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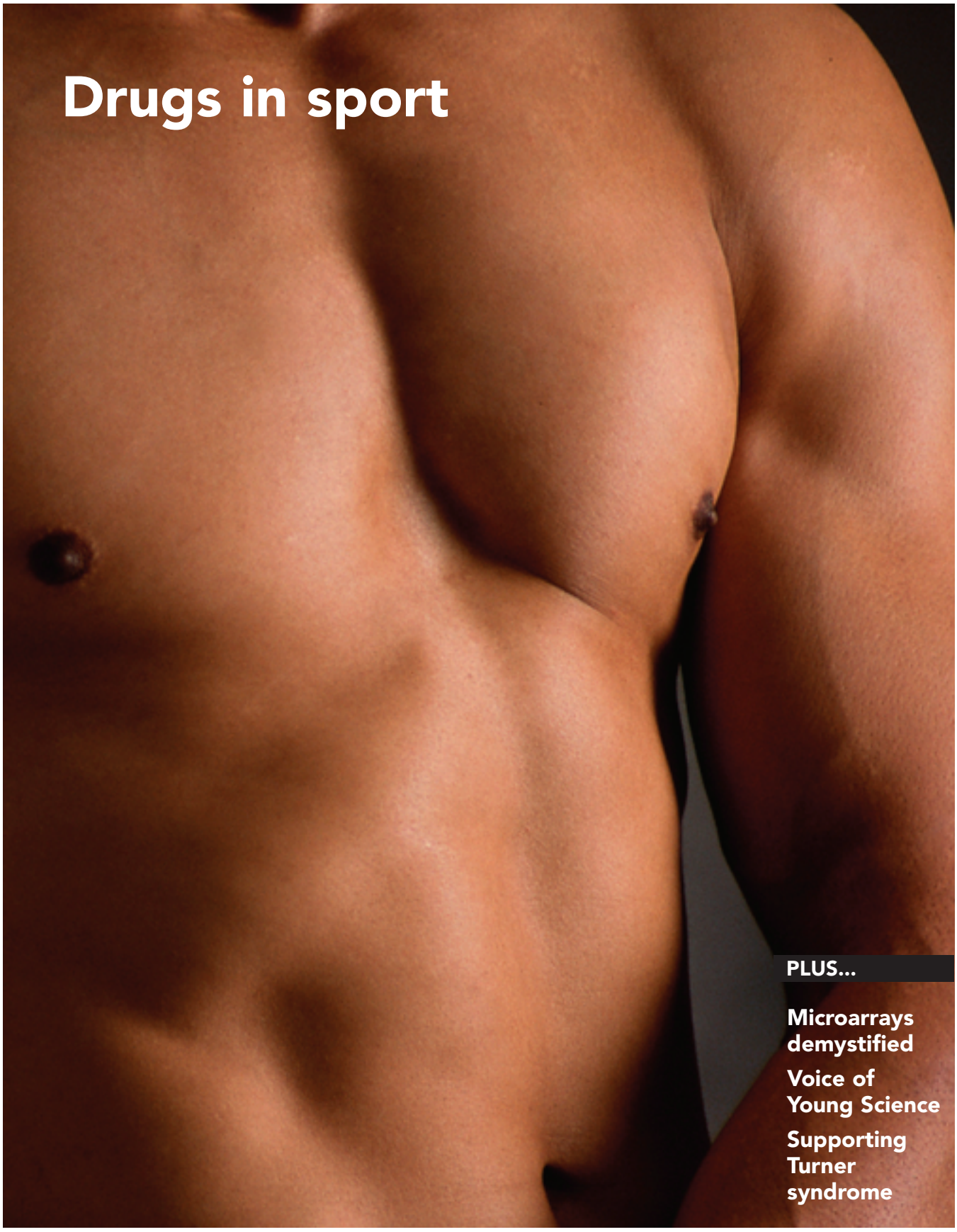
THE NEWSLETTER OF THE SOCIETY FOR ENDOCRINOLOGY NUMBER 74 • WINTER 2004/2005

THE Endocrinologist



Drugs in sport

PLUS...

Microarrays demystified

Voice of Young Science

Supporting Turner syndrome

The Endocrinologist

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Deadline for news items for the Spring 2005 issue: **20 December 2004**.
Please send contributions to the above address.

England was merry England, when
Old Christmas bought his sports again.
'Twas Christmas broach'd the mightiest ale;
'Twas Christmas told the merriest tale;
A Christmas gambol oft could cheer
The poor man's heart through half the year
Sir Walter Scott

It's the silly season again, with Christmas fast approaching and the frantic shopping, card sending and filling of festive stockings and kitchen cabinets. But once all preparations have been made, ales have been drunk and merriment subsided, there's lots of interesting reading in this issue of *The Endocrinologist*.

Christmas may bring sport (in one form or another) but there is little chance that Santa will pop some performance-enhancing drugs in your stocking. On page 9, Andrew Kicman and Vivian James give us an enlightening overview of drug abuse amongst athletes, the use of steroidal and non-steroidal hormones, and the problems associated with their detection and side-effects. As a sequel, a body builder talks frankly with Jane Shepley about his past relationship with androgenic steroids (see page 11). And whilst on the subject of androgens, page 13 sees Richard Anderson's review of a new book on testosterone.

Talking about science with the media is always a gambol/gamble: will the evidence be reported correctly or will it acquire a touch (or more) of sensationalism? The Society recently sent four young endocrinologists to attend 'Voice of Young Science: Science in the British Media'. On page 7, Deborah Wake and Alicia Parkes report back on the meeting and explain why scientists should be embracing the timely opportunity to educate the public through the media.

Hotspur relates a heart-warming tale about a patient who tried to fix him up with a date (page 12). Will this sustain him for 'half the year' and will we ever know the consequences apart from the consultation fee? Hot(spur) dates withstanding, this issue also features some very interesting 'Hot Topics' (page 14) and hot technology. Tim Rutherford provides an illuminating account of DNA microarrays on page 12, and suggests how this technology can be used both as a diagnostic tool and for formulating new hypotheses.

Finally, cheering news from the Turner Syndrome Support Society. Established 5 years ago under the auspices of the Child Growth Foundation and now independent, the spotlight article on page 8 outlines their activities and the support they have given to the thousands of girls and their families with this cradle-to-grave condition.

So on the note of Sir Walter Scott's mightiest ale, merriest tale and cheering the poor man's (and woman's) heart through half the year (and hopefully longer), the Society wishes you a happy Christmas and New Year.

SAFFRON WHITEHEAD

Promotion in mind?

If you're looking for that certain *je ne c'est quoi* to boost your promotion prospects then we may be able to help. In return for the considerable support you give the Society at all levels of its business, we are pleased to offer letters of support to members who would find them beneficial.

The Society will support members of the scientific or clinical community who have contributed to its running, and who are at the level of lecturer or above. So if, for example, you have chaired a session or spoken at a Society meeting, and you would like the Society to endorse your promotion application, let us know. Just contact Rachel Evans or Julie Cragg in the Bristol office (info@endocrinology.org).

Calling medical undergraduates!

Awards of £1000 from the Clinical Endocrinology Trust are available to undergraduate medical students to fund a project of up to 3 months' duration on any aspect of endocrinology.

The grants are expected to cover laboratory and other expenses. Research will normally take place in the UK under the guidance of a supervisor. A 500-word report must be submitted to the Trustees upon completion, and an abstract may be submitted to a future BES meeting. A further £1000 will be awarded for the best report.

See www.endocrinology.org/sfe/grants.htm for further details of how to apply. The deadline is **30 April 2005**.

Medals

Following plentiful nominations and a ballot, the Society is delighted to announce the following winners of its medals for 2005-2006.

Society for Endocrinology Medal 2005: Prof John Connell (Glasgow)
European Medal 2005: Prof Adriana Maggi (Milan)
Asia & Oceania Medal 2005: Dr Kenji Kangawa (Osaka)
Dale Medal 2006: Prof Jock Findlay (Clayton, Victoria)
Transatlantic Medal 2006: Dr David Mangelsdorf (Dallas)

Prizes Galore!!

Congratulations to the oral communication winners at the 195th Society for Endocrinology meeting that took place recently in London. Two prizes were awarded one in the clinical category and one in the basic science category.
Clinical: Marie Freel (Glasgow), S MacKenzie (Glasgow), E Friel (Glasgow), M Ingram M (Glasgow), E Davies (Glasgow), R Fraser (Glasgow), A Dominiczak A(Glasgow), M Caulfield (London) and J Connell (Glasgow).
Basic: R Fowkes (London and San Francisco), PV Tran (San Francisco), SF Akana (San Francisco), CR Carey San Francisco), MF Dallman (San Francisco) and HA Ingraham (San Francisco).

Two posters were awarded prizes at the same meeting, again one in the clinical category and one in the basic science category.
Clinical: PL Brown, HL Stoddart, KK Sidhu, TP Milligan and JM Burrin. (London)
Basic: D Patel, F Appleby-Dean, J Cox and DG Johnston. (London)

Clinical Fellowship

Dr Alia Munir from Sheffield is the recipient of the Society for Endocrinology/ Clinical Endocrinology Trust Clinical Fellowship. We congratulate Alia, who received the award following a rigorous process of peer review, marking and an interview. Our grateful thanks go to the Clinical Endocrinology Trust for their financial contribution to this 3-year award.

Members on the move...

S Baldeweg to University College London; M Elrishi to Leicester Royal Infirmary; R Iles to Middlesex University; K S Leong to Arrowe Park Road, Wirral; M Quinkler to Universitätmedizin, Berlin; A Tahrani to Royal Shrewsbury Hospital.

SIGnificant News!

The Society is very proud of the newly established Special Interest Groups, they are…..

Bone and Mineral, headed by Bronwen Evans
PCOS and the metabolic syndrome, jointly headed by Steve Atkin and Harpal Randeva
Pituitary, headed by Rob Fowkes
Steroids, headed by John Honour

If you are a member of the Society and are interested in joining any of the above SIGs or have any queries, please contact Rachel Evans in the Bristol office (rachel.evans@endocrinology.org).

The main aims of the SIGs are……

- Provide a focus for sub-specialties within endocrinology, to strengthen the discipline and form a community for promotion of interdisciplinary interests
- Organise small meetings for focussed groups, either individually or as part of the annual November meeting
- Increase the profile of endocrinology as a speciality

SOCIETY CALENDAR

16 February 2005
Society for Endocrinology Clinical Cases Meeting
Royal Society, London, UK

4-6 April 2005
24th Joint Meeting of the British Endocrine Societies
Harrogate International Centre, Harrogate, UK
(see advert on page 4)

5 July 2005
Molecular Endocrinology Workshop at Summer School
St Aidan's College, Durham, UK
(see advert on page 5)

6-7 July 2005
Advanced Endocrine Course at Summer School
St Aidan's College, Durham, UK
(see advert on page 5)

8 July 2005
Clinical Practice Day at Summer School
St Aidan's College, Durham, UK
(see advert on page 5)

30 August-1 September 2005
Society for Endocrinology Endocrine Nurse Training Course
John Macintyre Centre, Edinburgh, UK

7-9 November 2005
196th Meeting of the Society for Endocrinology
Royal College of Physicians, London, UK

BES 2005

24TH JOINT MEETING OF THE

British Endocrine Societies

4-6 April 2005

HARROGATE INTERNATIONAL CENTRE

Register Now! **www.endocrinology.org/sfe/BES2005**

Plenary lectures

CR Kahn

J Sandahl Christiansen

J Franklyn

K Korach

T Visser

Clinical management workshops

Endocrine sequelae of childhood cancer

Endocrine manipulations in the transsexual

HRT in women - who should get what

Diagnosis and management of steroid deficiency

Symposia

Endocrine complications of systemic disorders

Hyperinsulinism-induced hypoglycaemia

Cardiovascular endocrinology

Endocrinology of the kidney

Novel approaches for defining oestrogen action

Hypothalamic-pituitary-adrenal axis and inflammation

Intracellular transport of steroids

Regulation of ovarian folliculogenesis

Thyroid disease in pregnancy and childhood

Not forgetting

Oral communications

Molecular endocrinology workshop

Clinical cases

Poster presentations

and an exciting social programme!

The POC for the BES 2005 would like to thank all of the corporate members of the Society for Endocrinology for their sponsorship and continued support at the BES meeting.

Ardana Bioscience Ltd *for sponsoring a satellite session.*

Ipsen Ltd *for sponsoring a satellite session, the wine reception at the BES banquet, providing the delegate wallets, pads and pens*

Novartis Pharmaceuticals UK Ltd *for sponsoring a satellite session and Clinical Expert View 8: Diagnosis and management of neuroendocrine tumours of the pancreas and gut, particularly carcinoids.*

Pfizer Ltd *for sponsoring a satellite session, the BES final programme book, the welcome reception and the 'buffet and boogie' social event.*

Schering Health Care Ltd *for sponsoring a satellite session.*

Serono Pharmaceuticals Ltd *for sponsoring the Nurses tea and Clinical Expert View 1: Precocious puberty*

Servier Laboratories Ltd *for sponsoring Clinical Expert View 10: Interpretation of bone mineral density and markers of bone metabolism.*

Other exhibitors attending the meeting are: Eli Lilly and Company Ltd, Ferring Pharmaceuticals Ltd, Genzyme, Novo Nordisk Pharmaceuticals and OBI-DSL

Sponsorship opportunities are still available: contact Feona Horrex (Tel: 01454-642212; Email: conference@endocrinology.org).

For further information contact
BES, 22 Apex Court, Woodlands,
Bradley Stoke, Bristol BS32 4JT, UK
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Email: info@endocrinology.org;
Web: www.endocrinology.org/sfe/confs.htm)

COMMITTEE NEWS - *The latest from each of the Society's committees*

COUNCIL OF MANAGEMENT In addition to responding to the proposal from EFES for the formation of a European Society of Endocrinology (see details on page 3), Council suggested that criteria for travel grants should be revisited, to widen the eligibility of basic scientists. They have also approved:

- financial statements for the year to 30 April 2004
- reappointment of the auditors (Chantry Vellacott DFK)
- the reserve policy for the main Society fund
- applications for Corporate Membership from Ferring Pharmaceuticals Ltd and Servier Laboratories Ltd
- the Society's new officers (from November 2005): John Wass as Chairman, Julia Buckingham as General Secretary, and David Ray as Programme Secretary
- guidelines for interaction between the Society and commercial companies
- recommendations from the Committees Review Working Party regarding the remits and structure of all the Society's committees (committee members will receive the revised remits shortly)
- the concept of a new, distinct Corporate Liaison Committee to establish a method for regular two-way communication between the Society and endocrinology in industry.

AWARDS The Society for Endocrinology/Clinical Endocrinology Trust Clinical Fellowship has been awarded to Alia Munir (further details on page 3).

BES The abstract deadline has just passed for the BES 2005 meeting in Harrogate and registrations are starting to come in. The BES Committee are actively supporting the Programme Organising Committee for the European Congress of Endocrinology (ECE) to be held in Glasgow on 1-5 April. This committee first met in October, and the Local Organising Committee will meet in December.

CLINICAL Jayne Franklyn (Birmingham) will be the 2005 Clinical Endocrinology Trust Lecturer. The Committee have approved the draft scope of the Society's contribution to the strontium ranelate appraisal by NICE. They have also identified that the Society's statement on somatostatin analogues in acromegaly needs revision. Pierre Bouloux has agreed to remain as Programme Advisor until the end of his term as chair of the 2006 Programme Organising Committee for the ECE/BES meeting. Alongside a call for elected members, this committee also seeks two SpR representatives.

NURSE As well as compiling suggestions for nurse sessions at the November 2005 and BES 2006 meetings, development of the 2005 training course programme is underway, on 'Reproduction - from birth to the menopause'.

PROGRAMME Attendance at the 2004 Society meeting was over 400 with all strands well attended over the three days. The committee discussed plans for the programme for 2005, including a Clinical Endocrinology Trust Lecture for the Starling centenary. The preliminary programme will be available next May. The Committee have welcomed the new Programme Secretary, David Ray, who will be shadowing Ann Logan until the next AGM.

PUBLICATIONS Items on the agenda for the next meeting include the Society journals' recent move to HighWire, new Editors-in-Chief for *Journal of Endocrinology* and *Endocrine-Related Cancer*, pharmaceutical corporate influences in publishing, the Starling centenary and Open Access.

SCIENCE Martin Hewison is the new Council representative, replacing Robert Abayasekara. K Docherty, M Korbonits, I McEwan and J Pell have now joined the committee. Members have been asked for nominations, to enable Committee member rotation and representation of a wide range of interests. Feedback from BES 2004 and the Molecular Endocrinology Workshop at Summer School 2004 was very positive. A working party to review Society meetings, set up by Ann Logan, will address requests that chairs of oral communication sessions are more proactive in eliciting audience questions.

OBITUARY

D K O'Donovan

Denis Kenry O'Donovan, or 'DK' as he was known to all, graduated from Newman's Catholic University Medical School in Dublin (later to become University College Dublin). He undertook his postgraduate work under J C Collip in Magilll University, Montréal, before returning to Dublin to take up clinical appointments in St Vincent's and St Luke's Hospitals. Later he became Professor of Medicine at University College Dublin.

One of the pioneers of Irish endocrinology, DK was a towering figure in Irish medicine, making an immeasurable contribution to clinical medicine, teaching and research. He stimulated both deep affection and awe in generations of medical students as they passed through Ireland's largest medical school, and many of them later achieved prominence both at home and abroad.

DK was a founder member of the Society for Endocrinology in 1946, as well as the Thyroid Club and more recently the British Thyroid Association. At home he helped found the Irish Endocrine Society and was its second President (1978-1980). In addition to his personal commitment to research, DK chaired the Medical Research Council of Ireland for an unprecedented 13 years from 1973 to 1986.

His major clinical and research interest was the investigation of thyroid disease. Many colleagues and students remember 'DK's little fingers', as he recorded a syndrome combining developmental anomalies of the fifth digit with goitrous disease. On his retirement he expanded this work to study the hypothesis that thyroid hormone guided or influenced the evolution of *Homo sapiens*.

In his 95th year, and despite being retired for many years, DK maintained a lively interest in research and was preparing a paper entitled 'Thyroid hormone in the ascent to man' in the days before he died on 28th February. He is survived by Phyllis, his wife of 65 years, seven children and eleven grandchildren.

PETER SMYTH

With regret

We are sorry to announce the deaths of Sir Gordon Wolstenholme, Honorary Member of the Society, and Professor G E Lamming, who was a Senior Member. We hope to publish obituaries at a later date.

Voice of Young Science

The Society recently secured four places for Young Endocrinologists to attend 'Voice of Young Science: Science in the British Media'. Organised by Sense About Science, this workshop was held in London on 17 September 2004. Two of the delegates, Deborah Wake and Alicia Parkes, now examine the media's role in communicating science.

So 'science is the new post modernism'. No longer for nerds, it's trendy, sexy and in demand ... hooray! From dinner table conversation to the latest reality TV show, health and science issues are enjoying a surge of public interest. As active members of the scientific community, we should be embracing this timely opportunity to educate and inform a knowledge-thirsty public through the media industry.

But there are many recent examples of science being misreported, over-sensationalised or clearly biased in the news: 'MMR causes autism', 'Mobile phones cook your brain', 'Kisses may lead to cot death'. It is no wonder that scientists feel irritated at times with the British press. This workshop helped bridge the gap between scientists and the media, and dismissed the misconception that the two are 'in opposition'.

The event was a pilot, which explored communicating science to a wider audience. Its interactive forum allowed enthusiastic young scientists from various disciplines to hear and question prominent figures from science and the media. Professor Adam Finn, Dr Rachael Batterham and Dr Carly Stevens told the delegates about their experiences, both positive and negative, when their research hit the headlines. Later, the tables were turned when Alex Kirby from BBC Online, Tom Fielden from the Today programme, Anna Fazackerley from *Times Higher* and Mark Henderson from *The Times* fielded a barrage of questions from the delegates.

There are clear conflicts of interest between journalism and science, as Mark Henderson freely admitted, 'We work in different timescales and have different daily pressures. At the end of the day we [the press] have to write eye-catching stories and sell newspapers.' However, Alex Kirby believes that there is a genuine desire within the media to 'educate, inform and entertain … in that order'. There was no representation from the tabloid newspapers, who may have had a more difficult corner to defend.

It was clear from the event that the media industry is keen for young scientists to speak out. Approaching the media with clear soundbites will reduce errors. We also have a responsibility to ensure that the public is correctly informed after inaccurate or unfair reporting.

Fundamentally, there is a need for better communication between scientists and journalists. The London Science Media Centre, which served as the venue for this forum, is a great example of how that gap can be narrowed. Fiona Fox, the Centre's founder, explained how it provides PR support for scientists and expert scientific liaison for the press. This includes a database of 1000 scientific experts that journalists can approach when reporting scientific stories.

There is a need to move away from an environment where scientists and health professionals feels threatened, manipulated or misquoted to a more open and balanced approach. We all have a duty to educate and advise the public about important, critically reviewed breakthroughs, and we should take a proactive role to ensure clear, educational and unbiased reporting. This workshop encouraged better understanding between scientists and journalists, and so events like this may go some way to achieving that goal.

DEBORAH WAKE
ALICIA PARKES

Following the success of this inaugural event, Sense About Science are likely to run a similar workshop next year. The Society will again endeavour to secure places for Young Endocrinologists. If you would be interested in the 2005 event email jane.shepley@endocrinology.org.

Victim support

A new organisation, Victims of Animal Rights Extremism (VARE), has been established for people who have been threatened or attacked by animal rights extremists. Launched in the House of Commons at the end of April, VARE has two objectives. First, it will provide advice, information and mutual support to people who are the target of extremists. Secondly, it will serve as a focus for lobbying the Government to bring in tougher laws against extremism.

The group is entirely dependent on voluntary effort, mostly from the Research Defense Society, and has very little funding. Its website at www.vare.org.uk contains advice and information about animal rights attacks and what can be done to protect against them.

Towards a European Society of Endocrinology

In response to the proposal of the Executive Committee of EFES to form a European Society of Endocrinology, the Chairman of the Society for Endocrinology sent out a questionnaire to all members in May.

Members' responses to the questionnaire were presented to the Council of the Society for Endocrinology, and a response to EFES was formulated - the Society is in support of the formation of a European Society of Endocrinology and an annual meeting of this should be held every September / October.

The Society response was presented to EFES in November, as were the responses from all the European Societies. Twenty-four societies attended in all.

The combined decision of the European Societies was to form a European Society, and to hold an annual European meeting ideally during the last week in April or the first week in May. This obviously has implications for the timing of the BES meeting, and this will be discussed by the Society's working group on meetings.

Thank you to all those members who contributed to the questionnaire.

SPOTLIGHT ON THE

Turner Syndrome Support Society

The Turner Syndrome Support Society (TSSS) was established 5 years ago under the auspices of the Child Growth Foundation. However, rather than just affecting 'growth', Turner syndrome (TS) is a cradle-to-grave condition that needs lifelong treatment. The prime aim of the TSSS is to support patients and their families. It also aims to educate the public as well as health and education professionals about the condition. The TSSS believes that patients should be viewed holistically, as this could eliminate or at least ease several problems associated with the syndrome.

Within 6 months of becoming independent, the TSSS was involved with NICE's assessment of paediatric GH treatment. Though daunting, we were complimented on our professionalism and gained a reputation as a credible organisation. This helped to raise our profile, resulting in more contact with doctors, who then pointed their patients in our direction.

TS occurs in 1:2000-1:2500 live female births, and there are at least 11 000 girls and women in the UK with the syndrome. However, only a small percentage of these have been diagnosed. Ideally diagnosis should be made at birth, or at least in early childhood. Sadly this is not the case, and the TSSS is contacted by patients who have been diagnosed in their late teens or later, including one call from a 70-year-old women who had just learnt she had TS!

We would like to think that we have played a small part in the recent improvement in the average age at diagnosis by publishing our book, *Turner syndrome: lifelong guidance and support.* This book was launched at the 2002 meeting of the British Society for Paediatric Endocrinology and Diabetes, and has been very well received by doctors and patients alike. Containing everything you need to know about TS, it will be updated regularly in line with the latest research and treatments.

The TSSS maintains a good relationship with the medical profession, including endocrinologists, gynaecologists and geneticists. We have encouraged the development of adult TS clinics around the UK, and are now working with specialists to help smooth the transition from paediatric to adult care. In some regions, girls are still being discharged to the care of their GP who, with the best will in the world, will have limited knowledge of TS and the monitoring and treatments that allow patients to lead a normal healthy life.

Doctors and nurses kindly donate their free time to speak at our open days and weekend annual conference for members. Many have told us how much it benefits them, as they learn more about life with TS. In fact, we are now in the happy position of occasionally having too many willing speakers! By the same token, the TSSS provides members to speak at training days organised by the medical profession, who share their day-to-day experience of TS to help others.

Like other small charities, funding is a problem, but the TSSS has been fortunate to have support for projects by unrestricted educational grants from pharmaceutical companies that produce GH. This has enabled us to produce information about TS, like the book mentioned above, a DVD/CD (*Talking about Turner syndrome*), and booklets on specific topics like *Education and TS*. Members raise funds to help with the costs of running the society. Our only paid employee, the Executive Officer, runs the office, whilst the society is run by a dedicated team of volunteers who serve as trustees and committee members. The TSSS web site and quarterly newsletter 'ASPECTS' are produced by volunteers with a personal interest in TS.

Our prime aim will remain unchanged, but we recognise that there will be an increasing need for patients, health professionals and the TSSS to work together to improve knowledge of TS and care of those with the syndrome. In its first 5 years, the TSSS has made an excellent start and we now look forward to working with the Society for Endocrinology and other members of the BES to build on this foundation.

For further information about the work of TSSS and a publications list, contact TSSS, 12 Irving Quadrant, Hardgate, Clydebank G81 6AZ (Tel: 01389-380385; Fax: 01389-380385; Email: turner.syndrome@tss.org.uk; Web: www.tss.org.uk).

Dealing with doping

Two of the leading experts in sport-related drug abuse give an insight into this notorious and newsworthy field of endocrinology.

'Drug abuse scandal' makes a good headline as yet another athlete fails a drug test. The abuse of performance-enhancing drugs in sport is undoubtably a matter of concern, and the media would have you believe it's widespread, despite the relatively low incidence of positive dope tests. Although the extent of doping is debateable, few doubt that the rewards of sporting success (financial and otherwise) are powerful incentives for some competitors to look for every possible means of improving performance, even given the risks to reputation and health.

Less widely publicised is the use of such drugs generally in society, especially anabolic-androgenic steroids, for cosmetic benefits. Anabolic steroids may be regarded (wrongly) as a relatively harmless method to aid development of bulging muscles and 'six pack' stomachs. Surveys estimate that up to 5% of UK gym users take these drugs, rising to 25-50% amongst competitive body-builders. Although they are prescription-only medicines, they are relatively easy to obtain via the 'underground market' or the internet.

For amateur competitors, the major hazard is the potentially adverse effect on health. But in professional sport, careers are in jeopardy. Sport's governing bodies are obliged to operate a surveillance programme to meet the requirements of the World Anti-Doping Agency (WADA). WADA-accredited doping control laboratories analyse over 150 000 samples worldwide each year. Adverse findings are reported in 1-2%, mainly due to anabolic steroids like testosterone and nandrolone. The lack of established procedures to detect anabolic peptide administration (human GH, insulin and IGF-I) makes it difficult to ascertain the extent of their abuse. It is, however, generally accepted that GH is highly valued as a performance-enhancing drug, not least because it is difficult to prove abuse. GH tests are currently being refined for use in WADA-accredited laboratories.

The need to examine so many samples is a major challenge for the endocrine analyst. It is not enough to be able to screen rapidly for more than 100 different drugs, many in minute amounts. Positive findings must be confirmed to a degree that will withstand legal challenge should the case reach a disciplinary hearing.

Analyses for drugs and their metabolites almost exclusively rely on chromatographic separation followed by mass spectrometry for identification. Criteria for confirmation are agreement of retention time with a reference sample, and concordant data, with a minimum of three diagnostic ions being mandatory. The detection of a foreign (xenobiotic) anabolic steroid or its metabolite(s) in urine is considered proof that there is a case to be answered.

So-called designer drugs pose a major problem. Chemical modification may allow a drug to escape detection during screening, yet it retains pharmacological activity. For example, tetrahydrogestrinone is formed by saturation of the ethinyl group of the progestogen gestrinone. It was found in a urine sample given by British athlete Dwain Chambers, but only following characterisation of the residue

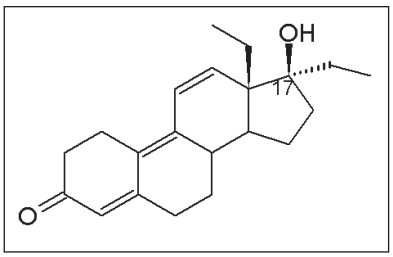

FIGURE 1 Structure of tetrahydrogestrinone (THG). Saturation of the ethinyl group of the progestogen gestrinone (addition of four hydrogens across the carbon-carbon triple bond) forms THG.

from a spent syringe that was provided anonymously to the US Anti-Doping Agency. Other designer drugs may as yet be undetectable. It is clearly not ideal to have to wait for someone within the sporting community to alert the authorities, and a more general screening process for anabolic steroids to highlight any suspicious compound is urgently needed.

Some performance-enhancing hormones are produced naturally, so detecting their administration is difficult. In the case of testosterone, the approved test determines the ratio of testosterone concentration to that of its naturally occurring inactive epimer epitestosterone. The resulting T/E ratio is independent of the dilution of the urine. Normally, T/E approximates 1 but after administration of testosterone the urinary excretion of testosterone increases and hence the ratio augments. In the past, accredited laboratories reported any samples with a ratio greater than 6 but from next year the WADA will implement the lowering of the laboratory reporting threshold to a ratio of 4. This test has been largely successful for over 20 years, but it can be circumvented by co-administering epitestosterone with testosterone, and it is difficult to establish rapidly whether an individual is a natural biological outlier, i.e. someone who normally has an elevated ratio.

Determining the carbon isotope ratio of the excreted steroids has significantly advanced the detection of natural androgen administration, and is increasingly important in drug control. The $^{13}C/^{12}C$ content of endogenously produced steroids reflects the average

continued overleaf

Dealing with doping

Continued from previous page

found in ingested carbon sources. However, testosterone in pharmaceuticals is mainly synthesised from soya-derived sitosterol, which has a lower ^{13}C content (see figure 2). Isotope ratio mass spectrometry can detect the abnormally low isotopic ratio of testosterone metabolite(s) in urine associated with testosterone administration.

Immunoprocedures are acceptable in detecting protein hormone abuse, though the increasing sensitivity of mass spectrometry, with its better discrimination, will probably soon become the method of choice.

Analytical sensitivity is crucial to identify athletes who cease drug administration in anticipation of a test. But such sensitive tests may give positive results following the ingestion of a contaminated dietary supplement. Athletes regard nutrition as vital in maintaining fitness. For many, inclusion of specialised dietary supplements is obligatory, and the number available is huge. However, in a survey by the Cologne WADA-accredited laboratory, 15% of the supplements tested contained steroids banned by WADA as performance-enhancing drugs, which were not declared on the label. Any athlete using these supplements is therefore at risk of testing positive, despite the amounts of steroid being small and in almost all cases not having any significant pharmacological effect.

The cause of contamination is unknown. One hypothesis for the occurance of the problem is possible cross-contamination during the manufacture of certain supplements. However, the result for the athletes can be potentially disastrous. Recently a number of professional tennis players, including Greg Rusedski, the British number 2, tested positive for 19-norandrosterone, a metabolite of a number of prohibited 19-norsteroids. In these cases, the disciplinary tribunal accepted the players' claim that the contaminated supplements had been provided by coaches who had been employed by the tournaments' organisers, and so the players were therefore exonerated from blame. But few athletes can avail themselves of such a defence, and attempting retrospectively to locate the source of the steroid is extremely difficult.

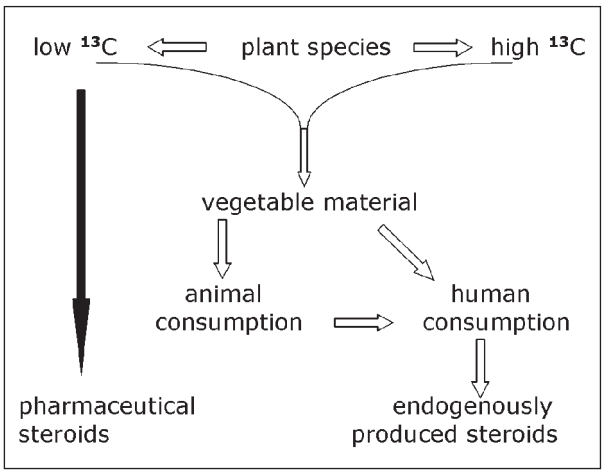

FIGURE 2 Endogenously produced steroids have a $^{13}C/^{12}C$ content that reflects the average of that in the carbon sources ingested, whereas testosterone in pharmaceutical formulations is mainly synthesised from sitosterol obtained from the soya plant, which has a smaller ^{13}C content. Isotope ratio mass spectrometry can be used to detect testosterone administration by determining whether an abnormally low isotopic ratio of testosterone metabolite(s) is present in urine.

The Association of Tennis Professionals has become so concerned over the problem that it has announced that it is making available to competitors supplements which have been analysed to ensure that they are free of any banned substances

Although hormones and other drugs are sometimes appropriate for the effective treatment of disease, abuse courts the risk of potentially serious unwanted effects. Unfortunately, this is often disregarded, maybe through ignorance, or because the perceived reward is thought to justify the risk. Two extreme examples come to mind. Body-builders may exploit the powerful anabolic effects of insulin, which is inexpensive and easier to obtain than GH, despite the risk of catastrophic hypoglycaemia if too large a dose is administered. Top-level athletes have been known to use erythropoietin (Epo) to increase their haemoglobin concentration and oxygen delivery to their tissues, but the resultant increase in blood viscosity is associated with a greater likelihood of thrombotic events, like myocardial infarction and strokes. An immunoprocedure to detect administration of Epo has recently been implemented.

Anabolic steroids are often administered in much greater doses than those used for legitimate treatment. They are sometimes taken in combinations ('stacking') over cycles of 6-12 weeks, followed by an off-period, although some body-builders take them virtually continuously. In these doses they have numerous adverse effects, many of which are insidious as they only become apparent after chronic administration (many months to years). These include liver damage associated with the orally active C-17 alkylated steroids, cardiovascular effects like lipoprotein profile changes and left ventricular hypertrophy, and irreversible virilisation in women. Permanent scarring can result from severe cystic acne. The psychological effects are difficult to evaluate scientifically, but anabolic steroid abuse has been implicated in some cases of violent behaviour ('roid rage') and even murder. Adverse physiological manifestations can also have subtle psychological effects, for instance when individuals perceive that onlookers are surprised to hear a deep voice coming from a woman or observe a man with obvious gynaecomastia.

GPs or clinical endocrinologists may well see patients who seek advice because they are abusing hormones, or who exhibit symptoms that may be caused by these agents. One-third of the respondents to a small survey of general practices had seen patients whom they knew or suspected were anabolic steroid users. Most had seen fewer than three in a year, but it is important for physicians to be aware of the effects of such drug abuse, if only to avoid the need for lengthy and unnecessary follow-up investigations.

Controlling the abuse of hormones is difficult and expensive. The adverse effects can be extremely damaging and may affect not just the abuser, but also those with whom they come into contact. Education of athletes in particular, and indeed of the general population, may be the best way to deal with what appears to be a growing problem.

ANDREW KICMAN
VIVIAN JAMES

Vivian James is Emeritus Professor of Chemical Pathology, University of London and Andrew Kicman is Head of R&D at the Drug Control Centre, Department of Forensic Science and Drug Monitoring, King's College London. They served as Chairman and Scientific Secretary respectively on the UK Sport Expert Committee enquiring into Nandrolone.

A sportsman speaks

Drug misuse in sport causes health problems. So why do people do it? Jane Shepley interviewed a professional body builder and gives us a candid insight into his sports drug culture.

As a lithe young man, John (not his real name) was an all round sportsman. In his thirties he began weight training, and his ambition drove him to compete at the highest level. At 5 feet 10 inches (178cm) tall, John's weight increased from 10.5 to 18 stone (67 to 114kg), and he competed in national competitions at 3% body fat (the average for a man of this age is about 15%). All this was possible with a lot of hard work, and a lot of drugs.

John trained 'naturally' at first, but he believed that performance enhancers like steroids and other hormones were vital for success. 'There is no point competing without them,' he told me, 'I couldn't even have beaten the women.'

When asked how common drug use was in his sport, John stated without hesitation that '99.9%' of competitors in the largest arenas, are assisted by steroids. So what about drug testing? 'If it was effective there'd be no-one left on stage!' was John's personal view. He added that even in the largest 'natural' body-building competitions, touted as completely drug-free, he believed that 90% of competitors took steroids, but knew how to avoid getting caught by using masking substances and drugs that are degraded quickly in the body.

Although body-building has a bad name for being rife with drugs, it is by no means alone. It is thought that in other sports such as football, cycling, athletics and rugby it is also extremely widespread. 'I know this business inside-out and there is no way that those rugby forwards get to the size they are without steroids, no matter how hard they train,' opined John.

Body-builders often obtain drugs from gym owners, but John preferred to seek dosage advice elsewhere, believing their interest was financial rather than in the health of their 'clients'. He instead surrounded himself with those he called the 'top people' for advice on optimising his performance, both naturally and with drugs. He particular rated his physiotherapist, himself a successful body-builder. John described him as an 'intellectual' with decades of experience and a deep knowledge of hormonal performance enhancers, apparently gleaned from scientific journals.

With guidance from his advisors, John said he would go to his dealer with a detailed shopping list, including 12- to 14-week courses of androgenic steroids. These enabled John to train harder and get much bigger, but also caused water retention. To be 'dry' in competitions , and best show off his physique, John would stick to anabolic steroids. In addition to these John used insulin (3-10IUs) first thing in the morning and directly after exercise on four training days each week. Two hours after each insulin dose he would take a shot of GH, which he described as the "champagne of hormones" due to its premium and scarcity. Whereas steroids are manufactured and imported to the UK in bulk (John estimated that the size of the international blackmarket industry was comparable to that of cocaine), growth hormone is supplied through theft from production lines and pharmacies or, more tragically, sold to dealers by low-income parents of children with GH deficiency.

Finally, John would use tamoxifen to counteract gynaecomastia, and duretics to help him 'dry out' before competitions.

With this extensive cocktail of drugs, it is no surprise that John's habit cost £6000-£7000 per year, with another £3000 on supplements, vitamins and antioxidants to further improve performance and minimise the side effects of the drug regime.

Although John was disciplined in his drug regime and apparently had knowledgeable advisors, he admitted that side effects were rarely discussed in his early years of competing. 'No-one in the gym talks about it, and no-one really cares anyway because they think it won't happen to them,' he related. Sporting ambition would seem to outweigh any fear of impotence, particularly as body-builders are thought to suffer from 'reverse anorexia': obsessional behaviour like anorexia nervosa, but with a drive to get bigger rather than smaller.

John stopped taking steroids 4 years ago, following medical advice after a blood clot formed in his thigh. He was told that this, along with arthritis in his hip, could result from extended steroid use. But John remains unconvinced, believing that his blood clot is more likely due to his strict low fat diet. In his opinion, the worst side effects have been the depression and low sex drive caused by hypogonadism. He confesses, 'I've been off the gear for nearly 4 years now, but my testosterone has not recovered.'

It was apparent that John had always paid great attention to his lifestyle and training, including his drug regime, so as to excel at his chosen sport. Though I had heard of a widespread drug culture in body-building, I was surprised at John's matter-of-fact approach. Far from being coy or regretful about 'abusing' drugs, he spoke of how he 'used' them as one aspect of an essential and well disciplined training regime in order to compete, and win, internationally.

And had it all been worth it? His reply, 'Absolutely, and I'd do it all again, but next time I'd start younger.'

JANE SHEPLEY

The views expressed are those of the interviewee and do not necessarily represent those of the staff or members of the Society for Endocrinology.

Making the most of microarrays

An advanced research technique or a diagnostic tool? Tim Rutherford takes a look at DNA microarrays and explores the future for this exciting new tool in endocrinology.

DNA microarrays can evoke feelings of fear, scepticism and horror: fear of the complexity, scepticism at the volume of uninterpretable data and horror at the costs of commercial arrays. Nevertheless, they are a natural tool in endocrinology, where transcriptional changes are usually a major primary response of the cell. Is the scepticism justified? Will microarrays remain esoteric or will they become a routine tool?

They are based on standard hybridisation technologies, like Northern blotting or FISH (fluorescence *in situ* hybridisation). Rather than immobilising the test RNA and labelling the probe, the test RNA is labelled (usually with a fluorescent dye) and the gene-specific probes are immobilised on a solid substrate. Probes can be printed onto glass slides, with anything from 100 to 20 000 genes represented on each. In addition to commercial manufacturers, many academic laboratories have facilities to print microarrays, but it takes a great deal of skill to reproducibly print them at a good quality. Alternatively, proprietary techniques developed by Affymetrix allow them to chemically synthesise up to 100 000 different oligonucleotide probes on a single glass chip.

The physical aspects of using microarrays are quite straightforward. Hybridisation and washing are easy in automated 'hyb' stations, and scanning takes no more than 10 minutes per array. Quantitating the spots on a scanned image is a semi-automated process, and no harder than deriving quantitations from Q-PCR plots. The shock comes when trying to interpret the vast amount of data produced by a large array! Research applications of microarrays involve a voyage into the unknown.

Diagnostic applications, however, will not need data interpretation from scratch. They will use pre-optimised decision-making algorithms (something familiar to many labs), based on a specific set of informative genes. In contrast to whole genome arrays, manufacturers are now moving towards small specific arrays for specific diagnostic purposes.

How do microarrays compare with Q-PCR? In terms of absolute sensitivity, Q-PCR is much more sensitive. Current microarray techniques require around 10µg total RNA, unless an amplification step is added, so this may limit their application. In terms of detecting differences, the two methods are comparable. Twofold changes in gene expression can reliably be determined, but smaller changes are hard to measure with confidence. Both methods require high quality RNA, which can be a problem in the clinical context, as well as rigorous procedures and assay design.

What about cost? Commercial microarrays are horrifically expensive, due to the very high design, development and set-up costs. But the manufacturing costs are low and prices can be expected to fall dramatically with time, increased volume and market competition. It can never be sensible to use a microarray for a single gene assay, but when the screening of a dozen or more genes is required, it may become a genuine and even economical alternative to Q-PCR, as you get a dozen or more results for the price of one.

The tools of biomics allow us to study multiple elements, whether genes, RNA transcripts, proteins or small metabolites, in a single assay. This allows a discovery-led approach to research. We do not approach a problem with a specific hypothesis and a single question, but instead with a large questionnaire. The results often lead us to new hypotheses.

In diagnostics, our discoveries may lead to a specific and informative assay, which can be worked up with more conventional single-assay techniques. Sometimes the patterns of gene or protein expression are highly diagnostic, but no single gene or protein gives reliable information in isolation. Here, looking at the complexity of gene expression in a key set of diagnostic genes may give much more information and a more reliable diagnosis than a single gene diagnostic. Microarrays, including DNA microarrays, may indeed be a diagnostic tool of the future.

TIM RUTHERFORD, ST GEORGE'S HOSPITAL MEDICAL BIOMICS CENTRE

Consultation with a matchmaker

I have no strong moralistic views about the existence of private practice. Certainly, compared with other specialties, an endocrinologist is unlikely to make much money through such practice, unless they adopt a 'focused therapeutic strategy' to 'cure' common problems such as obesity or sexual dysfunction.

On one morning each week, I see patients with the full breadth of endocrine problems in a spacious ex-merchant's house, now used as a private medical centre. A singular attraction for me is that this is the only medical practice in my working week that consists of a consultation between just myself and a patient.

All NHS clinics are teaching/training clinics and the room always buzzes with junior doctors, clinical attachments and students. Make no mistake I like teaching and training, but I also relish the chance to return to traditional professional basics: just the doctor and the patient with the dialogue uninfluenced by others.

It is probably also true that, in this setting, private patients articulate more readily their own opinions on health issues than the average NHS patient. Indeed, sometimes they will express views on non-medical topics. It was during a clinic a while ago that I met with Sally, who was just such a patient - and I was the topic!

I had treated her a number of years ago for Graves' disease. Eventually she required radioactive iodine, developed hypothyroidism, was treated with thyroxine, and had been clinically and biochemically euthyroid for several years. She attended annually for a check on her thyroid status and mild thyroid eye disease. She was a bubbly, engaging, positive young woman, who filled the room with chuckles and life. I was fond of her, she had real attitude. For one so young, she

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Testosterone: action, deficiency, substitution

Eds E Nieschlag & HM Behre, Cambridge University Press, 2004, 3rd edn, 737pp, £75/$130 (Hbk), ISBN 0-521-83380-9

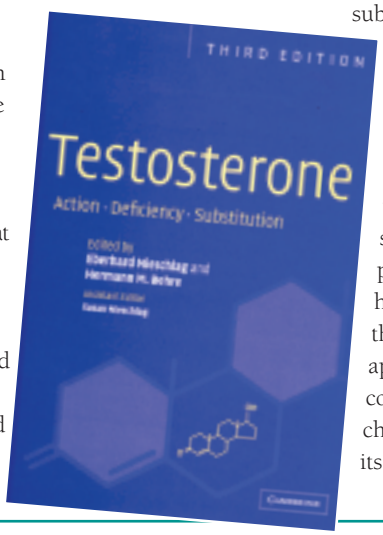
This is the third edition of what has become a standard reference work on all things androgenic. It is much enlarged compared with the previous (1998) version, with 737 pages split into 24 chapters, and a more spacious and attractive layout, which greatly increases readability. This expansion reflects growing interest, both clinical and scientific, in testosterone therapy, and the novelty of having a real and increasing choice in treatment options.

The German-biased list of contributors reflects its Münster editorial base. However, there is sufficient input from across Europe, the USA and Australia to reflect the state of the art. As before, there are important contributions from industry, with chapters from Organon (orally active steroidal androgens), Merck (5α-reductase inhibitors) and Jenapharm (SARMs).

These new chapters, with others on erythropoiesis, erection, the pathobiology of androgens in women, and dehydroepiandrosterone and androstenedione, replace three on transdermal androgen therapy. There is thus a shift in emphasis towards the broader roles of testosterone in male physiology, although, for example, the chapter on erythropoiesis contains much that is duplicated elsewhere. Each chapter concludes with a box of key messages: very useful when there is a wealth of data to assimilate, as is the case for cardiovascular disease.

The book begins with an updated overview of androgen synthesis and action, including speculation regarding a membrane androgen receptor akin to the new progesterone receptors. The following chapters cover the molecular biology and pathophysiology of the androgen receptor. They offer good summaries, but there is some overlap (e.g. relating to CAG repeat length, prostate cancer, and cardiovascular disease).

Subsequent chapters provide reviews of testosterone's role in traditional settings, including behaviour, spermatogenesis, hair, bone, muscle, and the prostate. The last is a tour de force including historical data from the 1940s through to a detailed analysis of the molecular biology of prostate hyperplasia and cancer. The chapter on muscle contains the superb studies conducted since the last edition, which explore the 'anabolic' effects of testosterone.



Kaufman and colleagues provide a thoughtful overview of androgens in male senescence, and the chapters from industry illustrate with a more biochemical flavour where we might be going. The chapter on androgens in women is particularly welcome, and covers the limited data on female androgen therapy. The treatment of hyperandrogenism in women, surely the most common testosterone-related condition seen by endocrinologists, is, however, missing. Perhaps better coverage is too much to expect from this book, with its heavily male emphasis, but the excellent chapter by Burger and Casson raises expectations that are then unfulfilled.

There is much to commend in this book, and while it has omissions, it remains an impressive overview. The change in emphasis reflects this subject's growing importance. Appropriately, the increase in bulk is muscle, not flab. It will be particularly useful for those wishing to broaden or update their knowledge of the effects of testosterone on diverse organs and systems. Chapters relating to prescribing practice in hypogonadism will appeal more to those new to the area, and at times appear rather didactic when compared with the flavour of other chapters, but this book easily justifies its place on the shelf.

RICHARD ANDERSON

Consultation with a matchmaker

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had already experienced several big hits: one infant death and one of her two remaining children afflicted with autism. She never complained about how life had treated her.

Towards the end of the consultation, having completed the medical review and discussed our respective holiday plans, she suddenly turned to me and asked, 'Are you ready?'

I was lost, I said, 'I have already examined you and you are fine.'

'No,' she said, 'are you ready?'

'Ready for what, Sally?'

'A date,' popped out from her oval mouth like a small explosion.

I should explain that my wife died 2 years ago. In a reasonably close-knit community this was common knowledge. I have to say I was thrown by the turn of the conversation and the loss of control. I felt very vulnerable. I mumbled a few sentences about coming out of a very traumatic emotional experience, when it dawned on me that she was not the least bit interested in the staging of my emotional rehabilitation. In reality, Sally was the reincarnation of Yente, the matchmaker from 'Fiddler on the Roof'. She fixed dates not emotions! She now moved into overdrive...

'I know the perfect woman for you; she likes walking, music. One of the six Benson sisters, Ruth, the prettiest one of them all. In fact they say it was because she was so pretty that she never married.'

I begged that she make no arrangements yet as I was not quite ready. How to end such a consultation? My customary handshake? Or should I give her a hug for showing a unique interest in my well-being, albeit just for the purposes of matchmaking? No, bad idea to start embracing young female patients at this (or indeed any) stage of a medical career. It was only when I heard myself ask 'Which one of us pays for this consultation?' that I realised I had recovered my composure.

'HOTSPUR'

Hot Topics

Catch up on leading research from the Society's journals courtesy of Jolene Guy, Gawain Lagnado, Richard Foulsham and Mona Munonyara.

Stem cell therapy for diabetes

Patients with type 1 diabetes may soon have an alternative treatment option. In their enlightening commentary, Burns and co-authors explain recent advances in stem cell biology that raise hopes of transplanting stem cell-derived tissue instead of human primary islets of Langerhans, and would effectively remove insulin dependency. A lack of donors has previously made transplantation difficult. However, with the creation of embryonic stem cells that are immunologically autologous with the patient, functional pancreatic β-cells may be produced and the donor problem avoided.

Is stem cell treatment really feasible? In the authors' view, two main issues remain to be resolved. The first is which stem cells to use, and the second whether insulin-producing cells derived *in vitro* need to undergo the same developmental pathway that leads to β-cell differentiation *in vivo*.

As the immune system may be primed to destroy even immunologically autologous pancreatic β-cells, the best research strategy may be to focus on generating cells that function as β-cells, but which are not recognised by recipients' immune system. **JG**
(See the full article in Journal of Endocrinology ***183(3)****, December 2004)*

Hypothalamic releasing factors

A century after the term 'hormone' was first coined, Guillemin begins our series of commemorative *Centenary reviews* with an insightful article on the hypophysiotrophic peptides, a field of research he has led for many years.

This is not just an enthralling account of progress in methodology, nomenclature and understanding of these hormones' physiology and medical endocrinology. It also expertly summarises current knowledge by referencing the latest studies that employ cutting-edge molecular biology techniques. The result is a thoughtful description that encapsulates the full range of physiological function and localisation of the hypothalamic releasing hormones, and highlights newly discovered, often surprising, autocrine and paracrine activities. It will be an invaluable reference to the endocrine community.

Looking to the future, Guillemin anticipates possible applications for this research in diverse aspects of clinical medicine, from cardiac function to imaging and control of tumour growth. **GL**
(See the full article in Journal of Endocrinology ***184(1)****, January 2005)*

Receptors run like CLOCKwork

Organisms appear to anticipate and adapt to rhythmic changes in their environment. Recent genetic and biochemical approaches have identified the genes that contribute to the generation of these rhythms. Rev-erbα is an orphan member of the nuclear receptor superfamily found in the nuclei of cells in most animal tissues. It is a constitutive transcriptional repressor and is expressed in a circadian rhythm.

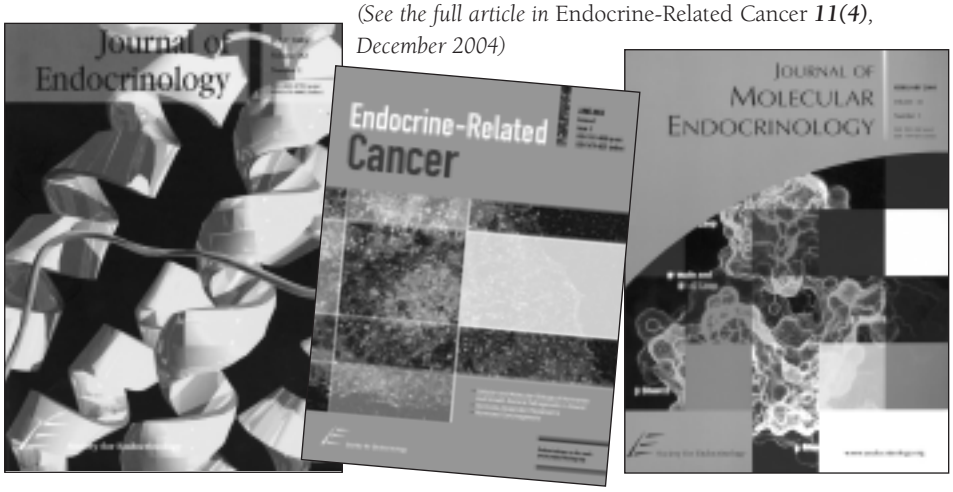
Here, Triqueneaux and co-workers report that two isoforms of Rev-erbα mRNA are generated through the use of two different promoters. The promoter regions of these isoforms contain DNA sequences that are the same as E-box DNA, which is known to function as a response element to core circadian clock components such as the CLOCK-BMAL1 heterodimer, involved in the transcription of clock-regulated genes. They have also found evidence for the presence of this activity in zebrafish and mice. This demonstrates that CLOCK is an important regulator of Rev-erbα in evolutionary distant vertebrates, and suggests a role for Rev-erbα in the circadian clock output. **RF**
(See the full article in Journal of Molecular Endocrinology ***33(3)****, December 2004)*

GnRH in malignancy

GnRH and its receptor (GnRHR) have been detected in breast, endometrium, ovarian and prostate cancers. Native GnRH, as well as GnRHR agonists and antagonists, has been shown to inhibit proliferation of cancer cells in a dose- and time-dependent manner. Consequently, GnRH and GnRHR have attracted considerable interest as therapeutic targets for hormone-dependent cancers. In this comprehensive review, Harrison and colleagues give an overview of GnRH/GnRHR cell signalling and expression, then evaluate the use of GnRH analogues in various malignancies, including findings from their own original research.

The authors have demonstrated that GnRH-PAP, a conjugate of GnRH and pokeweed antiviral protein, inhibited growth of cells expressing GnRHRs, including prostate and breast cancer cell lines. In comparison with control cells, cytotoxicity was 50-fold increased in the cancer cells.

This new and open field of biology is limited by lack of functional data in native cells, and further studies are needed to elucidate the physiological roles of GnRH and GnRHR in normal and cancerous tissues. **MM**
(See the full article in Endocrine-Related Cancer ***11(4)****, December 2004)*



AICOG 2005: All India Congress of Obstetrics and Gynaecology

Aurangabad, India, 6-9 January 2005.

Contact: Conference Secretariat AICOG 2005, Ashwini Hospital, 12, Samarthnagar, Aurangabad - 431 001 (MS), India (Tel: +91-240-2348731; Email: conference@aicog2005.com; Web: www.aicog2005.com).

CSSAM/ISSAM North American Congress on the Aging Male

Vancouver, Canada, 2-5 February 2005.

Contact: Irwin Kuzmarov, CSSAM/ISSAM North American Congress on the Aging Male, Kenes International, 17 Rue du Cendrier, PO Box 1726, CH-1211 Geneva 1, Switzerland (Tel: +41-22-9080488; Fax: +41-22-7322850; Email: aging@kenes.com; Web: www.kenes.com/aging).

1st National Conference on Obesity and Health

Manchester, UK, 7-8 February 2005.

Contact: Hannah Leach, Index Communications Meeting Services, Crown House, 28 Winchester Road, Romsey SO51 8AA, UK (Tel: +44-1794-511331/2; Fax: +44-1794-511455; Email: ncoh@indexcommunications.com; Web: www.obesityandhealth.co.uk).

Society for Endocrinology Clinical Cases Meeting

London, UK, 16 February 2005.

Contact: Ann Lloyd, Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: ann.lloyd@endocrinology.org; Web: www.endocrinology.org/sfe/train.htm).

8th Mayo Clinic Endocrine Course

Kohala Coast, HI, USA, 27 February-5 March 2005.

Contact: William Young, Mayo Clinic, 200 First Street, Rochester, MN 55905, USA (Tel: +1-507-2842191; Fax: +1-507-2845745; Email: young.william@mayo.edu; Web: www.mayo.edu/cme).

5th European Congress on Clinical and Economic Aspects of Osteoporosis and Osteoarthritis

Rome, Italy, 16-19 March 2005.

Contact: YP Communication, Boulevard G Kleyer 108, 4000 Liège, Belgium (Tel: +32-4-2541225; Fax: +32-4-2541290; Email: yolande@piettecommunication.com).

9th Pan Arab Conference on Diabetes

Cairo, Egypt, 22-25 March 2005.

Contact: Pan Arab Conference on Diabetes, 19 Nasouh Street, Zeitoun, Cairo 11321, Egypt (Tel: +20-2-2131868; Fax: +20-2-2723693; Email: info@arab-diabetes.com; Web: www.arab-diabetes.com).

35th Congress of the International Union of Physiological Sciences

San Diego, CA, USA, 31 March-5 April 2005.

Contact: IUPS 2005, The American Physiological Society, 9650 Rockville Pike, Bethesda, MD 20814-3991, USA (Tel: +1-301-6347160; Fax: +1-301-6347241; Email: iups2005@the-aps.org; Web: www.iups2005.org).

Fertility 2005 (4th Joint Meeting of BAS, BFS and SRF)

Warwick, UK, 2-6 April 2005.

Contact: Debbie Walker, World Event Management, Summit House, Woodland Park, Cleckheaton BD19 6BW, UK (Tel: +44-1274-854100; Fax: +44-1274-854110; Email: fertility2005@world-events.com; Web: www.jointukfertility.co.uk).

BES 2005: 24th Joint Meeting of the British Endocrine Societies

Harrogate, UK, 4-6 April 2005.

Contact: British Endocrine Societies, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: info@endocrinology.org; Web: www.endocrinology.org/sfe/confs.htm).

Do Corticosteroids Damage the Brain? Symposium in Honour of Professor Joe Herbert

Cambridge, UK, 7 April 2005.

Contact: Michael Hastings, MRC Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH, UK (Tel: +44-1223-402307/402411; Fax: +44-1223-402310; Email: mha@mrc-lmb.cam.ac.uk; Web: www.anat.cam.ac.uk/jhsymposium).

4th Congress of the Mediterranean Society for Reproductive Medicine (MSRM)

Cote d'Azur, France, 7-9 April 2005.

Contact: Dr Ashraf Samir, PO Box 125, Ibrahimieh, Alexandria 21321, Egypt (Tel: +20-3-3595043; Fax: +20-3-3595044; Email: drashraf@aast.edu).

1st International Congress on 'Prediabetes' and the Metabolic Syndrome: Epidemiology, Management and Prevention of Diabetes and Cardiovascular Disease

Berlin, Germany, 13-16 April 2005.

Contact: Kenes International (Tel: +41-22-9080488; Fax: +41-22-7322850; Email: prediabetes@kenes.com; Web: www.kenes.com/prediabetes).

ATA 2005: Horizons in Thyroidology

Baltimore, MD, USA, 15-17 April 2005.

Contact: American Thyroid Association, 6066 Leesburg Pike, Suite 650, Falls Church, VA 22041, USA (Tel: +1-703-9988890; Fax: +1-703-9988893; Email: admin@thyroid.org; Web: www.thyroid.org).

Diabetes UK Annual Professional Conference 2005

Glasgow, UK, 20-22 April 2005.

Contact: Conference Team (Tel: +44-20-74241156; Email: conferences@diabetes.org.uk).

16th IFCC-FESCC European Congress of Clinical Chemistry and Laboratory Medicine

Glasgow, UK, 8-12 May 2005.

Contact: EuroMedLab Glasgow 2005 (Tel/Fax: +44-141-4341500; Email: euromedlab2005@meetingmakers.co.uk; Web: www.glasgow2005.org).

48ème Journées Internationales d'Endocrinologie Clinique

Paris, France, 19-20 May 2005.

Contact: Dr G Copinschi, Laboratory of Experimental, Brussels Free University, CP 618, 808 Route de Lennik, B-1070 Brussels, Belgium (Email: klotz@ulb.ac.be; Web: www.endocrino.net).

1st Educational EUGOGO Course on Graves' Orbitopathy

Thessaloniki, Greece, 26-27 May 2005.

Contact: Gerasimos Krassas (Tel: +30-2310-479633; Fax: +30-2310-282476; Email: krassas@the.forthnet.gr; Web: www.ghsociety.com/index_eugogo.html).

6th Puberty Conference

Evian, France, 26-28 May 2005.

Contact: Catherine Hellstedt, Congrex Sweden AB, Karlavägen 108, PO Box 5619, SE-114 86 Stockholm, Sweden (Tel: +46-8-4596637; Fax: +46-8-6619125; Email: catherine.hellstedt@congrex.se; Web: www.congrex.com/puberty2005).

ECO 2005: 14th European Congress on Obesity

Athens, Greece, 1-4 June 2005.

Contact: Triaena Tours and Congress SA, Atchley House, 15 Messogion Ave, 115 26 Athens, Greece (Tel: +30-210-7499315; Fax: +30-210-7705752; Email: congress@triaenatours.gr; Web: www.eco2005.gr/index.html).

Gonadal and Nongonadal Actions of LH/hCG

Turku, Finland, 3-4 June 2005.

Contact: Nafis Rahman, Department of Physiology, University of Turku, Kiinamyllynkatu 10, FIN-20520 Turku, Finland (Tel: +358-2-3337577; Fax: +358-2-2502610; Email: lh-congress2005@utu.fi; Web: www.lh-congress2005.utu.fi).

ENDO 2005

San Diego, CA, USA, 4-7 June 2005.

Contact: The Endocrine Society, 8401 Connecticut Avenue, Suite 900, Chevy Chase, MD 20815-5817, USA (Tel: +1-301-9410200; Fax: +1-301-9410259; Email: endostaff@endo-society.org; Web: www.endo-society.org/scimeetings).

2nd Joint Meeting of the European Calcified Tissue Society and the International Bone and Mineral Society

Geneva, Switzerland, 25-29 June 2005.

Contact: European Calcified Tissue Society, PO Box 337, Patchway, Bristol BS32 4ZR, UK (Tel/Fax: +44-1454-610255; Email: admin@ectsoc.org; Web: www.ectsoc.org).

Bone and Tooth Society Annual Meeting

Birmingham, UK, 4-5 July 2005.

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

Society for Endocrinology Molecular Endocrinology Workshop at Summer School

Durham, UK, 5 July 2005.

Contact: Ann Lloyd, Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: ann.lloyd@endocrinology.org).

Advances in the Molecular Pharmacology and Therapeutics of Bone Disease

Oxford, UK, 6-7 July 2005.

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

Society for Endocrinology Advanced Endocrine Course at Summer School 2005

Durham, UK, 6-7 July 2005.

Contact: Ann Lloyd, Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: ann.lloyd@endocrinology.org).

Society for Endocrinology Clinical Practice Day at Summer School 2005

Durham, UK, 8 July 2005.

Contact: Ann Lloyd, Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: ann.lloyd@endocrinology.org).

International Symposium on Paget's Disease

Oxford, UK, 8-9 July 2005.

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

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a breakthrough treatment for acromegaly…

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(pegvisomant powder and solvent for solution for injection)

IGF-1 normalisation is within reach

Somavert® (pegvisomant) Prescribing Information.
Presentation: Somavert powder and solvent for solution for injection is supplied in vials containing 10mg, 15mg or 20mg of pegvisomant. After reconstitution, 1ml of solution contains 10mg, 15mg or 20mg of pegvisomant. **Indications:** Somavert is used in the treatment of patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalise IGF-I concentrations or was not tolerated. **Dosage:** Adults including elderly: A loading dose of 80mg should be administered subcutaneously under medical supervision. Following this, 10mg reconstituted in 1ml of water for injections should be administered once daily. Dose adjustments should be based on serum IGF-I levels, measured every four to six weeks, and appropriate dose adjustments made in increments of 5mg/day in order to maintain the serum IGF-I concentration within the age-adjusted normal range. The maximum dose should not exceed 30mg/day. Children: The safety and effectiveness of Somavert have not been established. **Contra-indications:** Hypersensitivity to pegvisomant or any of the excipients. **Warnings and precautions:** Growth hormone-secreting pituitary tumours may sometimes expand, causing serious complications (for example, visual field defects). Treatment by Somavert does not reduce tumour size. All patients with these tumours should be carefully monitored. Serum concentrations of alanine aminotransferase (ALT) and aspartate transaminase (AST) should be monitored at four to six week intervals for the first six months of treatment with Somavert, or at any time in patients exhibiting symptoms suggestive of hepatitis. Evidence of obstructive biliary tract disease should be ruled out in patients with elevations of ALT and AST or in patients with a prior history of treatment with any somatostatin analogue. Administration of Somavert should be discontinued if signs of liver disease persist. In patients with diabetes mellitus, doses of insulin or hypoglycaemic medicinal products may need to be decreased. Patients should be advised to use adequate contraception if necessary. The use of Somavert in combination with other medicinal products for the treatment of acromegaly has not been extensively investigated. **Pregnancy and lactation:** Somavert is not recommended during pregnancy and lactation. **Interactions:** Interactions between Somavert and other medicinal products have not been evaluated in formal studies. Patients receiving insulin or oral hypoglycaemic medicinal products may require dose reduction of these therapeutic agents due to the effect of Somavert on insulin sensitivity. Somavert cross-reacts in commercially available growth hormone assays. Treatment should therefore not be monitored or adjusted based on serum growth hormone concentrations reported from these assays. **Side effects:** In clinical trials, for patients treated with Somavert, the majority of adverse reactions to Somavert were of mild to moderate intensity, of limited duration and did not require discontinuation of treatment. The most commonly reported adverse events considered related to Somavert occurring in ≥ 5% of patients with acromegaly during the clinical trials were injection site reactions 11%, sweating 7%, headache 6%, and asthenia 6%. Most injection site reactions characterised as localised erythemas and soreness, spontaneously resolved with local symptomatic treatment, while therapy continued. The development of isolated low-titre anti-growth hormone antibodies was observed in 16.9% of patients. The clinical significance of these antibodies is unknown. **Overdose:** There is limited experience of overdosage with Somavert. In the case of overdose, Somavert should be discontinued and not resumed until IGF-I levels return to within or above the normal range. **Legal category:** POM. **Date of revision:** March 2004. **Package quantities, Marketing Authorisation numbers and basic NHS price:** Somavert 10mg, (30 vials of powder & 30 vials of solvent), EU/1/02/240/001, £1500. Somavert 15mg, (30 vials of powder & 30 vials of solvent), EU/1/02/240/002, £2250. Somavert 20mg, (30 vials of powder & 30 vials of solvent), EU/1/02/240/003, £3000 & (1 vial of powder & 1 vial of solvent), EU/1/02/240/004, £100. **Marketing Authorisation Holder:** Pfizer Limited, Sandwich, Kent CT13 9NJ, United Kingdom. Somavert is a registered trade mark. Ref: SV 1_3. Further information is available on request from: Medical Information Department, Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey KT20 7NS. **Date of Preparation:** April 2004. **Item code:** SOM 124.

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