthesis or inhibited the metabolism of a host of hepatic proteins, among them the renin substrate angiotensinogen, several clotting factors, sex hormone-binding globulin, corticosteroid-binding globulin and thyroxine-binding globulin.

Activation of the renin-angiotensin system is the main cause of oral contraceptive-induced hypertension in susceptible women. An activation of the blood clotting cascade which is not completely compensated for by increased fibrinolysis seems to be the main mechanism for the three- to fourfold increase in the risk of thromboembolism in users.

The further evolution of oral contraceptives was mainly driven by the hope of minimising side-effects, while the extremely high contraceptive efficiency of the first oral contraceptive on the market could not be improved. Only one year after Enovid®, the first European oral contraceptive (Anovlar®) containing only 50µg EE and 4mg norethisterone acetate was available. Epidemiological studies seemed to indicate that lowering the dosage of EE (and possibly of the synthetic progestogens) would lead to better tolerability (e.g. reduced breast tenderness or weight gain) and to fewer non-reproductive complications. Today’s conventional oral contraceptives contain between 20 and 35µg EE and microgram amounts of second or third generation derivatives of ethinylated 19-nortestosterone.

Other interesting developments have been the introduction of 17-hydroxyprogesterone derivatives with anti-androgenic properties for women with acne or hirsutism (e.g. cyproterone acetate), and of the progestagenic and anti-mineralocorticoid spironolactone derivative drospirenone for women with a tendency to fluid retention and an increase in blood pressure. Both are used in combination with low-dose EE.

However, these oral contraceptives still have a prothrombotic effect, although their EE content is low. The thromboembolic risk associated with the recently introduced transdermal combined contraceptive Evra® does not seem to be any better than modern oral contraceptives, since it also uses EE. This, unlike natural oestradiol, seems to affect hepatic protein synthesis independent of its route of application.

In postmenopausal hormone replacement therapy, the transdermal route of oestradiol application seems to be devoid of a prothrombotic risk. Development of a transdermal combined hormonal contraceptive with oestradiol instead of EE would provide a great next chapter in this endocrine story.

WOLFGANG OELKERS

The first 60 years continued from page 14

spend on promoting endocrinology over the next few years. We expect that the results for 2005-2006, which will be finalised in August, will add to this. The uncertainty surrounding publishing income means that we mustn’t go mad, and in particular we mustn’t make plans to spend money we haven’t earned yet (in case we don’t), but we can certainly identify some additional services over the next few years.

The Society held a strategic review late last year, and the spring Council meeting approved outline plans resulting from this. So look out for a number of new grants and other funding opportunities aimed at supporting scientists, clinicians and nurses in endocrinology. We are also looking at using some of the money, often in collaboration with other organisations, to help address some of the wider questions:

► can we encourage more good young scientists and doctors to opt for a career in endocrinology?
► can career structures for scientists be improved?
► can we encourage more schoolchildren to opt for a bioscience degree?
► can the negativity of parts of the public towards animal experimentation be countered?
► how can we increase awareness of endocrinology among the general public?

SUE THORN

WOLFGANG OELKERS

FEAT URES

An insight from Wolfgang Oelkers into the past, present and future of the pill that revolutionised society.
A TIME TO MAKE FRIENDS:
THE 'GOAL' OF GERMAN ENDOCRINOLOGY

Even if you hadn’t known before, this issue of The Endocrinologist will have ensured that you are aware of the forthcoming 2006 FIFA World Cup in Germany. Co-operation between endocrinologists in Europe and internationally is increasingly important, and so the World Cup’s slogan ‘A time to make friends’ applies just as well to German endocrinology.

Endocrinology in Germany has a long history. In the mid-1800s, Arnold Adolph Berthold showed that the effects of castration in birds could be reversed by ectopically transplanting the testis into the body cavity, leading to the conclusion that the testes released a substance that controlled secondary sexual characteristics. In 1840, Carl von Basedow from Merseburg described the symptoms of hyperthyroidism, and in 1893 the physiologists Joseph von Mering and Oskar Minkowski first described the development of diabetes following a pancreatectomy.

The 20th century saw Bernhard Zondek from Berlin describe the presence of ovarian hormones and gonadotrophins in 1927, and together with Selmar Aschheim he developed the first biological pregnancy test. From 1929, the chemist Adolf Friederich Butenandt followed their observations and succeeded in clarifying the chemistry of ovarian and testicular hormones, receiving the Nobel Prize for Chemistry in 1939.

From these early roots, endocrine research and patient care have developed and reached the very highest standards in Germany. A substantial number of endocrine centres in Germany have researchers at the forefront of clinical and basic science. This is especially true in areas like neuroendocrinology, regulation of appetite, energy metabolism and body weight, molecular genetics of endocrine disorders, diabetes and thyroid hormone metabolism.

Even in the earliest days, endocrine research in Germany involved collaboration between physicians and basic scientists like physiologists and chemists. This approach will continue to be vital for the future of endocrinology, which will depend on joint ventures and co-operation between researchers from different countries working in the fields of medicine, molecular and cellular biology, biochemistry, pharmacology, physiology, education, industry and public health. They will form an integrated force that will increase the understanding of the hormonal network at the genetic, molecular, cellular and regulatory level. Undoubtedly, endocrinology has a central role in addressing medical problems in ageing societies. There are also challenges for endocrinology. The most significant are to improve public awareness in order to get adequate recognition of the discipline in universities, general hospitals, outpatient services and health policy, and to attract young scientists and clinicians to plan their careers in endocrinology.

The German Society of Endocrinology, which was established officially in 1964 and now has more than 1500 members, is one of the largest professional endocrine societies in Europe. Its main objectives are the promotion of research, both basic and clinical, and ensuring that scientific knowledge is transferred to the clinical environment.

One of the Society’s top priorities is to realise this by fostering ties with other European societies through Europe-wide research projects, and by establishing communication channels for exchanges between colleagues across Europe. Consequently, this year’s annual congress was held with the Dutch Endocrine Society, and the next year’s meeting will be organised with the Austrian Society of Endocrinology. In 2008, Germany will host the 10th European Congress of Endocrinology in Berlin (www.ece2008.com).

Making friends will help create the networks we need to further improve the prevention, diagnosis and treatment of endocrine disorders, leading to an improved quality of life for all.

THOMAS GUDERMAN

Endocrine-Related Cancer

You can now make your papers free to all, immediately upon publication, in Endocrine-Related Cancer online.

Benefits to authors include:
• Immediate free availability of your published article to all
• No extra costs for colour illustrations online
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If you prefer not to pay this fee, only subscribers will have access to your article for the first 12 months. Review articles will continue to be freely available upon publication without any charge.

Endocrine-Related Cancer (impact factor 4.597) is a not-for-profit journal of the Society for Endocrinology. Find it online at http://erc.endocrinology-journals.org, and the Society’s other journals at www.endocrinology-journals.org.

Full details of this free access option are at http://erc.endocrinology-journals.org/preview_misc/Free_Access_Announcement.dtl.
British endocrinology: what's in a name?

The fact that English is the chosen spoken language at most international endocrine meetings in Europe carries with it certain advantages and disadvantages for the UK endocrinologist. As a generalisation, and with notable exceptions, it means that UK speakers have greater confidence in their presentation skills, fluidity of argument, potential use of humour and capacity to deal with questions, when compared with most (but certainly not all) non-UK presenters.

On the other hand, the UK endocrinologist is rarely fluent in any language other than their own, which compares unfavourably with other European endocrinologists. They can average appear to be able to converse in two or three languages, making them appear more civilised, cultured and worldly.

As I progressed through my own medical career and attended more European meetings, I fought hard to overcome my English stereotype. This was not to the extent of learning a foreign language in any detail, but rather in my 'embrace' of certain European habits - in particular, the personal greeting.

By upbringing I was taught that the handshake was sufficient, but this is grossly inadequate in Europe, where all the women are greeted with kisses. The problem is how many kisses? For instance, in France it is two, but in Belgium and Holland three kisses are expected. This national variation has been the source of much personal physical discomfort for an uncomplicated male English endocrinologist like me. If unaware of the personal greetings requirement of an individual country, or the country of origin of a particular female endocrinologist, one stops at two kisses. But then if she turns out to be a triple kisser, great pain is inflicted when, stationary at the time that the female rotates her head to offer her cheek for the third time, one’s nose receives a severe and unexpected blow: a risk directly proportional to the size of one’s hooter.

And the breakdown of barriers across Europe has brought a new danger - men. I was always aware that I might run into a male kisser from France or southern Europe. However, the influx of endocrinologists from former eastern European countries has now brought a new risk, the bear hug-induced rib fracture.

I do not wish to convey the impression that European meetings are anything but pleasurable. After all, the security body search at the airport is as close as many UK endocrinologists ever get to a sexual encounter. Indeed, it is said that some members of the Society for Endocrinology deliberately leave their phone in their pocket to trigger the security alert and guarantee a search.

Many of my thoughts have been stimulated by the forthcoming football World Cup finals, and the need to distinguish between patriotism and nationalism. England is one of the favourites and the finals are being held in Germany. The history of conflict between these two countries doesn’t just encompass two world wars but more importantly football rivalry! Individuals deal with those issues in different ways.

Lytton Strachey (of the Bloomsbury set) was a conscientious objector during the first world war. He was taken to court to defend his stance and was asked by the lawyer, ‘What would you do if you found a German soldier molesting your sister?’ to which he replied, ‘I would attempt to interpose my body between the two of them.’

The language was much tougher, however, when I attended the annual meeting of the German Endocrine Society in Essen recently. A very eminent German endocrinologist gave an excellent lecture on the usefulness of the German pegvisomant database. Yet what struck me forcefully was the military nature of the language he used. For instance, rather than ‘we are gathering clinical and biochemical data in treated acromegals’ he reported that ‘these are studies carried out under field conditions’ - and his data were not merely collected but ‘captured’.

His speech set alarm bells ringing, forcing me to confront events in my own department. My ex-boss, ex-senior consultant colleague, who retired nine years ago, had casually mentioned that, in his spare time away from the golf course, he was learning German. His consultant replacement, a man whom I had a major hand in selecting, is Scottish (as was evident when I saw him play goalkeeper in a unit five-a-side match). But the precision of his haircut should have given away the fact that he is (as I have since discovered) half-German. I retired from the NHS at the end of 2005, noting with further mild amusement that my final research fellow is German: talented, delightful but definitely German. Finally, there was the appointment of my successor. I knew of UK interest, but yet again there was a solitary German candidate. I was away at the time of the interviews and, on my return, was curious to know the outcome. The result was crystal clear as soon as I opened the door to my office - I saw it immediately - a large bath towel draped expansively across my chair!

I remain calm, not sick as a parrot or over the moon about what is happening here. Indeed I plan a few days’ holiday in Berlin next week. I will also use the opportunity to take a look at a few potential venues for future meetings of the British Endocrine Societies.

‘HOTSPUR’
Mammary involution in IGFBP-5 transgenic mice

- IGFBP-5 mediates involution of the mammary gland. Mammary involution comprises two major phases. The initial phase sees dramatic increases in rates of apoptosis, while in the second phase activation of extracellular proteases occurs, including the plasmin and matrix metalloproteinases (MMPs). Prolactin is capable of inhibiting both of these phases in rats.

In this study, Flint and colleagues examined whether mammary involution could be inhibited by prolactin in mice as it is in rats. They aimed to determine whether prolactin could inhibit cell death and prevent increased expression of plasmin and MMPs in mouse mammary gland, and to examine whether the effects of prolactin are influenced by expression of IGFBP-5 as a transgene.

They found that prolactin inhibited involution in wild-type but not transgenic mice expressing IGFBP-5. This suggests that IGFBP-5 antagonises prolactin signalling in mammary epithelium. Prolactin inhibited gene expression of MMP-3 and MMP-12 but not tissue plasminogen activator or plasmin in wild-type and transgenic animals. The authors provide evidence that prolactin’s effect on MMP expression is likely to be indirect. The study demonstrates that prolactin is a potent inhibitor both of cell death, an effect which is suppressed by IGFBP-5, and of MMP expression, which is independent of IGFBP-5. JM (See the full article in Journal of Molecular Endocrinology 36(3), June 2006)

CaR and familial hypocalciuric hypercalcaemia

- The calcium-sensing receptor (CaR), expressed in the parathyroid and kidney, is central to maintaining calcium homeostasis by regulating parathyroid hormone (PTH) release and renal calcium reabsorption. Mutations in this receptor can therefore disrupt calcium homeostasis. The predominantly asymptomatic disorder familial hypocalciuric hypercalcaemia (FHH) results specifically from heterozygous inactivating mutations in the CaR which cause an elevation in the set point for calcium-activated PTH suppression, leading to hypercalcaemia.

In three FHH families, Ward and colleagues have identified three novel mutations in the CaR, one of which has a strong dominant-negative effect over wild-type receptors. Individuals who are heterozygous for this CaR mutant receptor show relatively severe hypercalcaemia and increased PTH levels. When compared with another inactivating mutation which has a stronger dominant-negative effect over wild-type receptors (and was discovered previously by these authors), a positive correlation between strength of dominant-negative effect and severity of hypercalcaemia/PTH levels becomes apparent.

Here, the authors clearly demonstrate a relationship between the strength of the dominant-negative effect of a naturally occurring CaR mutation and biochemical severity of FHH, thus supporting existing evidence that the type of mutation is a significant factor in dictating the severity of FHH. VN (See the full article in Clinical Endocrinology 64(5), May 2006)

Prolactin in joint protection

- Prolactin has a broad range of physiological functions, including promoting cell survival, and can be found in the synovial fluid of joints. Zernierio and co-workers have studied the expression and action of prolactin receptor subtypes in articular cartilage, to discover whether the hormone acts as a regulator of chondrocyte survival.

Prolactin receptor expression was analysed in the femoral epiphyseal cartilage of male postpubescent and adult rats, establishing the expression of long form receptor mRNA in chondrocytes and its translation into significant quantities of protein. Prolactin itself inhibited serum deprivation-induced chondrocyte apoptosis in a dose-dependent manner.

This study confirms that prolactin is one of several hormones that promote chondrocyte survival and help maintain synovial joint surfaces. This potentially occurs by upregulation of the Bcl-2 proteins that otherwise decrease in serum deprivation-induced apoptosis. Isolated chondrocytes are able to generate prolactin, while other survival factors have to diffuse from the joint synovial fluid, suggesting that prolactin is a specific autocrine mediator of cartilage renewal. This action could be exploited therapeutically to prevent the degradation of articular cartilage responsible for rheumatological conditions such as arthritis. HJ (See the full article in Journal of Endocrinology 189(2), May 2006)

IGF and breast cancer risk

- A great deal of basic science has demonstrated the importance of IGFs in breast cancer growth. Many studies have shown a clear role for IGFs as potent mitogens for breast cancer cells in vitro, acting with the IGF-I receptor to promote proliferation, inhibit apoptosis and promote malignant transformation.

However, evidence from epidemiological studies has been much more mixed. The true role of IGFs in breast cancer risk remains ambiguous. Two studies have investigated this role further, and both feature much larger sample populations than previous reports. Schernhammer and colleagues report that no association was found between three markers - GH, IGFBP-1 and IGFBP-3 - and breast cancer risk, and furthermore no association between IGF-I levels and premenopausal breast cancer risk. Meanwhile, Rinaldi and colleagues report a significant increase in breast cancer risk in women whose serum IGF-I and IGFBP-3 levels are in the upper fraction of the normal range. While no significant association was found in younger women, the reported correlation was most pronounced in women whose tumours were diagnosed after 50 years of age. AL (See the full articles in Endocrine-Related Cancer 13(2), June 2006)
Zuckerman: Scientist Extraordinary

B Donovan, BioScientifica Ltd, 2005, 506pp, £24.95 (Society members £18.50), ISBN 1 901978 24 9

’Solly Zuckerman was a rare creature, for few scientists have managed to play such a central part in national affairs ... to some [he] is a legendary but shadowy figure who shunned the limelight, while enjoying the manipulative process ... did he use or abuse his power?’

So reads the description in the preface of this lengthy volume devoted to the life, achievements, contributions and (in parts) less than successful endeavours of the late Lord Zuckerman in diverse social, academic and political arenas.

His adopted style was Baron Zuckerman of Burnham Thorpe in the County of Norfolk, and the Zuckerman archive held in the University of East Anglia was obviously a rich source for the material gathered in Donovan’s tome. There are 21 chapters that have intriguing titles including Scientific controversies, Invasion of Europe, New broom at the zoo, Zuckerman and the civil service, The biological effects of explosions and British bombing policy, Adviser at war, Defence and Zuckerman as a scientific adviser.

Clearly there are sections for almost all those with interests in politics, academia, central government or many other facets of our society. Bernard Donovan is to be congratulated on collating and synthesising such a wealth of information from many diverse sources.

As this review is for The Endocrinologist, comments on Zuckerman’s inputs into endocrine matters are most pertinent. Bernard Donovan describes with great clarity the lengthy and often acrimonious exchanges between Solly Zuckerman and Geoffrey Harris on the controversial topic of hypothalamo-hypophysial relationships. Of course, Donovan’s own significant contribution to this area, while working alongside Harris, provided him with a ringside seat to witness the debate! This makes most interesting reading, but it is a shame that the author does not come down more decisively as to whose accounts were ultimately proven to be endocrinologically correct.

The final chapter of the book includes a telling quotation (from an American Sunday magazine): ‘I have a bet with my wife that Solly Zuckerman is the most famous scientist in Europe. I claim he’s a bookie. Who is right? ... Zuckerman would have been dismayed by the question ... let alone the correct answer.’ Frustratingly the answer is not immediately apparent, although Donovan notes in a paragraph entitled ‘Eminence grise’, on page 495, that Zuckerman was a ‘fixer’ (quoting Marcia Williams). Is this an answer or are there more sinister conclusions, one wonders?

In reading this well researched semi-biographical account of, overtly, a most influential, truly enigmatic scientist/politician of the 20th century, one may remain uncertain whether the answers to the questions posed in the preface have been truly answered. Perhaps they cannot be, but Bernard Donovan has provided much of the information (and key literature sources) to allow an informed judgement from whatever politico-scientific stance one begins.

IAN W HENDERSON