

THE **Endocrinologist**

TSH - TIPS FROM TADPOLES



PLUS...

DNA Microarrays
Demystified

Journals in Cyberspace

Loads of Funding
Opportunities

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Deadline for news items for
the Spring 2001 issue: **5 January 2001.**
Please send contributions to the above address.

Welcome to the Autumn issue of *The Endocrinologist*. We hope that you have all had a restful summer and aren't too horrified by the thought of being back to work. What's that I hear, it's like you've never been away! Well, we have much to stimulate your flaccid neurons in this issue.

This year's publication of the human genome sequence and the realisation that it comprises upwards of 100 000 genes begs the question of what do all these genes do? The discipline of functional genomics aims to answer this and one strategy employed is gene expression profiling using DNA microarray technology. On page 8 Claire Johnson describes the theory, practice and potential of this exciting new technique, demonstrating how it will impact on our understanding of physiology and disease.

As scientists and practising endocrinologists it is very easy to overlook the patient experience. On page 9 Patsy Perrin provides us with a very moving insight into how she lives with acromegaly. Read on to John Lazarus' page 11 revelations of the alternative life of thyroid hormones

and you will be amazed at what they get up to once away from the thyroid.

Following our lively debate at BES 2000 on publishing in the next millennium, on page 10 Steve Byford describes how the Society's publications are moving forward into the electronic age. We really are at the forefront of this publishing initiative, an essential strategy as the future clearly lies in cyberspace. If you haven't yet realised, this newsletter (with searchable links) is now available in full on the Society's Web site. Go check it out and let us know what you think.

We would also like to flag up the large number of funding opportunities that the Society provides for members, particularly young endocrinologists, many of which are advertised in this issue. Travel grants, research grants, studentships and fellowships are all currently available through the Society so don't miss the chance to help fund your work.

Together with all the usual news, views, reviews, announcements and events, this issue promises to re-engage you in the wonderful world of endocrinology. Happy reading.

ANN LOGAN
DIANA WOOD

Prize Studentship 2001

The Society for Endocrinology is pleased to announce its sixth studentship, which will support a student studying for a higher degree in the field of endocrinology. The stipend will be £11 500 pa (rising by £1000 pa to £13 500 in Year 3) plus university fees and a bench fee of £8000 pa.

Candidates must have graduated recently, or expect to graduate in 2001, with a good honours degree in a biological science. Applications must be made by the student on the appropriate application form. They should include a synopsis of the project and be supported by their prospective supervisor, who must be a member of the Society for Endocrinology.

Further details and application forms are available from Ann Lloyd in the Bristol office (ann.lloyd@endocrinology.org) or from the web (www.endocrinology.org/sfe/prstud.pdf). The closing date is **12 January 2001**. Interviews will be held in late February.

Non-Clinical Research Fellowship

The Society's next Non-Clinical Research Fellowship will be awarded in February 2001. The award is intended to assist investigators who expect to make their career in endocrinology and who have already demonstrated their research ability. It will enable the successful candidate to advance their research career. The grant is awarded for a maximum of 3 years.

The deadline for applications is **29 December 2000**, and forms are available from Ann Lloyd in the Bristol office (ann.lloyd@endocrinology.org) or from the web (www.endocrinology.org/sfe/nonclin.pdf). Interviews will be held in January/February 2001.

Congratulations!

The Society is pleased to congratulate Ann Logan, Editor of *The Endocrinologist*, who has been awarded a Chair in Molecular Neuroscience by the University of Birmingham; Malcolm Parker, Programme Secretary, who has been awarded a Chair in Molecular Endocrinology by Imperial College School of Medicine and will be Director of their new Institute of Reproductive and Developmental Biology; and Christopher Edwards, who has been appointed Vice-Chancellor of Newcastle University from 1 January 2001.

Basic Science Review Lecture

Congratulations to Dr Andrew Bicknell from the University of Reading, who submitted the winning abstract for the Young Endocrinologists Basic Science Review Lecture, as judged by the Awards Committee. Dr Bicknell will present his lecture during the Young Endocrinologists session on Monday 20 November during the Society's annual meeting at the Royal College of Physicians in London.

191ST MEETING OF THE SOCIETY FOR ENDOCRINOLOGY

Royal College of Physicians, London
20-21 November 2000

Plenary lectures, symposia (including an Endocrine-Related Cancer symposium), Nurses session, Young Endocrinologists session, debate, oral communications and posters

Conference grants are available to UK Young Endocrinologists
(see page 4 or www.endocrinology.org/sfe/yenou.pdf)

Further information available from the Bristol office (Email: info@endocrinology.org)

Free Journal Access for Junior Members

From 1 January 2001, Junior Membership will replace the Society's Student Membership category.

Junior Members will be entitled to free online access to the full text of the Society's journals: *Journal of Endocrinology*, *Journal of Molecular Endocrinology* and *Endocrine-Related Cancer*.

To qualify, members should be under 30 or earning less than a specified figure, currently £20 000. Date of birth details will be required on the annual renewal invoice and application form in order to qualify as a Junior Member.

Members on the move...

S F Ahmed to Royal Hospital for Sick Children, Glasgow; **C S Arun** to Royal Liverpool Hospital; **K D Bhoola** to Technikon-Natal, Durban; **A M Clarkson** to Texas Tech University Health Sciences Center, Lubbock; **D Cuthbertson** to Ninewells University Hospital, Dundee; **D Dove** to Wexham Park Hospital, Slough; **A H Heald** to University of Manchester Medical School; **M D Julian** to Instituto Cajal, Madrid; **A Robertson** to Conway Institute of Biomolecular and Biomedical Sciences, University College, Dublin; **M F Saftou** to CHBS, Endocrinology Department, Lorient, France; **K Smith** to University of Dundee.

SOCIETY CALENDAR

20-21 November 2000
**191st Meeting of the
Society for Endocrinology**
London, UK

12 February 2001
Clinical Cases Meeting
London, UK

26-29 March 2001
20th Joint Meeting of the BES
Belfast, UK

Young Endos get Out and About!

Grants are available from the Clinical Endocrinology Trust for Young Endocrinologists to visit clinical departments outside their Calman rotation, in order to see endocrinology practised in a different setting. Up to £500 is available for visits within the UK, with £1000 for visits elsewhere in Europe.

Applications should be made in writing to the Treasurer at the Society's Bristol office by **1 February 2001** and should include:

- a brief outline of why you propose to visit a particular department
- details of your destination and the date and length of your intended visit (1-2 weeks)
- details of cost of travel and accommodation and an outline of your timetable.

The letter will also need to be signed by the head of your department and the head of the department you propose to visit.

Applicants should be members of the Society for Endocrinology who are under 35 and have signed up with the Young Endocrinologists' discussion list. To join this list, please send a message to the list owner at young-endocrinologists-request@mailbase.ac.uk

Endocrine Nurses

Nurse members will soon receive a mailing of our courses up to 2003! The programme will cycle through themes covering the pituitary, thyroid/parathyroid, reproduction, growth and development, and endocrine oncology, and venues will alternate between the north and south of the country. Please let us know what you would like covered under each of the themes - and your suggestions for speakers. Don't forget to volunteer yourself or a colleague! Our fourth training course, *Reproduction - from birth to the menopause* held on 4-6 September attracted 57 delegates.

Our next committee meeting is on 11 December 2000. Please tell us of any issues you would like explored.

MAGGIE CARSON

Another year older (but not deeper in debt)

The end of June saw the end of another financial year. We briefly contemplated writing an article on the Society's financial position, but you wouldn't read it, would you? So here are the highlights in note form.

Where does the Society get its money?

- Income from our three journals
- Income from our agreement with Blackwell Science regarding *Clinical Endocrinology*
- BioScientifica's profits
- Commercial exhibitors and sponsors at conferences etc
- Registration fees for training courses and other activities
- Income and capital gains from our investment portfolio
- A grant from the Clinical Endocrinology Trust towards our PR activities

And how do we spend it?

- Grants: three fellowships, three studentships, conference grants, grants for Young Endos to attend the November meeting or visit other labs, grants to other meetings...
- Producing and distributing our three journals
- *The Endocrinologist*
- The November meeting (which is free for members)
- Training courses, clinical days and other events
- Running the Society, its offices and its committees
- Activities such as public relations

Our usual aim is to spend all the income from the Society and its reserve fund. In 1999/2000, we budgeted to have a deficit, but achieved a surplus. This year we are budgeting a bigger deficit, due to additional activities (you could view this as spending last year's surplus). Again, we hope to out-perform the budget; if we make a surplus, the extra goes to fund more grants.

JULIA BUCKINGHAM AND SUE THORN

November Meeting Grants

Grants of up to £150 are available to Student and Young Endocrinologist Members to attend the Society meeting in London on 20-21 November 2000. This is in addition to the normal annual overseas conference grants. Extended deadline for receipt of applications: **6 November 2000**.

For details and forms contact Chris Davies or Julie Cragg in the Bristol office, or see the Society's Web site.



THE 5th INTERNATIONAL CONGRESS OF
NEUROENDOCRINOLOGY

BRISTOL • UK

31 August -
4 September 2002





Contact Helen Gregson at BioScientifica for details
Tel: 01454-619347 Email: ICN2002@endocrinology.org
Web: www.bioscientifica.com/icn2002.htm

Awards for Support Groups

Patient support groups do invaluable work in helping patients live with their conditions. Many groups rely on volunteers or a small number of staff, and the resulting high workload means that there is rarely time to expand the organization's activities.

In recognition of this, the Society and the Clinical Endocrinology Trust (CET) have just distributed over £11 000 to endocrine patient support groups. Small groups working with endocrine-related disorders were invited to apply for up to £2000 to fund specific projects that would directly benefit patients.

We received 22 applications, which were judged by a panel representing the Society, the CET, and patient groups. The standard was very good, with well thought-out projects and realistic goals. Allowances were made for the size of the support groups and their stage of development. The successful projects are listed below.

The excellent response means that further awards will probably be available next year. Meanwhile, for information about patient support groups in endocrinology, contact Victoria Withy or Tom Parkhill in the Bristol office.

AWARD-WINNING GROUPS

Addison's Disease Self-Help Group £1000 to print patient guidelines

Amarant Trust (*providing information on the menopause and related conditions*) £2000 for patient leaflet

Anorchidism SG £759 for various small projects, including newsletter printing and mailing, installation of second phone line, etc.

Association for Cushing's Treatment and Help £350 to print patient booklet

Congenital Adrenal Hyperplasia SG £500 to print patient leaflet

The Gender Trust (*helping gender dysphoric, transsexual, or transgenderist patients*) £1600 to maintain office services

Medical Advisory Service (*general helpline*) £1500 to provide nursing staff with background training in endocrinology

The Pituitary Foundation £1995 to reprint leaflet on diabetes insipidus

Verity (*polycystic ovaries self-help group*) £1374 to print patient information booklet

School's Out!

July saw the Society's first Summer School. Four excellent courses made up our premier training event, the latter part of the week having the added benefit of CME registration.

The Young Endocrinologists Day started the week, with a basic introduction to some difficult topics. This time it was 'Intracellular signalling' and 'Secretory pathways and measuring secretion'. Small workshops in the afternoon allowed interactive discussion in an informal way.

'Novel and innovative techniques in molecular biology' was the theme of Tuesday's Molecular Endocrinology Workshop sessions. The excellent programme provided useful information for both laboratory and clinical endocrinologists.

Record numbers of delegates attended the Advanced Endocrine Course over the next 2 days. The programme was a mixture of clinical and basic science sessions, covering important topics in the training of clinicians in endocrinology and diabetes. The speakers included many leading names in endocrinology.

The School's finale was the Clinical Practice Day, with the themes 'Salt and water balance' and 'Female reproductive endocrinology'. These were very well received, and attended by consultants and many SpRs who had stayed on from earlier in the week.

We received very positive feedback regarding the scientific content and the venue for all the courses, with delegates considering the whole event a great success. Thanks are due to Rob Fowkes, Claire Stewart, Andy Levy, John Bevan and everyone else who helped organize the week.

It is planned to alternate venues between the north and south of the country, and York is a strong contender for next year. See you there!

JULIE CRAGG

THE BRITISH ENDOCRINE SOCIETIES AWARDS

supported by Pharmacia

The British Endocrine Societies, together with Pharmacia, are delighted to announce the seventh in a series of awards for clinical and basic science research proposals in the field of endocrine growth factors.

The successful proposal will receive the major award of £10 000. In addition, the panel will award five travel grants of £500 to the runners up.

The awards will be announced at the 20th Joint Meeting of the British Endocrine Societies, in Belfast on 26-29 March 2001.



Pharmacia

Application forms are available from
Helen Gregson, British Endocrine Societies
17/18 The Courtyard, Woodlands,
Bradley Stoke, Bristol BS32 4NQ, UK
Tel: 01454-619347; Fax: 01454-616071;
Email: helen.gregson@endocrinology.org
Web: www.endocrinology.org/sfe.conf.htm
Deadline for applications is 8 January 2001

2000
SUMMER
SCHOOL



Ernst Knobil

Ernst Knobil was born in Berlin in 1926. His family subsequently moved to Paris, and then to North America where he graduated from Cornell in 1948, and joined Samuel Leonard's laboratory there. His first paper, 'Beta-glucuronidase activity in rat uterus', was published in *Endocrinology* in 1950 and he received his PhD in 1951.

Ernst's postdoctoral studies, with Roy O. Greep in Boston, were on adrenal cortical function in the rhesus monkey, and the relationship between mother and fetus in rats and monkeys. He was appointed instructor at the Department of Physiology of Harvard Medical School in 1953 and Assistant Professor in 1957. His work on the species specificity of GH was renowned. Harvard selected him as a Markle Scholar in Academic Medicine (1956-1961).

In 1961 he was appointed the first Richard Beatty Mellon Professor of Physiology and Chairman of the new Department of Physiology at the University of Pittsburgh School of Medicine, a position he held for 20 years. He founded the Center for Research in Primate Reproduction and built the Pittsburgh Primate Center. Ernst made a significant contribution towards understanding the regulation of the reproductive cycle in the macaque. He stressed the fundamental role of the ovary in the regulation of the menstrual cycle and correctly assigned what he called a 'permissive role' to the hypothalamus. He discovered that gonadotrophin secretion is pulsatile in nature, opening a new field in chronobiological research and identifying new therapeutic options for human diseases. Ernst was President of The Endocrine Society (1976) and of the American Physiological Society (1979).

In 1981 he became Dean of the University of Texas Medical School at Houston and the H Wayne Hightower Professor in the Medical Sciences. He was also appointed Director of the Laboratory of Neuroendocrinology at the same institution, and continued his research on the role of the hypothalamus in the regulation of reproduction in the macaque. After his tenure as Dean ended in 1984, he continued to work at the University of Texas, earning the title of Ashbel Smith Professor of the University of Texas-Houston Health Science Center, and remaining Director of the Laboratory of Neuroendocrinology until he closed it in 1997.

Ernst died of pancreatic cancer on 13 April this year. He was greatly admired by his students and colleagues, and is survived by his wife, Julane Hotchkiss, four children and three grandchildren.

LUCIANO MARTINI. INSTITUTE OF ENDOCRINOLOGY, MILAN

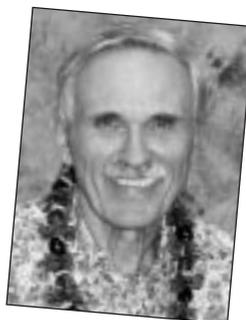
Frederick C Greenwood

Frederick Greenwood joined the Department of Biochemistry and Biophysics of the University of Hawaii in 1968, from the Imperial Cancer Research Centre in London.

He became the Director of the Pacific Biomedical Research Center in 1973, and during his 27-year tenure attracted an estimated \$80 million for research and training. Among Dr Greenwood's many contributions to endocrinology were the energy and visibility he brought to the study of relaxin, qualities which were a driving force in advancing the field. He was a great mentor, scientist, and friend.

He died on 8 August after a lengthy battle with liver cancer. He is survived by his wife, Dr Gillian Bryant-Greenwood, and four children. A memorial fund has been established in his memory. Donations may be made to the University of Hawaii Foundation and sent c/o Pacific Biomedical Research Center, University of Hawaii at Manoa, 1993 East-West Road, Honolulu, HI 96822, USA.

CAROL BAGNELL



Konrad Norymberski

Konrad Norymberski was born in Poland and educated at the University of Zurich. He worked initially for Syntex SA in Mexico as they began large scale synthesis of steroids from natural plant sources. In the late 1940s, he joined the Rheumatism Research Unit at Sheffield's Nether Edge Hospital.

At that time, reliable analytical methods for corticosteroids were lacking, and Dr Norymberski set out to remedy this deficiency. An early description of the technique that he developed (along with C J W Brooks) was published in *The Lancet* in 1953. With others, he developed his methods over the next decade, the refined techniques becoming the basis of urinary corticosteroid assays for many years thus providing an essential tool for investigation and management of adrenal cortex disease.

By 1957 the MRC established a Research Unit for the Chemical Pathology of Steroids at the Jessop Hospital, Sheffield, under his direction. In 1963, Dr Norymberski moved to the University of Geneva where, amongst other projects, he investigated steroid microreactions in the vapour phase. He subsequently returned to Sheffield to continue his work on chemical reactions useful in steroid assays at the Department of Zoology, attracting distinguished collaborators from the UK and overseas.

He was a member of the Editorial Board of *Journal of Endocrinology* from 1964 to 1977.

Dr Norymberski retired in 1979, moving to London where he lived quietly, keeping in touch with colleagues and reading. He died on 24 February aged 81. We offer our sympathy to his wife Elizabeth and acknowledge with respect the contributions of an innovative and inventive steroid chemist.

R E OAKEY

William Taylor

We are sorry to announce the death of Dr William Taylor of Tynemouth on 1 July. An obituary will follow in a later issue.

Eli Lilly HypoCCS Award

This award is made annually to recognize achievements in the study of hypothalamic-pituitary diseases and their impact on peripheral receptive tissues or organs. It comprises a certificate and \$20 000, and will be presented at the HypoCCS Symposium in Bruges, Belgium in March 2001. The recipient will be invited to give a lecture and submit a manuscript for publication in the proceedings.

For further information regarding nominations, contact Pierre C Sizonenko, Division of Paediatric Endocrinology and Diabetology, Department of Pediatrics, HUG, 1211 Geneva 14, Switzerland (Fax: +41-22-3824588; Email: Pierre-Claude.Sizonenko@hcuge.ch). Deadline for receipt of nominations: **15 November 2000.**

European Science Exchange Programme

The Royal Society's International Programme provides grants for scientific research visits to and from the UK, for periods from a week up to 2 years. Note that grants are not available for those undertaking clinical medical research. For further information, see www.royalsoc.ac.uk

Grants for BES 2001

Grants are available from the Clinical Endocrinology Trust to attend BES 2001. Contact Chris Davies on 01454-619036 or email info@endocrinology.org for further details. Deadline for applications: **8 January 2001.**

Webspinning

Highlighting the best on the Web

Clinical Trials

www.clinicaltrials.gov/ct/gui/c/r

Clinical trials are probably now followed more closely than ever before. This may explain the apparent explosion of sites offering information on the topic. Hosted by the NIH and the National Library of Medicine, this site has a clean and simple interface, focusing on a searchable database. A search for 'growth factors' generated 61 hits, 'thyroid' 22 hits, while 'HRT' and 'endocrine tumour' gave 6 and 2 hits respectively. Each hit is linked to additional information about the study in question and, in most cases, background information about the disease. All very simple, clean and useful.

SERVICES: L, D, O (miscellaneous information); STRONG POINTS: Search engine, interesting information; WEAK POINTS: Nothing significant; RATING: Excellent.

Gene Chips (DNA Microarrays)

www.gene-chips.com/

A site to answer the question, 'What is a DNA microarray?'. This interesting site is not affiliated to Affymetrix or other gene technologies. Instead, it is the product of computational chemist Leming Shi, who has compiled a nice collection of links, most of which are relevant. A useful section links to companies involved in gene chip science. Rough spots include links to sites that no longer exist or require a subscription. Although it's not quite ready for prime time, Gene Chips is off to a good start.

SERVICES: L; STRONG POINTS: Links; WEAK POINTS: Broken links; RATING: Good.

Molecular Sequence Analysis: A Guide

www.sequenceanalysis.com/

The molecular biology community has been needing a guide like this for ages. This site aims to transform beginners into professional users of online molecular biology Web sites. One of the strengths of the site is its extraordinarily simple design; no one will be intimidated by the interface. Users will find tutorials and links to all the important molecular biology sites, accompanied by well-written descriptions of everything from common algorithms to 'how to search databases'. I applaud the excellent service it provides.

SERVICES: L, O (online tutorial); STRONG POINTS: Fits a perfect niche, well-compiled; 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: a.logan@bham.ac.uk.

Spicy solution?

Patients with type II diabetes may benefit from the inclusion of cinnamon in their diet. Richard Anderson and colleagues at the US Agricultural Research Service's nutrition labs have shown that a spice restores the ability of patients' fat cells to respond to insulin. Clinical trials of a cinnamon extract are to begin shortly. (Originally reported in *New Scientist*, 12 August 2000.)



DNA Microarrays: High throughput biology

June's announcement of the first working draft of the human genome represented a triumph for the global high throughput DNA sequencing effort. However, whether human biology turns out to be governed by 35 000 or 150 000 genes, we only understand the function of a tiny fraction of the expressed genome. To capitalize on the results of the human genome project, high throughput methods are required to add context to gene sequence and accelerate our understanding of function.

The most powerful technique currently available is gene expression profiling, using DNA microarray or 'chip' technology. This can measure the expression levels of thousands of genes in parallel, from relatively small amounts of RNA, identifying when and where genes are switched on and off in physiological and pathological processes. Recent publications have illustrated the power of this technology in gene identification, functional assignment and molecular pathology. Accessing, applying and analysing microarray experiments present both challenges and opportunities.

Microarray technology is often considered the preserve of pharmaceutical companies and a few generously funded academic institutes. Fortunately, this is changing with the cost of equipment and off-the-shelf microarrays falling, institutes and research councils setting up in-house microarray facilities and collaborations between industry and academia. The *Nature Genetics* supplement 'The Chipping Forecast' (1999 **21** Suppl 1-60) contains several excellent reviews on array technology and how to set up microarray facilities.

Briefly, the two major types of microarray are the spotted cDNA array and the *in-situ* synthesized oligonucleotide array. Spotted cDNA arrays can be fabricated in any lab with access to a robotic array spotter and cDNA libraries. Pre-made cDNA microarrays and services are also available (e.g. Incyte GEM™ microarrays). Most commonly, RNA from two samples, labelled with different fluorescent dyes, is hybridized competitively with a single array. The ratio of the amount of dye detected at each cDNA spot represents the differential expression of the gene in the original samples. cDNA arrays can be produced to fit the exact needs of a lab. The collection of cDNAs on the array can be modified easily, and any organism for which cDNA clones exist can be arrayed. However, it is time-consuming to choose and sequence-verify thousands of clones.

In-situ synthesized oligonucleotide microarrays can be supplied off the shelf and quality controlled (GeneChip® from Affymetrix and FlexJet™ DNA Microarrays from Rosetta Inpharmatica). Short oligonucleotide sequences are used to represent genes and multiple oligonucleotides are present for any one gene. In the case of Affymetrix GeneChips®, one sample is labelled and hybridized to one array. Once the data have been captured, differential gene expression can be calculated by comparing two chips electronically 'on the fly', without the need to go back into the lab and physically perform the comparison.

A major application of DNA microarrays is in candidate gene identification. For example, tissue samples from non-affected and diseased patients are compared, and the roles of genes that are differentially expressed can be studied. Drawbacks of this approach are the accessibility of good quality human material, genetic variability between samples, the presence of multiple cell types and secondary effects due to the influence of a persistent disease state. Cell culture models have the advantage of being more controllable, and can be directed to observe a specific biological process. *In vivo* processes can be studied in animal models in a more controlled manner than in human tissue. In practice, a

combination of all these approaches plus information from other sources will yield the most meaningful data.

Recently, the effects of thyroid hormones on the rat liver were investigated by Feng *et al.* using DNA microarrays (*Molecular Endocrinology* 2000 **14** 947-955). This identified a number of differentially expressed genes involved in a wide range of functions, thus providing a wealth of new information and plenty of scope for future research. Such studies often highlight genes with no known function. This is an area where the large volume of data collected can be used to good effect.

Iyer *et al.* (*Science* 1999 **283** 83-87) exposed fibroblasts to serum for 24 hours and determined the expression of over 8000 genes at 12 time points. Genes with similar expression profiles were grouped together or 'clustered'. On inspection, it was apparent that in many cases genes with similar functions appeared in the same cluster. It was speculated that unknown genes in a cluster might also be involved in the function. Similarly, genes with assigned functions may be found to have additional functions. It would seem logical for genes involved in the same process to be co-regulated. After all, genes do not work in isolation but in concert, and are subject to numerous controls, interactions and cross-talk. To understand physiological and disease-related processes we must look at the global picture of gene expression.

An exciting development on this theme is molecular classification. Acute myeloid leukaemia (AML) and acute lymphoblastic leukaemia (ALL) require different therapies for successful treatment, but can be distinguished only by a combination of highly specialized tests. In a landmark paper (*Science* 1999 **286** 531-537), Golub *et al.* described how a molecular 'signature' could be generated for each class of leukaemia using gene expression profiles. This has far-reaching implications for the diagnosis, prognosis, treatment and management of cancer and possibly other diseases. Microarray technology may well become an integral part of the diagnostic laboratory.

The ability to display and interrogate data, and extract

'...far-reaching
implications for
the diagnosis and
management of
disease'

meaningful analyses, is often the rate-limiting step. It is no easy task to set up bioinformatics tools in-house, and even data storage can produce many headaches! Many established statistical methods have been applied effectively to the analysis of microarray data (reviewed by Sherlock, *Current Opinion in Immunology* 2000 12 201-205) and a few companies now offer comprehensive software packages (e.g. GeneSpring™ from Silicon Genetics).

In the midst of the excitement surrounding microarrays, it must be remembered that only one aspect of the gene expression machinery is being recorded: transcription. A change in transcription does not necessarily lead to an equivalent change in protein. Furthermore, post-translational modifications such as phosphorylation and glycosylation cannot be determined. So why is so much effort being directed at microarrays? The simple answer is that whilst progress is being made in proteomics, current techniques do not have the high throughput, ease of use and instant gene identification that microarrays enjoy. Each technique will have its own advantages and disadvantages, and ideally they can be used to complement each other.

Regardless of the pros and cons of performing gene expression microarray experiments, there is no doubt that the technology is making a significant impact on our understanding of physiology and disease, and will continue to do so for some time.

CLAIRE JOHNSON, PFIZER LTD
(See also 'Web spinning' article on page 7 for relevant Web site review)

Living with Acromegaly...

An insight into endocrine disease, as viewed through the eyes of a patient.

Before acromegaly I was known for my boundless energy. Skiing, walking, dancing and playing music all figured highly in my life, and I enjoyed a good job as a project manager. Three years on, the chronic loss of energy means that most of this has gone, and I am still unable to work.



anything they have decreased; I can't do things I did last year.

How has this affected me? I look well and am usually able to disguise being completely 'knackered'. I can pull out the stops and be full

of life and energy for a few hours. The aftermath is a feeling of being run over by a bulldozer - which lasts for days. On a good day I'm optimistic about regaining health, on a bad day it's a corner I prefer not to look round. There are some things I can't face thinking about, especially the shape of my future.

So how do I manage my life? Well, I lost my job and am unlikely to be able to regain that level of income when I do regain fitness. With my job went a good salary, stimulation and companionship. Now I rarely ask people what they do, as it's a question I find hard to answer myself. I'm unable to continue active hobbies and am frustrated with lack of finances and physical energy. One of the worst hurdles is coping with the annual interview with the DSS for Invalidity Benefit, knowing that I look OK, have no visible impairments and probably know more about endocrine conditions than they do.

What replaces my previous dreams? The dream of walking in the Picos d'Europa is on hold and walking in the Lakes is off the agenda - some days the Thames Path seems like Helvellyn. But I fight it and go for a walk on most fine days, with my dogs who pull me along when I start flagging.

I'm a positive person, so I make the most of this (temporary?) situation. I have more time for friends, family and other hobbies such as music, and I certainly take life more slowly. I try to learn as much as possible about my condition and have great faith in my medical support. I'm an active Trustee with the Pituitary Foundation whose literature and support helped me so much in the initial days, and who appreciate my skills.

I still need my dream - it will emerge from the mists soon.

PATSY PERRIN

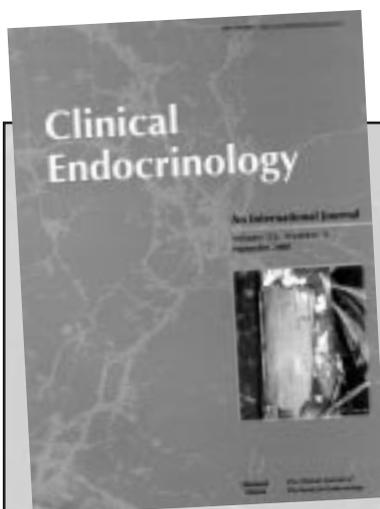
Diagnosis was swift, and came as a relief as it explained why I was feeling so terrible. I expected an operation followed by radiotherapy and to be back at work after a couple of months. (The other acromegaly patient within my GP's practice was able to return to work soon after his trans-sphenoidal hypophysectomy, without the need for radiotherapy.)

'...some days the Thames

Path seems like Helvellyn'

A large tumour was removed, and I immediately started to feel and look better. Radiotherapy caused minimal problems. I started Sandostatin LAR a couple of months later and felt an immediate improvement as GH levels fell again. However, after 3-4 months I remained easily exhausted. I was advised that this wasn't unusual, and so prepared for a wait - which turned out to be a long one!

It seems that I'm 'complicated'. Further diagnosis identified enlarged parathyroid glands; MEN1 is also suspected. The high dosage of Sandostatin LAR has brought GH levels down, but restoration of energy and stamina remains elusive. If



Clinical Endocrinology

The official clinical journal of the Society for Endocrinology

From 2001, Society members will be able to access *Clinical Endocrinology* online, as well as receiving the paper edition, for £56.57+VAT. Members who wish to receive the paper edition only can still do so for £46. See your membership renewal form for full details.

Watch this Cyberspace!

It's all sorted then! The Society's journals are on the Web, so we're poised ready for the brave new electronic future. It's time for a rest, leaving our happy readers to click away feverishly with their mice.

Well, no, I don't think so. Our e-journals have certainly not finished developing. It's true that all our home-grown journals are available as full text, together with free advance abstracts, tables of contents, review articles and commentaries. You can view them via links from our home page - www.endocrinology.org. That's fine if you know about the Society, or are a regular reader of its journals. But there are readers out there who would never think of visiting our Web site, even though the articles may be exactly what they're looking for. That's why we started adding links from the bibliographic entries in PubMed/Medline (www.ncbi.nlm.nih.gov/PubMed/). If you locate articles from our journals that way, the full text is only a click away - especially for *Endocrine-Related Cancer*, for which you don't even need to be a subscriber!

We've taken this idea further. Organizations like SwetsNet Navigator, EBSCO Online, RoweCom Information Quest and Minerva Electronic Online Services make journals from many different publishers available and searchable via one Web site, and libraries often subscribe to e-journals via this route. By entering into agreements with these services to include abstracts with links to our articles, we will attract people who aren't currently our core readers.

We've also improved the (free) search engine on our own Web site, so that you can now make much more refined searches. In addition, if you'd like to be alerted to new articles as they are published, you can now have the table of contents emailed to you as soon as the full text is available.

Another route to material is via reference lists in other articles. How refreshing if you could go straight to an intriguing article from where it was cited! We have brought this a step closer. The online reference lists for *Journal of Endocrinology* and *Journal of Molecular Endocrinology* now include links to the PubMed/Medline entries for the cited articles, and from here you can often click straight through to the relevant article on the publisher's Web site. In addition, we provide links from citations in our reference lists directly to the articles in selected journals, such as *Journal of Biological Chemistry*, *PNAS* and many others - including our own journals, of course! We will add the same features to *Endocrine-Related Cancer*'s reference lists very soon.

We also plan to join the recently announced CrossRef project, which will ultimately enable us to introduce reference list links directly to and from articles in online journals from most of the world's major publishers.

All of that will improve your access to articles published in our journals, and to related articles published elsewhere. But how can we help you get your papers published more quickly in the first place? This is where ESPERE comes in (the acronym stands for Electronic Submission and Peer Review). It's a collaborative project, involving several learned society and commercial publishers, started by our very own Sue Thorn. A trial version of this system went live in June, which means

that you can now submit your paper electronically to *Journal of Endocrinology*, via a simple, friendly Web interface. At the click of a mouse, our referees and editorial board members can then download your manuscript from ESPERE's secure Web server - the system ensures that the normal confidentiality is maintained. An online version of the referees' report form is on our Web site, which means that the entire review process can be conducted electronically. We've already received a number of submissions via this route from around the world, and we hope to learn a great deal from the process in order to make further improvements in the future. The publication of your papers need no longer be held up by postal delays!

As you can see, a lot of work has gone into the continuing development of the Society's electronic journals. But far from indicating that we've got the electronic revolution pretty much sewn up, I think this is just the beginning. We currently produce our e-journals by an extension of the method used for the printed versions. Their appearance reflects this - they are still largely electronic copies of our printed journals. If we're to continue to meet our readers' and authors' needs, this may well have to change in the future. If we wish to retain the option of involvement in forthcoming e-publishing initiatives, including more sophisticated and richly structured searching, linking and archiving services, we shall need to place the electronic version much more squarely at the centre of the way we work. As a result, we're now investigating how we might do that, and hopefully speed up the entire publication process at the same time.

If the heady world of online research journals leaves you yearning for something simpler, I'm happy to announce that your favourite newsletter, *The Endocrinologist*, is now available in full on the Society's Web site. It's fully searchable, too! Just follow the links from the home page - you don't need a password.

Now **that** seems pretty sorted, after all.

STEVE BYFORD

20TH JOINT MEETING OF THE

**British
Endocrine
Societies**

26-29 March 2001

**Belfast Waterfront Hall
and Hilton Hotel, Belfast**

Please contact Helen Gregson (Tel: 01454-619347;
Email: helen.gregson@endocrinology.org) for a preliminary programme



Abstract deadline:
29 November 2000

From Tadpoles to TSH

When you were children you watched your frog-spawn develop into tadpoles, which then metamorphosed by stages into frogs. Little did you realize then that this metamorphosis is critically dependent on adequate ambient thyroid hormone concentrations, and the development of functional thyroid hormone receptors in the tails of the tadpoles!

The development and neurological maturation of the human nervous system in the fetus is also dependent on thyroid hormone. During the first trimester of pregnancy, before the fetal thyroid is functional, placental transfer of thyroxine occurs. Studies (mainly in rats) have shown deranged neuronal architecture and impaired neuronal maturation, particularly in the cerebellum, in those fetuses where mothers were rendered hypothyroid before or during pregnancy.

The human counterpart to these observations was first observed in the iodine-deficient areas of the world. Iodine deficiency does not occur in the UK, although several areas of continental Europe are still affected, and an increased incidence of thyroid dysfunction in children has been described in these regions. In severe deficiency, cretinism ensues, and over the past 20 or 30 years it has been realized that iodine deficiency encompasses a wide spectrum of disorders. These range from very mild psychomotor impairment through increasingly severe cognitive impairment states, in addition to the

occurrence of various neurological syndromes (e.g. spastic diplegia).

The critical feature of the various degrees of iodine deficiency is a low circulating maternal thyroxine concentration, especially during early gestation. For many years, it has also been observed that children with congenital hypothyroidism at 5-day neonatal screening develop a higher IQ if treated before the age of 2 weeks than children whose treatment is started later.

What about pregnancy in areas which are not iodine-deficient? Recent data have highlighted several important issues. First, it is known that about 10% of pregnant women have circulating thyroid peroxidase (TPO) antibodies and a proportion of these may be expected to have high TSH with relatively low thyroxine. Secondly, a study reported in the USA showed that the prevalence of high TSH during gestation was about 2.5% (*Clinical Endocrinology* 1991 **35** 41-46).

Last year, an important paper by Haddow *et al.* published in the *New England Journal of Medicine* (1999 **341** 549-555) compared the IQ of children aged 7-9 born to mothers who were known to have a high TSH in mid-gestation, and who were untreated, with control children born to mothers who were known to have a normal TSH during pregnancy. Twenty per cent of the 'high TSH' children had an IQ below 85, compared with 5% of the control children - a highly significant difference. The study was carefully carried out and a wide range

of psychological tests performed. In addition, a previous study by Pop *et al.* (*Clinical Endocrinology* 1999 **50** 149-155) showed a decrease in the developmental index in infants born to mothers with high TSH in early pregnancy compared with control infants.

Clearly, there may be a case for screening for TSH in early pregnancy and intervening with thyroxine treatment in those women found to have high TSH levels. Several questions remain unanswered:

- is there a critical stage of pregnancy when a high TSH is potentially more damaging to brain development (perhaps in early gestation before fetal thyroxine production)?
- in those women who have TPO antibodies, does a normal TSH in early pregnancy remain normal for the rest of gestation?
- if thyroxine therapy is administered, will this prevent the IQ decrement observed by Haddow *et al.*?

To date, there are no randomized trials available to answer these questions. While there may be a considerable cost involved in screening all pregnant women for TSH (together with the attendant anxieties), this must be balanced by the opportunity to counter one cause of mental impairment, and thereby provide a genuine health gain in the community. After all, we still screen for syphilis in the UK, with an incidence of 1 in a million.

Meanwhile, I am pleased to report ongoing interest and thyroid research in the world of tadpoles. If the tadpoles can have thyroxine, why not the human fetus?

JOHN H LAZARUS



11th Workshop on Vitamin D

Nashville, May 2000

“An insight into the so-called non-genomic action of 1,25D₃ was provided in the rapid responses session. Anthony Norman presented interesting data to suggest that 1,25D₃ can modulate VDR-mediated genomic responses downstream of its rapid response. All the presentations pointed to the presence of the elusive VDR membrane receptor, with putative cross-talk mechanisms occurring via non-genomic and nuclear VDR action.

In the vitamin D hydroxylase session, Satyanarayana Reddy summarized the actions of a vast array of vitamin D metabolites, demonstrating that the biological activity of 1,25D₃ represents a combination of the actions of the natural hormone and its metabolites. R Bland and S Zehnder demonstrated extra-renal expression of 1 α -hydroxylase, as well as further analysis of its expression in the kidney proximal tubule and collecting duct.

The VDR and gene regulation session included a talk by Mark Haussler on work demonstrating the importance of novel VDR polymorphisms which may have a major impact on intestinal calcium absorption and susceptibility to osteoporotic fractures. The final session included interesting work by Roger Bouillon, suggesting that vitamin D may protect keratinocytes against UVB-induced cell death, accompanied by a suppression of the sunburn-related cytokine interleukin 6.”

ENDO 2000 - 82nd Annual Meeting of the Endocrine Society

Toronto, June 2000

“The symposium on chromatin remodelling and transcription was especially interesting. When performing day-to-day genetic analysis, it is easy to forget that eukaryotic DNA does not exist as a freely accessible double helix, but is wrapped in nucleosomes. The lectures reminded us of this and highlighted the resulting increased complexity. The workshop presentations were also very useful, particularly Peter Cooper’s, on use of the BLAST sequence database. Some of the statistics were rather impenetrable, the useful hints will make my future use of BLAST much more efficient.”

“This year’s focus was ‘back to Toronto roots’ - diabetes. Michael Bliss gave a splendid account of the struggles leading towards the discovery of insulin in 1920s Toronto. David Harlan followed with exciting data on the first steps towards Banting’s idea in the 20s - controlling diabetes by β -islet transplantation. The novel approach to islet preparation and transplantation left all eight diabetic patients who participated insulin-independent a year after the transplant.

I had been looking forward to posters on Ghrelin, a novel endogenous ligand for the GH secretagogue receptor. This 28 amino acid protein is highly expressed in the stomach, with immunoreactivity in the arcuate nucleus of the hypothalamus, and has been found to release GH *in vivo*. Cyril Bowers showed, in several *in vivo* experiments, that Ghrelin’s properties concerning GH release are very similar to those of artificial GH secretagogues. Also of interest, Kamegai *et al.* reported that *i.c.v.* injections of Ghrelin upregulated NPY expression, while GHRH and somatostatin expression were unchanged - an action similar to that of GHRP-6. In an oral communication, I presented experiments using an RNase protection assay to quantitatively measure both forms of mouse Ghrelin (Ghrelin 28 and its splice variant Ghrelin 27). As expected, we found high expression in stomach and gut, but no expression was measurable in any other tissue, including the hypothalamus. Ghrelin is very much embarking on its career in GH physiology, and the relevance of these very low levels of expression remains to be seen.”

Hormonal & Neural Peptide Biosynthesis Gordon Conference

New London, July 2000

“Protein trafficking in the secretory pathway was well covered - the endocytic pathway seems to be getting even more complex! Protein:protein interactions abound, and many appear to be regulated by phosphorylation/dephosphorylation cycles. My main interest is the mechanism for protein sorting at the trans-Golgi network (TGN). It has always been thought that proteins enter secretory granules by interacting with a sorting receptor in the TGN membrane. At the last Gordon conference, the idea that carboxypeptidase E might be such a sorting receptor caused much controversy. This year, although some remain sceptical, data from Peng Loh (NIH) appear to be holding up, but it is also becoming apparent that there are interactions between some secretory proteins and specialized lipid domains of the TGN.

The classical view of the Golgi apparatus seems about to be challenged. Katherine Howell’s lab has produced some incredible high resolution, high voltage electron microscope tomographic 3D images. These appear to show a specialized endoplasmic reticulum associating with multiple Golgi cisternae, and that sorting to different compartments (e.g. lysosomes, plasma membrane) may occur from different Golgi cisternae. This would really rewrite the cell biology textbooks!”

Thanks to Scott MacKenzie, Nina Balthasar, Mark English and K Shennan for their contributions. The Society is pleased to be able to support its members with travel grants.

26th International Aldosterone Conference

Toronto, June 2000

“The discovery of non-genomic actions of aldosterone, and of extra-adrenal sites of production, means there is still much to be learned. My own work concerns its extra-adrenal synthesis, so I was most interested in the session on cardiac aldosterone. Perrin White presented RT-PCR analysis of steroidogenic gene expression in the human heart. He had detected a full complement of the relevant enzymes, with the exception of aldosterone synthase itself. Others have found evidence of aldosterone synthase in the heart, including Claude Delcayre’s group. They have now achieved cardiac overexpression of the aldosterone synthase gene in the rat. Their ongoing work will assess the effect of this on cardiac fibrosis, a phenomenon in which aldosterone is known to play a part.”

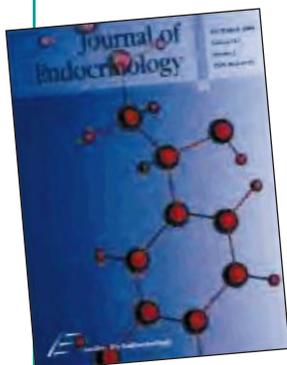
Hot Topics

Carolyn Cowey selects highlights from forthcoming issues of *Journal of Endocrinology* and *Journal of Molecular Endocrinology* (online versions at <http://journals.endocrinology.org>).

Dimethoate blocks StAR transcription

Researchers from Texas Tech University have investigated the mechanism by which dimethoate, an organophosphate insecticide, disrupts reproductive function in animals. Using the mouse MA-10 Leydig tumour cell line, Walsh *et al.* showed that dimethoate inhibited steroidogenesis by blocking transcription of the steroidogenic acute regulatory (StAR) gene. StAR is required for the rate-limiting transfer of cholesterol from the outer to the inner mitochondrial membrane.

(See the full article in *Journal of Endocrinology* **167**(2), November 2000)



Modulation of PTH by oestrogen

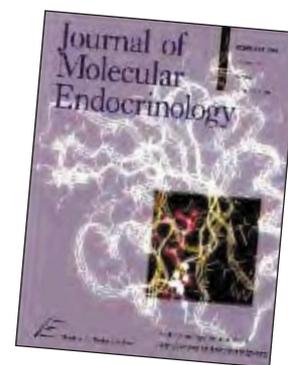
Research carried out by Nasu *et al.* from Kobe University School of Medicine has explored how the interaction between parathyroid hormone (PTH) and oestrogen works to cumulatively increase bone mass in patients with osteoporosis. Pretreatment with oestrogen decreased PTH-induced inhibition of osteoblast proliferation, and instead caused PTH to stimulate osteoblast function. Insulin-like growth factor-I mimicked the actions of oestrogen, and may be involved in the oestrogen-induced modulation of PTH.

(See the full article in *Journal of Endocrinology* **167**(2), November 2000)

RT-PCR for quantification of mRNA

mRNA quantification is useful for clinical diagnostics, and applications include monitoring responses to chemotherapy, or providing a molecular assessment of tumour stage. Bustin, from Queen Mary and Westfield College, London, reviews the use of the reverse transcription-polymerase chain reaction (RT-PCR), and the technical aspects involved in the quantification of transcription. Bustin advocates the use of RT-PCR for experiments requiring sensitive, specific and reproducible quantification of mRNA.

(See the full article in *Journal of Molecular Endocrinology* **25**(2), October 2000)



mER isoforms and tissue-specificity

Oestrogen receptor-alpha (ER α) and oestrogen receptor-beta (ER β) are ligand-regulated transcription factors that modulate target gene transcription, and oestrogen signal transduction. There are several splice variants for these receptors, and the proteins encoded for by these variant mRNAs could also affect oestrogen and anti-oestrogen action. Several splice variants of the rat and murine ER β (ER β 2) have been characterized. Due to the possibility of species-specific expression and therefore functional differences in ER variants, Lu *et al.* from the University of Manitoba, Canada, have examined the functions of mER β 2 using mouse cells. The researchers found that mER β 2 is both ligand- and promoter-specific. This mER β variant isoform can exert dominant negative transcriptional effects on both mER β 1 and mER α , the importance of which will depend on the relative expression of the mER isoforms and on co-expression of the ERs in the same cells. Differential tissue expression of the mER isoforms probably occurs, which could contribute to the mechanisms associated with tissue-specific oestrogenic and, possibly, anti-oestrogenic action.

(See the full article in *Journal of Molecular Endocrinology* **25**(2), October 2000)



First International Workshop on the Genetics of Bone Disease

17-21 March 2001

DAVOS CONGRESS CENTRE, SWITZERLAND

www.ectsoc.org

Organised by the European Calcified Tissue Society

Deadline for abstracts: 13 November 2000

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Dursley GL11 6DS, UK
Tel: +44 (0)1453 549929
Fax: +44 (0)1453 548919
Email: janetcrompton@compuserve.com

International Bone and Hormone Meeting

Queensland, Australia, 4-8 November 2000.
 Contact: Tel: +61-2-92473663; Fax: +61-2-92523375; Email: rosemmary@solnet.com.au.

Keynote Conference

London, UK, 6-10 November 2000.
 Contact: Millennium Festival of Medicine, BMA House, Tavistock Square, London WC1H 9JP, UK (Tel: +44-20-73836047; Fax: +44-20-73836220; Email: medicine2000@medicine2000.org; Web: <http://www.medicine2000.org>).

New Targets for Cancer Intervention

Eilat, Israel, 12-16 November 2000.
 Contact: American Association for Cancer Research, Public Ledger Building, Suite 826, 150 South Independence Mall West, Philadelphia, PA 19106-3483, USA (Tel: +1-215-4409300; Fax: +1-215-3519165).

HRT and Key Advances in Clinical Management of the Post-menopause

London, UK, 15 November 2000.
 Contact: Emma Bryce, Royal Society of Medicine, 1 Wimpole Street, London W1G 0AE, UK (Tel: +44-20-72903919; Fax: +44-20-72902977; Email: emma.bryce@roysocmed.ac.uk; Web: <http://www.roysocmed.ac.uk/diar/page4.htm>)

191st Meeting of the Society for Endocrinology

London, UK, 20-21 November 2000.
 Contact: Society for Endocrinology, 17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-619347; Fax: +44-1454-616071; Email: info@endocrinology.org; Web: <http://www.endocrinology.org>).

4th Meeting of the British Thyroid Association

London, UK, 22 November 2000.
 Contact: Malcolm Prentice, Mayday University Hospital, Croydon, Surrey CR7 7YE (Tel: +44-208-401-3034; Fax: +44-208-401-3487; Email: malcolm.prentice@mhc-bt.sthames.nhs.uk).

20è Journées Françaises d'Endocrinologie Clinique, Nutrition et Métabolisme

Paris, France, 24-25 November 2000.
 Contact: A Deshons, CERC, 7 rue du Capitaine Dreyfus, F-95137 Franconville Cedex, France (Fax: +33-1-34135976).

Key Advances in Clinical Management of Benign Prostatic Disease

London, UK, 30 November 2000.
 Contact: Trina Capps, Royal Society of Medicine, 1 Wimpole Street, London W1G 0AE, UK (Tel: +44-20-72902965; Fax: +44-20-72902977; Email: trina.capps@roysocmed.ac.uk; Web: <http://www.roysocmed.ac.uk/diar/page4.htm>).

International Conference on Progress in Bone and Mineral Research 2000

Vienna, Austria, 30 November-2 December 2000.
 Contact: Vienna Medical Academy, Alser Strasse 4, A-1090 Vienna, Austria (Tel: +43-1-40513830; Fax: +43-1-405138323; Email: medacad@via.at).

British Society for Immunology: Congress 2000

Harrogate, UK, 5-8 December 2000.
 Contact: Congress 2000, Triangle 3 Ltd, Triangle House, Broomhill Road, London SW18 4HX, UK (Tel: +44-20-88752423; Fax: +44-20-88752421; Email: meetings@immunology.org; Web: <http://www.immunology.org>).

2nd International Meeting on Social and Economic Aspects of Osteoporosis and Bone Disease

Liège, Belgium, 7-9 December 2000.
 Contact: Tel: +32-4-2541225; Fax: +32-4-2541290; Email: ypc@compuserve.com.

Techniques and Applications of Molecular Biology: A Course for Medical Practitioners

Warwick, UK, 11-14 December 2000.
 Contact: Dr Charlotte West, Department of Biological Sciences, University of Warwick, Coventry CV4 7AL, UK (Tel: +44-24-76523540; Fax: +44-24-76523701; Email: charlotte.west@warwick.ac.uk).

Joint Meeting of the SSF/VFS

Utrecht, The Netherlands, 15-16 December 2000.
 Contact: Dr JThJ Uilenbroek, Department of Endocrinology and Reproduction, Faculty of Medicine, Erasmus University Rotterdam, PO Box 1738, 3000 DR Rotterdam, The Netherlands (Tel: +31-10-4087581; Fax: +31-10-4089461; Email: uilenbroek@endov.fgg.eur.nl).

Biochemical Society Conference

Sussex, UK, 18-21 December 2000.
 Contact: Biochemical Society, 59 Portland Place, London W1B 1QW, UK (Tel: +44-20-75803481; Fax: +44-20-76377626; Email: meetings@biochemistry.org; Web: <http://www.biochemistry.org/meetings.htm>).

Endocrine Facets of Ageing in the Human and Experimental Animal

London, UK, 30 January-1 February 2001.
 Contact: Bursary Scheme Administrator, The Novartis Foundation, 41 Portland Place, London W1B 1BN, UK (Tel: +44-20-76369456; Fax: +44-20-74362840; Email: bursary@novartisfound.org.uk; Web: <http://www.novartisfound.org.uk/bursary.htm>).

3rd National Clinicopathological Conference on Pituitary Disease

London, UK, 31 January 2001.
 Contact: Dr Mark Vanderpump, Department of Endocrinology, Royal Free Hospital, Pond Street, London NW3 2QG, UK (Tel: +44-20-78302414; Fax: +44-20-78302416; Email: m.p.j.v@btinternet.com) or Dr GS Conway, Cobbold Laboratories, The Middlesex Hospital, Mortimer Street, London W1N 8AA, UK (Tel: +44-20-73809451; Fax: +44-20-76369941).

1st World Congress on the Fetal Origins of Adult Disease

Bombay, India, 2-4 February 2001.
 Contact: Ms Alifiya Motiwala (Tel: +91-22-6516439/6456763; Fax: +91-22-6516438; Email: mrcssc@vsnl.com; Web: <http://www.sneha-india.org>).

International Meeting on Steroids and Nervous System

Torino, Italy, 11-14 February 2001.
 Contact: G Panzica, Department of Anatomy, Pharmacology and Forensic Medicine, c.so M D'Azeglio 52, Torino, Italy (Email: giancarlo.panzica@unito.it; Web: <http://medicina.medfarm.unito.it/dipart/dafml/gcp/info/>).

Society for Endocrinology Clinical Cases Meeting

London, UK, 12 February 2001.
 Contact: Ann Lloyd, Society for Endocrinology, 17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-619036; Fax: +44-1454-616071; Email: info@endocrinology.org; Web: <http://www.endocrinology.org>).

1st Asian ISSAM Meeting on the Aging Male

Kuala Lumpur, Malaysia, 1-4 March 2001.
 Contact: Yenli Lim, Conference Manager, 1st Asian ISSAM Meeting, c/o Subang Jaya Medical Centre, 1 Jalan SS12/1A, Subang Jaya, 47500 Petaling Jaya, Selangor, Malaysia (Tel: +603-730-6777; Fax: +603-730-6571; Email: iliney@tm.net.my; Web: <http://www.apsir.org>).

Introduction to Molecular and Cellular Research

Wyndham Miami Biscayne Bay, FL, USA, 2-5 March 2001.
 Contact: Tel: +1-888-3636274; Email: ahall@endo-society.org; Web: <http://www.endo-society.org/scimtgscipub.htm>).

1st International Conference on the Genetics of Bone Disease

Davos, Switzerland, 17-21 March 2001.
 Contact: Janet Crompton, The Old White Hart, North Nibley, Dursley GL11 6DS, UK (Tel: +44-1453-549919; Fax: +44-1453-548919; Email: janetcrompton@compuserve.com; Web: <http://www.janet-crompton.com/genbone2001>).

British Society for Paediatric and Adolescent Gynaecology Annual Meeting

London, UK, 19 March 2001.
 Contact: R Stanhope, Institute of Child Health, Biochemistry, Endocrinology and Metabolism Unit, University College London, 30 Guilford Street, London WC1N 1EH, UK (Tel: +44-20-79052159; Fax: +44-20-74046191).

20th Joint Meeting of the British Endocrine Societies

Belfast, UK, 26-29 March 2001.
 Contact: British Endocrine Societies, 17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-619347; Fax: +44-1454-616071; Email: info@endocrinology.org; Web: <http://www.endocrinology.org>).

12th International Workshop on the Development and Function of the Reproductive Organs

Ma'ale Hachamisha, Jerusalem, Israel, 30 April-3 May 2001.
 Contact: Secretariat, Dan Knassim Ltd, PO Box 1931, Ramat Gan 52118, Israel (Tel: +972-3-6133340 ext 208; Fax: +972-3-6133341; Email: team2@congress.co.il).

International Conference: The Consequences in Adult Age of Endocrine Diseases in Childhood

Thessaloniki, Greece, 11-12 May 2001.
 Contact: Prof GE Krassas, Panagia Hospital, Department of Endocrinology and Metabolism, 22 N Plastira Str., N Krini, GR-55132 Thessaloniki, Greece (Tel: +30-51-447444; Fax: +30-51-282476; Email: krassas@the.forthnet.gr).

44è Journées Internationales d'Endocrinologie Clinique: - Obesity Come-back to Endocrinology

Paris, France, 17-18 May 2001.
 Contact: Dr G Copinschi, Laboratory of Experimental Medicine, Brussels Free University, CP 618, 808 Route de Lennik, B-1070 Brussels, Belgium (Fax: +32-2-5556239).

14th International Congress of Comparative Endocrinology

Sorrento, Italy, 26-30 May 2001.
 Contact: Studiocongressi, Via S Anna dei Lombardi 38, 80134 Napoli, Italy (Tel: +39-081-5511668; Fax: +39-081-5528835; Email: studiocongressi@napoli.com; Web: <http://www.napoli.com/studiocongressi>).

1st Joint Meeting of the International Bone and Mineral Society and European Calcified Tissue Society

Madrid, Spain, 5-10 June 2001.
 Contact: Tlesa, Londres 17, 28028 Madrid, Spain (Tel: +34-91-3612600; Fax: +34-91-3559208; Email: ibms2001@tlesa.es; Web: <http://www.intercongres-2001.com>).

5th European Congress of Endocrinology

Turin, Italy, 9-13 June 2001.
 Contact: CCI Centro Congressi Internazionale, Via Cervino, 60-10155 Torino, Italy (Tel: +39-011-2446911; Fax: +39-011-2446900; Email: efes2001@ibow.com; Web: <http://www.ibow.com/efes2001>).

EULAR 2001: Annual European Congress of Rheumatology

Prague, Czech Republic, 13-16 June 2001.
 Contact: Tel: +41-1-3839690; Fax: +41-1-3839810; Email: eular@bluewin.ch.

ENDO 2001: 83rd Annual Meeting

Colorado, USA, 20-23 June 2001.

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).

Bone and Tooth Society Meeting

York, UK, 3-5 July 2001.

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: <http://www.janet-crompton.com>).

Pediatric Endocrinology 2001

Montréal, Canada, 6-10 July 2001.

Contact: PedEndo Secretariat, 1110 Pine Avenue West, Montréal, Québec, Canada H3A 1A3 (Tel: +1-514-3983770; Fax: +1-514-3984854; Email: pedendo@ums1.lan.mcgill.ca; Web: <http://www.med.mcgill.ca/pedendo>).

29th British Congress of Obstetrics and Gynaecology

Birmingham, UK, 10-13 July 2001.

Contact: BCOG Secretariat, Congress House, 65 West Drive, Cheam, Sutton, Surrey SM2 7NB, UK (Tel: +44-20-86610877; Fax: +44-20-86619036; Email: info@conform.com).

Recent Progress in Hormone Research

Washington, DC, USA, 4-8 August 2001.

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).

27th Meeting of the**European Thyroid Association**

Warsaw, Poland, 25-29 August 2001.

Contact: Prof. Janusz Nauman (Email: euro-thyroid-assoc@cf.ac.uk).

20th International League of Associations for Rheumatology World Congress

Edmonton, Canada, 26-31 August 2001.

Contact: Tel: +1-905-2733080; Fax: +1-905-27323611; Email: healthcarecomm@sympatico.ca.

34th International Congress of Physiological Sciences

Christchurch, New Zealand, 26-31 August 2001.

Contact: The Conference Company, PO Box 90-040, Auckland, New Zealand (Fax: +64-9-3601242; Email: info@tcc.co.nz; Web: <http://www.iups2001.org.nz>).

11th International Society for Chromaffin Cell Biology (ISCCB-11) Meeting

San Diego, CA, USA, 3-11 September 2001.

Contact: Dan O'Connor, Department of Medicine and Center for Molecular Genetics, University of California, 3350 La Jolla Village Drive, San Diego, CA 92161-9111H, USA (Tel: +1-858-5528585 ext 7373 (office), 2632 (lab); Fax: +1-858-6426331 (office), +1-858-6426425 (lab); Email: doconnor@ucsd.edu; Web: <http://medicine.ucsd.edu/hypertension> or <http://elcapitan.ucsd.edu/hyper/>).

4th Biennial Congress of the European Society for Sexual and Impotence Research

Rome, Italy, 30 September-3 October 2001.

Contact: SC Studio Congressi, Via F Ferrara 40, 00191 Rome, Italy (Tel: +39-06-3290250; Fax: +39-06-36306897; Email: sc.congressi@agora.stm.it; Web: <http://www.essir2001.it>).

Clinical Endocrinology Update: 2001

Illinois, USA, 7-10 October 2001.

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).

American Society of Bone and Mineral Research

Phoenix, Arizona, USA, 12-16 October 2001.

Contact: Tel: +1-202-8571161; Fax: +1-202-2234579; Email: asbmr@dc.sba.com.

21st Joint Meeting of the British Endocrine Societies

Harrogate, UK, 8-11 April 2002.

Contact: British Endocrine Societies, 17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-619347; Fax: +44-1454-616071; Email: info@endocrinology.org; Web: <http://www.endocrinology.org>).

ENDO 2002: 84th Annual Meeting

San Francisco, California, USA, 19-22 June 2002.

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).

5th International Congress of Neuroendocrinology

Bristol, UK, 31 August-4 September 2002.

Contact: BioScientifica Ltd, 16 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-619347; Fax: +44-1454-616071; Email: icn2002@endocrinology.org; Web: <http://www.bioscientifica.com/icn2002.htm>).

28th Meeting of the European Thyroid Association

Goteborg, Sweden, September 2002 (dates to be confirmed).

Contact: Dr Ernst Nystrom (Email: euro-thyroid-assoc@cf.ac.uk).

Clinical Endocrinology Update: 2002

Oregon, USA, 6-9 October 2002.

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).

22nd Joint Meeting of the British Endocrine Societies

Glasgow, UK, 24-28 March 2003

Contact: British Endocrine Societies, 17/18 The Courtyard, Woodlands, Bradley Stoke, Bristol BS32 4NQ, UK (Tel: +44-1454-619347; Fax: +44-1454-616071; Email: info@endocrinology.org; Web: <http://www.endocrinology.org>).

ENDO 2003: 85th Annual Meeting

Philadelphia, Pennsylvania, USA, 4-7 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).

International Society of Endocrinology Congress 2004

Lisbon, Portugal, 1-4 September 2004.

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

SATELLITE SESSION

Do you have your finger on the pulse of testosterone replacement therapy? Prof Fred Wu invites you to get to the heart of the matter and come to a satellite session to be held at the 191st Meeting of the Society for Endocrinology:

Testosterone replacement: assessing its place in the men's health revolution

21 November 2000 (7.45 - 8.45 am)

ROYAL COLLEGE OF PHYSICIANS, LONDON

The session will address the following frequently asked questions and more:-

- How do you monitor testosterone therapy?
- Do you treat testosterone levels below 8 or 10 nmol/l?
- Should levels of SHBG be taken into account?
- Should we derive some index of free testosterone?

Programme**Chairman: Prof Fred Wu (Manchester)**

Critical issues in the management of testosterone replacement therapy
Prof Richard Ross (Sheffield)

Testosterone - the heart of the matter**Dr Hugh Jones (Barnsley)****A physiological approach****Professor Glenn Cunningham (Houston, USA)****Discussion and questions**

If you would like to receive further details regarding this session, please contact:

Helen Gregson, BioScientifica Ltd
16 The Courtyard, Bradley Stoke, Bristol BS32 4NQ
tel: 01454 619347, fax: 01454 616071
e-mail: helen.gregson@endocrinology.org

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at monthly intervals. Maintenance dosages vary but seldom exceed 1mg/day (3 IU/day). Dose requirements decline with age. **Contra-indications:** Hypersensitivity, active tumour, tumour therapy. Treatment should be discontinued after renal transplantation or if tumour growth recurs. **Special warnings:** Children should be regularly assessed by a specialist in child growth. Treatment should be instigated by a physician with special knowledge of GH insufficiency. No skeletal growth can be expected after epiphysial disc closure. Growth disturbance in chronic renal disease should be established by monitoring growth for 1 year on optimal treatment for renal disease. Monitor for glucose intolerance (if on insulin there may be need for dose adjustment); thyroid function; renal function in patients with chronic renal insufficiency; and in patients with history of an intracranial lesion for tumour progression or recurrence. In the event of severe or recurrent headache, visual problems, nausea and/or vomiting, a funduscopy is recommended. If papilloedema is

confirmed, a diagnosis of benign intracranial hypertension should be considered and if appropriate the growth hormone treatment discontinued. Experience with prolonged treatment in adults is limited. Experience above 60 years of age is lacking. **Interactions:** Concomitant glucocorticoid therapy may inhibit growth. **Pregnancy and lactation:** Contraindicated during pregnancy because of insufficient evidence of safety. The possibility that human growth hormone is secreted in breast milk cannot be discounted. **Undesirable effects:** Fluid retention with peripheral oedema and especially in adults carpal tunnel syndrome - normally transient. Mild arthralgia, muscle pain, paresthesia in adults usually self-limiting; rarely headaches in children (0.04/patient year). Formation of anti-somatropin antibodies are rare - where observed the antibodies have not interfered with response to Norditropin. Local skin reactions. Benign intracranial hypertension has been reported rarely. **Overdose:** Acute: hypoglycaemia with

subsequent hyperglycaemia. Long-term overdose may cause known effects of GH excess. **Pharmaceutical Precautions:** Store at 2° - 8°C in the outer carton or during use in Nordipen. Do not freeze or shake vigorously. **Legal category:** POM, CD4. Prices and marketing authorisation numbers: Norditropin SimpleXx™ 5mg/1.5ml: £117.10 PL3132/0131 Norditropin SimpleXx™ 10mg/1.5ml: £234.20 PL3132/0132 Norditropin SimpleXx™ 15mg/1.5ml: £351.30 PL3132/0133 Name and address of PL holder: Novo Nordisk Pharmaceuticals Limited, Novo Nordisk House, Broadfield Park, Brighton Road, Pease Pottage, Crawley, West Sussex, RH11 9RT. Nordipen®, Norditropin® and SimpleXx™ are trademarks Reference:

1. Müller *et al.* Horm Res 1999, in press.
2. Jakobsen LV, et al. Abstract P2/548 81st Annual Meeting of the Endocrine Society, San Diego, 12-15 June 1999.

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