

The Endocrinologist

THE NEWSLETTER OF THE SOCIETY FOR ENDOCRINOLOGY • ISSUE 77

AUTUMN 2005

Get set for Glasgow: ECE 2006

PLUS

America - a passport to success?

All change for Society meetings

Beyond the ovary in PCOS



Cover shows the Scottish Exhibition and Conference Centre in Glasgow, venue for ECE 2006

If members have any images that they think would make good covers for The Endocrinologist, the editorial office would be delighted to see them.

▶ It's that time of year when halls of residence fill with new students. Parents rush up and down the M1 in cars laden with duvets, pots and pans, sundry reading lamps and a guitar. All the way, the obligatory spider plant spills its potting compost over rucksacks and suitcases bulging with faded, designer-split jeans and converse baseball boots.

Meanwhile teachers prepare for another academic year. While finalising their timetables, they struggle with their consciences about whether to update their lectures and Powerpoint slides. There is that dull sinking feeling that summer is over, and those half-written papers and grant applications will have to be put on hold - yet again. Another year looms of balancing research, teaching, report writing and administration with the pressures associated with increasing numbers of students (due to unrealistic Government targets) and an increasing number of frozen academic posts (due to Government cut-backs).

But, despite all this, there are still the few who have evaded the lure of City finance and are trying to jump off the 3- to 5-year post-doc cycle and secure a permanent academic appointment. Even though new initiatives have been introduced to provide a career structure for non-clinical researchers, it is still very difficult to find an academic position in the UK. So what might increase your chances? Rob Fowkes (page 10) ponders on the advantages (and disadvantages) of 'doing' that post-doc in the USA, and whether crossing the pond enhances career prospects. Young endocrinologists will find his article particularly illuminating and useful when considering such a move.

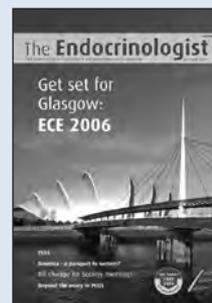
I know that the Government has sought to encourage postal voting, but the Society has gone one step further and now brings you e-voting! Page 3 explains how Ordinary Members can vote for Council members by email. So with one tap on the reply button there is no excuse not to take part. Society News also includes an update on the Society's revised strategy and invites your comments and suggestions (page 7).

One outcome that the Society wants to achieve is 'Improved public information and understanding'. In this respect, you might like to add your name to a database of scientists who are keen to talk to writers and demystify science (see SciTalk, page 7). Members might also like to think about airing or hiring their kilts for ECE 2006 on 1-5 April in Glasgow (for further details see pages 12 and 13), and look forward to a trip to London for the Society's 196th Meeting this November. The latter is the penultimate November meeting because, from 2007, the Society has decided to host just one premier meeting, every spring (more information on page 6).

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women. On page 8, Wiebke Arlt takes us beyond the ovary and up towards the adrenal in her overview of this syndrome. With some good basic clinical endocrinology to sink your teeth into, she provides evidence to counter the long-held belief that the hyperandrogenism associated with PCOS is of ovarian origin.

Finally we take a cultural turn from the Society and endocrinology towards classical music (page 11). Hotspur explains how he finally bonded with his hero, Wolfgang Amadeus Mozart, not when the horn concerto dropped in the all-time greats, but because he, like Mozart, disappointed his father. Leopold Mozart wrote to his son 'My dear Wolfgang, you convince me in all your letters that you go by the first wild idea that enters your head ... too much arrogance and self love ...' In comparison, Hotspur's father declared 'You see it's bad for business when I let you do the surgery for me.' And on that inharmonious note, read on.

SAFFRON WHITEHEAD



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Members: Mono - Half page £110
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Deadline for news items for the Winter
2005 issue: **14 October 2005**. Please send
contributions to the above address.

Calling all consultants!

2006 Clinical Excellence Awards

► The Society can now support nominations for the 2006 Clinical Excellence Awards. These awards are open to all consultants (including honorary consultants) who have been in post for more than a year. They seek to reward those who make the biggest contribution to delivering and improving healthcare, either through clinical service or through teaching and research in academic medicine, and have replaced the old distinction award system. We can support ten bronze awards and five silver/gold awards.

If you would like the Society to support your award application, complete a nomination support request form (available from the Bristol office) and return it to us, with a copy of your CV questionnaire (CVQ), by 31 October 2005. Based on this information, Society members will be objectively ranked for consideration on a scale of 0-5 by a panel of existing A and A+ award holders, by the end of November.

All citations for the Society's supported candidates will be written by the ranking panel during December 2005, using the Advisory Committee on Clinical Excellence Awards' (ACCEA) standard form, based on the information supplied by the candidate. The citation should reflect the following areas:

- (a) delivering a high quality service
- (b) developing a high quality service
- (c) managing a high quality service
- (d) research, education and training

The citation forms will be approved by the chair of the panel before being sent to the ACCEA by the Society, together with ranking information and Society details, in time for the 22 January 2006 deadline. CVQs will not be submitted.

Further details can be obtained from Rachel Evans in the Bristol office or from the ACCEA at www.advisorybodies.doh.gov.uk/accea/index.htm.

Clinical Review Lecture 2006 - call for abstracts

► Applications are invited from clinical endocrinologists who are no more than 6 years post-MD/MRCP (usually in the SpR grade) to present a 30-minute review lecture on any subject under the general heading of endocrinology. Applicants must be members of the Society who are under 35. Older applicants may be considered if there are extenuating circumstances. The successful applicant will be asked to present their lecture during the Clinical Cases Meeting on 15 February 2006 at the Royal Society of Medicine, London. The Society for Endocrinology will offer a £500 honorarium for this prestigious award. Full details can be found at www.endocrinology.org/sfe/train.htm.

Nominations needed!

► Please send your nominations for new members of the Clinical and Science Committees. Nomination forms can be obtained from www.endocrinology.org/sfe/commit.htm or from Christine Davis in the Society office (christine.davis@endocrinology.org).

Travel grant reminder

► Don't forget to apply for your travel grant to attend the ECE 2006 meeting. The deadline for applications is 15 December 2005.

NEW SERVICE FOR MEMBERS

E-voting

► 2005 sees the first opportunity for Ordinary Members to cast their votes for new Council members by email. Votes can be cast this way until 26 October, after which you may still vote using the paper ballot form included with your AGM papers in this mailing. Please ensure you only vote once. If you are an Ordinary Member and have not been invited to vote online, it means we either do not have your email address or your email bounced. Please contact christine.davis@endocrinology.org to ensure the Society has your correct email address.

MEMBERS ON THE MOVE

M Elmes to University of Nottingham;
F Hammer to University of Birmingham;
A E Michael to St George's Medical School, London; **H L Simpson** to Addenbrooke's Hospital, Cambridge;
A Swali to University of Birmingham;
S Ward to Great Ormond Street Hospital, London; **M Hewison** to Cedars-Sinai Medical Centre, Los Angeles.

Have you seen these members?

► We have lost track of the following members. If you know their whereabouts or contact details, please tell christine.davis@endocrinology.org. Also tell Christine if your name is listed but you have not moved, as your mailings are not reaching you.

- K A Al-Busadah** - University of Sheffield
- Ruth Andrews** - University of Edinburgh
- P G H Byfield** - Hammersmith Hospital, London
- John Cox** - Current Medical Literature Ltd, London
- D A Darko** - Home address, Northwood, Middlesex
- D R Ferguson** - University of Cambridge
- Stephen Harmer** - University of Reading
- I C Hart** - Pfizer Inc, Groton, CT, USA
- S L Howell** - King's College London
- J S M Hutchinson** - University of Aberdeen
- R Mihai** - Bristol Royal Infirmary
- P J A Moulton** - Whittington Hospital, London
- David O'Regan** - Home address, Cambridge
- Paul Peter** - Worcester Royal Hospital
- M J Scanlon** - St Mary's Hospital, London
- Mohamed Tadayyon** - GlaxoSmithKline Beecham Pharmaceuticals
- S Taheri** - Home address, Putney
- J J Turner** - Nuffield Orthopaedic Centre, Oxford
- Robert Ven** - University Hospital Gasthuisberg, Leuven, Belgium
- A K Viswanath** - Aberdeen Royal Infirmary
- J S Woodhead** - Welsh National School of Medicine, Cardiff

Committee News

The latest from
each of the
Society's
committees.

Council of Management

Details of the latest Council decisions and approvals will be reported in the next issue.

Awards

Recent activities include selecting the 2005 Young Endocrinologist Basic Science Review Lecturer (see page 6), as well as gathering nominations and conducting a ballot to determine the recipients of five Society medals in 2006 and 2007. Medal winners will be announced in the next issue, once ratified by Council.

Clinical

The 2006 Clinical Cases Meeting takes place at the Royal Society of Medicine on 15 February. Professor Krish Chatterjee has accepted an invitation to convene the clinical programmes for Summer School 2006 in Cambridge. Sessions for November 2006 and BES 2007 are being developed for submission to the Programme Committee. The interdepartmental peer-review initiative is progressing well, and the Committee is keen that it should benefit more endocrine units (see page 7 for further details).

Following the move to one main Society meeting per year, the Clinical Committee Strategy Group has looked at ways of strengthening clinical training and continuing education services. Ideas include adding a review lecture to the annual Clinical Cases Meeting, and replacing Summer School from 2007 with an October event covering endocrinology and diabetes, which would provide clinical training and consultant updates. They also discussed the potential of a road show or a BES event to attract more young clinicians to endocrinology, including a lunch with opportunities to meet senior clinicians.

Corporate Liaison

This new Committee is to serve as a forum for two-way communication and advice between the Society and industry, regarding issues related to regulation, therapeutic development and endocrinology. It is chaired by Professor John Connell and has representatives from the Society and its Corporate Members. The

Committee agreed on its scope and remit at the inaugural meeting, and also discussed the future of the Society meetings.

Nurses

The Clinical Endocrinology Trust has kindly provided a £5000 grant for nurse activities, and the Committee is deciding how best to distribute the funds to maximise benefits to nurse members. The content of the November 2005 Nurses session on 'Bone breaking disease' has been finalised, while that for ECE 2006 in Glasgow on 'Metabolic syndrome' will soon be confirmed. The suggested topic for November 2006 is 'The endocrinology of ageing', with 'Thyroid cancer' and 'Multiple endocrine neoplasia' being candidates for BES 2007. One or two Vice-chairs are sought within the Committee, to shadow the current Chair, Maggie Carson, for the remainder of her term of office.

Programme

The preliminary programme for this year's November meeting has been distributed and all abstracts have been marked. Final programme details are being finalised, with a satellite session by Shire Pharmaceuticals on Tuesday evening, and some exhibition space remaining on day 3 only. Sponsorship has been secured for three Special Interest Group sessions. This year's annual dinner will be at The Villandry. The Committee will meet in October to discuss suggestions for BES 2007. See page 6 for details of changes to the future of Society meetings.

Science

Programme suggestions for the November 2006 and BES 2007 meetings are being finalised. Three members are due to retire at the end of 2005 and the Committee is in the process of identifying potential new members (see page 3 if you would like to make a nomination). Dr Rob Fowkes has replaced Professor Martin Hewison as Programme Advisor.

The Science Committee Strategy Group has identified endocrine education as an area of concern for

basic scientists. Without a specific first degree in the subject, it is difficult to gain a sense of identity as an endocrinologist. A proposal for initiatives to support basic scientists will be formulated for the Society's strategic review.

Young Endocrinologists

The session at the 2005 November meeting includes the Basic Science Review Lecture and oral communications. Young Endocrinologists' posters should once again be labelled as such, to encourage senior members to chat to them about their work. Members of the Young Endocrinologists group will circulate during the poster session, providing information about grants and membership, as well as invitations to the Young Endocrinologists tea.

Abstracts from Young Endocrinologists will be included in the main part of ECE 2006, which will include a session on professional development. Council has approved clinical and basic science prizes for the best posters.

The Steering Group want to hear from any proactive and enthusiastic basic science members who would like to join the group and play an active part in Young Endocrinologist sessions at Society meetings. Please contact Julie Cragg (julie.cragg@endocrinology.org).

European Society of Endocrinology

History was made at a recent General Council Meeting of EFES (European Federation of Endocrine Societies). After consultation, member groups voted overwhelmingly to create a European Society of Endocrinology (ESE), to launch in 2006. Free membership is available when registering to attend ECE 2006 in Glasgow (see www.ece2006.com).



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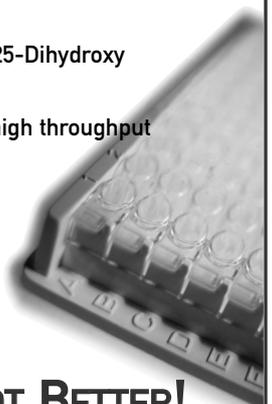
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CHANGE AHEAD FOR SOCIETY MEETINGS

► Over the last 6 months, the Society has conducted a major review of the arrangements for its meetings. Council has decided that, from 2007, the Society will host one premier meeting in the spring of each year, with the possibility of training courses, small focus groups and other events at other times. The meeting will be held at venues around the UK, rather than in London. It will include educational content and clearly defined basic, cross-over and clinical sessions.

The programme will be set by the Society's Programme Committee. It will be known as the 'Society for Endocrinology BES 20** meeting'.

'BES' will be retained as an acronym and logo only. Current members of the BES will be invited to submit proposals for sessions and will have their association with the meeting acknowledged in

return for circulating the preliminary programme to their members. The British Thyroid Association Lecture and prizes will continue.

The single Programme Committee will be chaired by the Society's Programme Secretary and initially formed from the Society's existing Programme Committee with some members of the BES Committee. Each annual meeting will have a Programme Organising Chair and Deputy, to take main responsibility for programme content, and another member of the Programme Committee (co-opted if necessary) will be responsible for local liaison. This will replace the BES Liaison Committee, the Local Organising Committee and the Society for Endocrinology Programme Organising Committee.

This means that November 2006 will be the last Society November meeting in its present format.

For further enquiries, please contact Rachel Evans (rachel.evans@endocrinology.org).

SOCIETY CALENDAR

7-9 November 2005
196th Meeting of the Society for Endocrinology
Royal College of Physicians,
London, UK
(see advert below)

15 February 2006
Clinical Cases Meeting
Royal Society of Medicine,
London

1-5 April 2006
8th European Congress of Endocrinology
incorporating the BES
Scottish Exhibition and
Conference Centre, Glasgow
Abstract deadline:
4 November 2005
(see advert on pages 12 and 13)

11-14 July 2006
Summer School
The Moller Centre, Cambridge

RAE 2008

The following members have been appointed to subpanels for the 2008 exercise. Several were nominated by the Society.

- Steve Bloom**, Other laboratory-based subjects
- Barry Furr**, Cancer studies
- Stephen O'Rahilly**, Other laboratory-based clinical subjects
- Nancy Rothwell**, Preclinical and human biological sciences
- Graham Russell**, Other laboratory-based clinical subjects
- Jonathan Seckl**, Preclinical and human biological sciences
- Paul Stewart**, Other hospital-based clinical subjects
- Raj Thakker**, Other hospital-based clinical subjects

Basic Science Review Lecturer 2005

► Dr Chris Burns from the NIBSC in Potters Bar is the winner of this year's Young Endocrinologist Basic Science Review Lectureship. He will present his lecture during the Young Endocrinologists session at the November meeting.

196th Meeting of the Society for Endocrinology

7-9 November 2005

Royal College of Physicians

11 St Andrew's Place, Regent's Park,
London NW1 4LE

Plenary lectures

- Ghrelin: discovery and physiological significance
- The evolution of primary aldosteronism
- Oestrogen receptors at work in living animals

Symposia

- Thyroid cancer
- Non-classical sites of action of classical hormones
- The placenta as an endocrine organ
- Hormone measurements - past, present and future
- Evolving aspects in the HPA axis

Debate

- Do postmenopausal women benefit from oestrogen therapy?

PLUS

Sessions for young endocrinologists and nurses, posters and oral communications.

Special interest group sessions

- Polycystic ovary syndrome
- Pituitary
- Bone and Mineral

Public lecture

- Stress, hormones and your health
- 5.30pm, Tuesday 8 November

For more information see

www.endocrinology.org/sfeconference2005

Endocrinology and Diabetes Day

Lectures

- Beta cell growth: implications for type 1 and type 2 diabetes
- Stem cells to cure
- The role of genetics
- Expert sessions
- Managing the younger, lean, newly diagnosed patient
- Update on new therapies for type 2 diabetes mellitus

Debate

- Insulin and overweight type 2 diabetes



Strategy Update

► As mentioned in the last issue, the Society plans to review its strategy in November 2005. Our current financial situation is favourable and far less constrained than during the last review, in 2003. It is an ideal opportunity to focus on new areas for development over the next 5 years, alongside our current services.

All four Officers, with key Committee Chairs and Society staff members, will take part in the review.

Our aims are to create:

- ▷ a better environment for clinical research and effectiveness
- ▷ improved public information and understanding
- ▷ better understanding of the Society and its aims

Society members will be consulted shortly and their comments fed into the Strategy Meeting. Please contact Rachel Evans (rachel.evans@endocrinology.org) for more information.

Congratulations

► We are pleased to congratulate **Professor Nancy Rothwell** who has become a Dame of the British Empire for services to science, and **Dr Peter Hindmarsh** and **Dr David Ray** who have been awarded Chairs.

Society's Diamond Jubilee

Next year sees the Society's 60th anniversary. This will be marked by special lectures at the November 2006 meeting. We are delighted to announce that Professor Steve Hillier will deliver the Jubilee Medal Lecture at this meeting. In addition, a special logo will be carried throughout the year on all the Society's journals and literature.

Society funds in good health

► The financial results for the year to 30 April 2005 were excellent. The surplus generated from Society activities, including investment income, was £139 000. In addition to this, BioScientifica passed £362 000 to the Society by gift aid, following an exceptional year. With investment gains of £69 000, the surplus for the year was £570 000. The BES meeting in Harrogate exceeded expectations with a surplus of £54 000. These results mean that the forthcoming strategic review can consider more ambitious plans for future Society activities. Congratulations to all involved.

Interdepartmental peer-review

► The Society's Clinical Committee began a scheme for peer-review of UK endocrine units in 2001. Its main aim is to improve services for endocrine patients. Each visit focuses on basic standards of endocrine care and service provision. It encourages an exchange of ideas and experience, and allows concerns to be voiced. The visit report provides 'levens for improvement' (e.g. highlighting needs for consultant expansion or specialist nurse provision, etc.) and can assist in negotiations with management. It also provides useful information for clinical governance and consultant revalidation. Visits are run on a voluntary basis and aim to support endocrinologists in the various centres. It is hoped that all UK endocrine centres will become involved. So far, Sheffield, Hull/York and Oxford/Reading have been visited. If you would like your centre to be considered for a visit, see www.endocrinology.org/sfe/peerreview.htm.

SciTalk: connecting scientists and writers

► **Playwrights, poets and novelists are beating a path to your door, in an unusual project to increase the credibility of scientists as characters in fiction.**

SciTalk aims to promote personal contact between scientists and writers: one-to-one and face-to-face. It's about the fun and challenge of questioning others as well as explaining what you do. If it helps fiction writers enjoy using science and including scientists as believable characters - and helps scientists learn how writers work and what they mean by 'research' - then it will have succeeded.

The idea was conceived by Ann Lingard, a novelist as well as zoologist and parasitologist, who developed SciTalk in collaboration with physicist and information scientist Peter Normington. Supported by the National Endowment for Science, Technology and the Arts, a database is already online at www.scitalk.org.uk. You can add your name to the pool of scientists who are keen to talk to writers and demystify science. Who knows, you might precipitate a host of endocrine epics! For further details, contact enquiries@scitalk.org.uk.

NEW CET PRIZE LECTURES

► We are pleased to announce two new prize lectures for Young Endocrinologists. We thank the Clinical Endocrinology Trust whose generosity has made the funds available. Winning lecturers will each receive an honorarium of £2500 and will present their lectures at the annual BES meeting commencing from 2007. A call for abstracts will be made in due course, so watch this space.

CET grant update

► In 2004, eight medical undergraduates each received grants of £1000 from the Clinical Endocrinology Trust to fund a project of up to 3 months' duration on any aspect of endocrinology. In addition, Christopher Hewitt from the University of Sheffield was awarded a further £1000 for submitting the best project report. Five students applied by the deadline this year. They are currently undertaking their projects and will report back in due course.

Beyond the ovary: steroids and PCOS

Wiebke Art
takes a fresh
look at a
common
endocrine
disorder.

► Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, affecting 5-15% of the female population. PCOS has a huge and possibly insufficiently acknowledged impact on the nation's health, as an early marker disease for cardiovascular risk.

At least half the women with PCOS are insulin-resistant and at an increased risk of developing the metabolic syndrome including obesity, hyperlipidaemia, high blood pressure and type 2 diabetes. Furthermore, chronic anovulation due to PCOS is the most frequent cause of female infertility. Related treatment consumes the largest part of fertility treatment costs in the UK. Pregnancy in PCOS, once achieved, is not straightforward either, with a tenfold-increased risk of gestational diabetes and pregnancy-related hypertension.

PCOS was first described in 1935 by Stein and Leventhal, who found bilateral polycystic ovaries in women with amenorrhea at autopsy. Nowadays, luckily, we can catch these women earlier. Many of them initially present with mild obesity and oligomenorrhea and hirsutism. Motivating them to comply with treatment may help to avoid the detrimental consequences of full-blown metabolic syndrome in later life. It is often useful to realise that these women may be genetically advantaged, as they would be the most likely to survive and even reproduce in times of extreme food restriction like poverty, hunger and war.

Though it is obvious to doctors that the term 'syndrome' implies that the underlying cause of disease is unclear, patients tend to interpret 'polycystic ovary syndrome' quite literally and anxiously look for treatment options to heal their ovaries. It is often difficult to explain the complexity of PCOS, that it is probably genetically determined and that it affects the whole endocrine-metabolic set-up. Patients therefore often wonder why dieting should get rid of cysts in their ovaries.

Most confusingly, the ultrasound appearance of polycystic ovaries is not necessarily a precondition for diagnosis. Two of the following are required for diagnosis of PCOS, according to the Rotterdam 2003 PCOS Consensus Workshop: (a) oligo- or amenorrhea, (b) clinical or biochemical signs of hyperandrogenaemia, (c) polycystic appearance of ovaries at ultrasound (as defined by more than 12 cysts with a diameter of 2-9 mm).

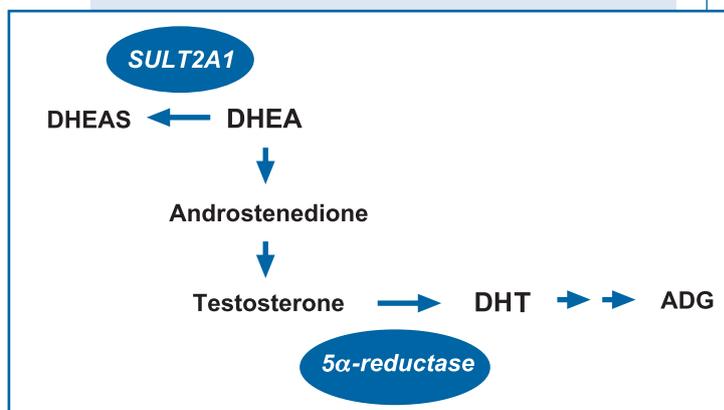
Furthermore, polycystic ovaries are not necessarily indicative of PCOS. The work of Steve Franks and others tells us that polycystic ovaries at ultrasound are seen in a considerable number of women, without concurrent clinical evidence of the syndrome. Whether polycystic ovaries without PCOS represent a pre-clinical stage of the disease or an unrelated entity is a matter for debate.

Importantly, endocrine researchers, like patients, tend to restrict their view of PCOS to the ovary, especially when considering the origin of hyperandrogenaemia, one of the syndrome's main clinical features. *In vitro* studies have shown excess androgen production by theca cells isolated from ovaries in PCOS. This includes increased activity of 5 α -reductase, resulting in increased conversion of testosterone to dihydrotestosterone (DHT), which binds the androgen receptor with tenfold higher affinity than testosterone.

However, whilst this seems to imply that the problem lies primarily in the ovary, earlier studies by Paul Stewart and colleagues provided indirect evidence that 5 α -reductase activity may generally be enhanced in PCOS. They found that patients had increased urinary baseline excretion of 5 α -reduced androgen and glucocorticoid metabolites. We have now revisited this concept using a dehydroepiandrosterone (DHEA) challenge test.

DHEA is a crucial precursor of human androgen synthesis, and we have previously shown that oral administration of DHEA leads to its efficient conversion towards androgens in women. Comparing women with PCOS and healthy controls, the oral DHEA challenge, preceded by dexamethasone suppression, was a tool to detect differences in downstream androgen generation. While levels of androstenedione and testosterone following DHEA administration did not differ between groups, women with PCOS showed significantly higher generation of DHT and the DHT metabolite ADG, i.e. upregulation of all androgens downstream of 5 α -reductase (see Figure).

This was further supported by urinary steroid excretion analysis, which revealed a significantly increased excretion of 5 α -reduced androgen, glucocorticoid and mineralocorticoid metabolites following DHEA administration. A general increase in 5 α -reductase activity will inevitably lead to enhanced androgen activation by



Downstream conversion of DHEA towards androgens, highlighting the two enzymes recently implicated in PCOS-related hyperandrogenaemia: 5 α -reductase (activating testosterone to DHT) and SULT2A1 (DHEA sulphotransferase, inactivating DHEA to DHEAS).

conversion of testosterone to DHT in peripheral target cells of androgen action. This clearly highlights the importance of liver and other target tissues in a novel, 'beyond the ovary' perspective on hyperandrogenaemia in PCOS.

Our recent study on the interconversion of DHEA and its sulphate ester, DHEA sulphate (DHEAS), may have exposed another novel perspective.

Only desulphated DHEA is biologically active and can be converted towards androgens. It has previously been assumed that DHEA and DHEAS interconvert freely and continuously, DHEAS being activated to DHEA by steroid sulphatase, and DHEA inactivated to DHEAS by DHEA sulphotransferase (SULT2A1). So DHEAS is usually seen as a circulating storage pool for continuous DHEA regeneration.

However, while DHEA administration yields rapid generation of active androgens, we showed that administration of DHEAS did not lead to an increase in either DHEA or downstream androgens. This suggests that SULT2A1 activity, i.e. the inactivation of DHEA to DHEAS, appears to be the rate-limiting step regulating the DHEA-DHEAS equilibrium, determining DHEA bioavailability. These *in vivo* findings were supported by concurrent *in vitro* experiments, demonstrating ample generation of DHEAS from DHEA in cultured liver cells, but a complete lack of conversion of DHEAS to DHEA.

Serum DHEAS measurements are generally used as an estimate of adrenal androgen generation. However, from our recent findings, it seems highly likely that serum DHEAS may not appropriately reflect corresponding levels of desulphated, biologically active DHEA. Serum DHEA and DHEAS may be concordant in the physiological situation, but will be discordant in pathological conditions, in particular if SULT2A1 activity is impaired.

Hyperandrogenaemia of adrenal origin is usually excluded by measurement of serum DHEAS. A woman with normal DHEAS and increased androstenedione levels is generally considered to have hyperandrogenaemia of primarily ovarian origin. Most women with PCOS show this pattern, so seeming to justify the concentration of research into PCOS-related hyperandrogenaemia on mechanisms underlying ovarian androgen hypersecretion.

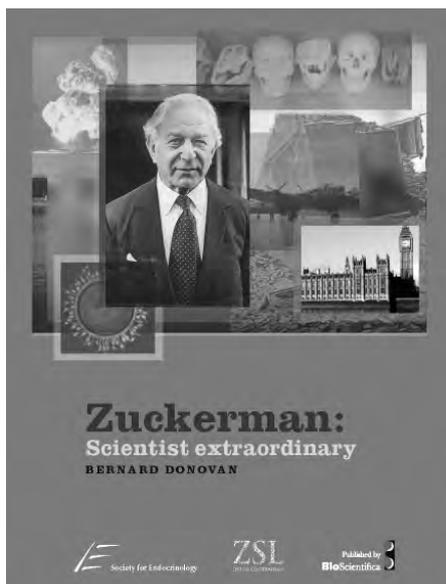
However, although serum DHEAS is normal, it may be that biologically active DHEA is pathologically increased, resulting in increased androstenedione through efficient downstream conversion of DHEA. Increased DHEA levels with concurrently low normal DHEAS levels would suggest impairment of SULT2A1 activity. Preliminary findings in a large PCOS cohort, which we presented at BES 2005, revealed that a significant proportion of women with PCOS showed exactly that pattern.

One could argue that increased DHEA levels may result from enhanced ovarian CYP17 activity, the enzyme responsible for DHEA biosynthesis. However, we have shown that dexamethasone administration yields a similar and near complete suppression of serum DHEA in both healthy controls and women with PCOS, suggesting a primarily adrenal origin of circulating DHEA in both groups. This leaves SULT2A1 impairment as a potential novel mechanism underlying hyperandrogenaemia in PCOS.

These two mechanisms, enhanced 5α -reductase activity and putatively impaired SULT2A1 activity, illustrate the importance of steroidogenesis in understanding the pathophysiology of PCOS. A systemic view, rather than an ovarian spotlight, is likely to generate further insights into this fascinating disease.

WIEBKE ARLT

New from BioScientifica!



Zuckerman: Scientist extraordinary By Bernard Donovan

Solly Zuckerman was a rare creature, for few scientists have managed to play such a central part in national affairs. An anatomist and authority in anthropological research before the war he became involved in investigating the effects of bombing and became the trusted confidant of air marshals and generals. He was the chief scientific adviser of successive governments, developing policies for the control of nuclear weapons. To some, Zuckerman is a legendary but shadowy figure who shunned the limelight, while enjoying the manipulative process. Did he use, or abuse, his power? Should he have done more to encourage the input of scientific advances to British industry? Or were his efforts frustrated by an unreceptive establishment? Such are some of the questions explored in Professor Donovan's definitive study.

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THE 'BEEN-TO-AMERICA' DEGREE

Rob Fowkes
looks at the
pros and cons
of a stint across
the pond...

► The lack of career structure for non-clinical researchers is a perennial problem for UK scientists. Although new initiatives, such as the RCUK fellowship scheme, try to redress the balance, it is still immensely difficult to secure an academic appointment in the UK. Spending time in a foreign research establishment, often in the USA, has traditionally been seen as a way to boost your chances of securing a lectureship. But does the 'Been-to-America' degree still have the desired effect?

Before you begin trans-Atlantic plans, do ask yourself why you want to go to the USA for post-doc experience. There's no right or wrong reason - but it's worth asking others who've been whether they feel they made the best decision. You should certainly consider how working overseas will help you on your chosen career path. If you don't want to be a principal investigator, do you really need to go abroad to improve your chances of getting another post-doc job in the UK? Table 1 summarises some points to consider in your decision making.

FOR	AGAINST
Experience	Inconvenience
May enhance career prospects	Enhanced career prospects not guaranteed
Challenge	Expensive
Access to resources	Unsettling
It's America	It's America

Make sure you choose what you are most comfortable with. As the old adage goes, it's better to regret something you have done than something you haven't.

Once you decide to work in the USA the decisions get even trickier. There's no perfect time to go. In some cases, it's best to go soon after completing your PhD, for your first post-doc. This can be better financially as you're less likely to be encumbered with responsibilities like property ownership, or to notice a poor currency exchange rate. But you need to be really sure about who you'll be working for, as the gulf between post-grad and post-doc can be large, and even larger in a foreign country. Will your boss in the USA give you the support you need?

If you go later in your research training, the issue of supervision/support will be less important, as you will be used to relying on yourself for motivation. But the complications at this stage will be more to do with the inconvenience and financial costs associated with moving abroad. You may have to make huge decisions about going with or without your partner, who will possibly have to make major sacrifices to accompany you. Post-doc salaries are not great in the USA, where many institutes have strict policies about paying foreign post-docs the equivalent of a newly qualified post-doc, regardless of actual experience. By far the best way to move to the USA is with your own salary covered in the form of a post-doc fellowship (see Table 2 for some funding suggestions).

Your experience will undoubtedly be more fruitful if you succeed in securing a fellowship, and will enhance your future career prospects even more. However, these

schemes are limited in number and extremely competitive, so you must consider alternative approaches.

It's good to have a short-list of groups that you'd like to work with, so you have a number of options. Try writing directly to the principal investigator of the group, and prepare an 'application pack' consisting of a letter of introduction tailored specifically to the group in question, your up to date CV (look at examples of US scientific resumes), and letters of support from respected academics. This approach can yield remarkable numbers of job offers (ten from six letters, in my case!). Good post-docs are hard to find the world over, so you should be optimistic. Once you've received some offers, consider those that you really find attractive and try to visit them for an interview. Of course, it's great if they offer to fly you out for the experience, but, if not, try and coincide these interviews with a trip to a meeting in the USA. It is extremely important to see where you might be spending the next 3 years of your life; after all, there's a world of difference between San Francisco and Syracuse.

'So much to do, so little time!' Once your decision to cross the pond is made, there will be numerous important logistical chores. Here's a brief list:

- ▷ Visa application (J-1 'exchange visa' for you, J-2 for a spouse) (see www.usembassy.org.uk/cons_web/visa/niv/exchange.htm)
- ▷ Salary and contracts
- ▷ Medical insurance
- ▷ Accommodation
- ▷ Relocation expenses
- ▷ Tax arrangements (both UK and USA)
- ▷ Saving some money

So, if you survive your time in the USA, is it worthwhile when (if) you return home? Generally, yes. Showing that your commitment to science extends to relocating abroad often looks good on applications for lectureships. Being associated with a good American principal investigator is also an invaluable benefit of having worked abroad. The experience of thriving in an 'alien' environment is good for your own personal development, and gives you a great opportunity to make new collaborative contacts and to 'get known'. Plan your experience well and it will serve you well in the future, but if you make rash decisions about where and when you move abroad, it could be the end of your research career (for better or worse!). Most importantly, enjoy yourself, work hard and remember the tea bags.

ROB FOWKES

TABLE 2: Potential sources of funding

Wellcome Trust - www.wellcome.ac.uk - Research Career Development Awards/Advanced Training Fellowships
BBSRC - www.bbsrc.ac.uk - David Phillips Fellowship
Royal Society - www.royalsociety.org - University Research Fellowships
American Heart Association - www.americanheart.org
NARSAD (Alliance for Research on Schizophrenia and Depression) - www.narsad.org
EMBO - www.embo.org - long-term fellowships (2 years)
Hfsp - www.hfsp.org - long-term fellowships (3 years)
Lalor Foundation - www.lalor.org - post-doctoral fellowships (up to 2 years).

Triumphs, disasters and Mozart

► **How many people are there to whom you would willingly kneel in gratitude, for all the pleasure they had given you during this life, if they walked into the room?**

A mere handful I suggest. For me, however, Wolfgang Amadeus Mozart would be top of the list. We have nothing in common. Much as I love listening to music, I can't even play a note on a single instrument. I spent a year in the violin class at school but was unable to open the case (not technically gifted either)! I so much wanted to share one common trait with the great man, but feel that my sporting interests, such as cricket, were unlikely to be of much concern to him.

I often think of Mozart as still alive, which is quite reasonable given that the broadcaster on Classic FM is prone to exclaim: 'Great news for Mozart! His horn concerto has moved up to number 125 in the all-time greats list!'

I have tried to picture his response to hearing such news. Would he whip his wings off in a soccer-style celebration and throw them to the crowd, or run towards Beethoven and Bach, shaking his triumphant fist in their faces, whilst all the time looking carefully over his shoulder to see if his disapproving father, Leopold, was about to censure such celebration?

Unfortunately, in the real world, the triumph of a successful medical diagnosis is usually short-lived. Shirley was a perfect example of this phenomenon. She was 30 years old, and I was investigating her for Cushing's syndrome; the disease was mild and intermittent, and it took me 3-6 months to conclude that she had Cushing's disease. With mild intermittent endocrine disease it can take that length of time to come to a diagnosis. Sometimes you just have to be patient and allow the diagnosis to come to you rather than forcing the pace unnaturally.

At clinic I informed Shirley that I was now certain that she had Cushing's disease. 'Good,' she said, 'that's the diagnosis my husband suggested.' 'Oh,' I said, 'I was unaware your husband is medically qualified.' 'He's not,' she replied, 'he's a farmer.' 'A farmer!' I spluttered, 'How on earth

did he diagnose Cushing's disease?' 'Easily,' she explained, 'he went to the library last Saturday and looked it up in a book.'

Resisting the temptation to wish foot and mouth disease had descended on his whole flock of sheep whilst he had been away from his post, I accepted the demolition of my diagnostic triumph quietly, if not graciously.

Sometimes, however, a disaster strikes when you have not, even fleetingly, enjoyed a preceding triumph. The week had started badly with Valentine's Day. I had received my first Valentine's card for 5 years. I was overjoyed until I opened it, only to find that the signed greeting consisted of 'best wishes'. Who sends a Valentine's card with 'best wishes'? That's the way you sign the card you send to your 10-year-old nephew recovering from his appendectomy! How much lower must a man's self-esteem fall? It must have been Aunt Polly who, aware of my lack of a social life, had sent it to me out of sympathy.

I decided to cheer myself up by going back to my roots in London for the weekend. I would stay with my father, a good-looking, youthful in appearance, single-handed GP in the East End. On such occasions I always offered to do my father's Saturday morning surgery so that he could have a lie-in. The surgery contained no difficult clinical problems that I

was aware of, and the weekend was enjoyed without a hitch.

It was Monday evening when he phoned. He always phoned on a Monday evening after such a weekend, to check I had arrived home without incident. Tonight, however, his voice was sterner than usual.

'That's the last surgery I will ever let you do for me,' he said.

'Why Dad? What did I do wrong? Wrong diagnosis? Wrong management?'

'Was it the facial palsy? Don't tell me the old boy has had a full-blown stroke,' I guessed wildly.

'No, it was Lennie Smith, who came into my surgery again tonight,' he stated calmly. 'When I finished dressing his toenail wound, Lennie turned to me and said, "I'm so glad to see you looking better, Doc, you looked awful on Saturday morning!"'

'You see, it's bad for business when I let you do the surgery for me,' Dad finished.

The conversation over, I reeled away from the telephone and, simultaneously, while aiming a kick at the cat, heard on Classic FM that Mozart's horn concerto had fallen to 150 in the list of all-time greats. It was at that precise moment it dawned on me that I had at last bonded with my hero, Mozart; both of us disappointed our fathers.

'HOTSPUR'



8th European Congress of Endocrinology incorporating the BES

1-5 April 2006

Scottish Exhibition and Conference Centre, GLASGOW, UK

The Society for Endocrinology is proud and privileged to host next year's European Congress of Endocrinology. Glasgow's impressive SECC will be the venue for the event, on 1-5 April 2006. The ECE 2006 meeting will, as its name suggests, attract delegates from all over Europe and the UK. The British Endocrine Societies meeting will be incorporated into the event, which will retain much of the character you have come to expect from this spring gathering.

Glasgow is a vibrant city surrounded by beautiful countryside. With a population of around 600 000, it is Scotland's largest city. Glasgow is easily accessible by road, rail or air. On Glasgow's elegant streets you will find some of the most beautifully preserved Victorian buildings. It is also a hub for cultural, sporting and leisure attractions.

The scientific programme is packed with sessions to appeal to clinicians and basic scientists alike. Leading researchers from across Europe and the USA will discuss their latest work in symposium sessions. Hear 'The expert's view' as experts present cases and draw comments from the audience; each session will run twice, so delegates can attend a wider range of topics. Clinical management workshops and oral communications will serve delegates with the whole range of current endocrine research. As always it is a pleasure to present the prestigious medal lecturers, who will complete the varied and stimulating programme.

And don't forget the social events! The annual sporting events that many associate with the start of a BES meeting - five-a-side football, tennis and golf - take place on Saturday 1 April. The evening entertainment includes both the informal and the formal. The inspiring ambience of Glasgow Science Centre will set the scene for the welcome reception on Saturday 1 April. City centre bar Tiger Tiger will give delegates a choice of three rooms in which to relax, socialise or dance the night away at an informal gathering. Sunday evening provides a chance to enjoy a complimentary drink and finger buffet. Finally, Tuesday's Congress dinner will be

PROGRAMME ORGANISING
CO-CHAIRS:

Professor Pierre Bouloux
(London, UK)

Professor Josef Köhrle
(Berlin, Germany)

LOCAL ORGANISING CHAIRMAN:

Professor John Connell
(Glasgow, UK)

**Abstract deadline
extended to:
4 November 2005**



www.ece2006.com

24th Joint Meeting of the British Endocrine Societies

Harrogate, UK, 4-6 April 2005

The Society is pleased to have provided grants to help its members attend these conferences. The next deadline for travel grant applications is 15 December.

See grant information on the Society's web site for more information.

The broad array of subjects at the meeting ensured an interest for everyone attending, from molecular biologists to neuroendocrinologists. Invited speakers included Professor Jayne Franklyn, who presented a novel viewpoint on our understanding of the causes of thyroid disease, and Professor Rod Flower, whose insightful talk included the latest information on annexin 1's role as a unique glucocorticoid mediator.

The oral communications on reproduction and growth, steroids and neuroendocrinology were of particular interest to me; they included a lot of exciting and innovative research. As a postgraduate student, I also found the Young Endocrinologist session very informative and helpful, especially the information and advice given by Dr Rob Fowkes about working as a post-doc in America (see his article on page 10 of this issue).

Overall, the meeting was an excellent opportunity for insights into current endocrine developments, as well as allowing scientists and clinicians to network and collaborate.

DEVINDER MEHET

The topics for the symposia and clinical workshops were well chosen and excellently presented. I found the expert sessions particularly useful, especially the one on precocious puberty and its treatment. The presentations on HRT were sensible and pragmatic: a helpful guide for clinical practice. I also found the sessions on endocrine manipulations in the transsexual educational and enlightening.

S SULIMAN

Society for Endocrinology Summer School

Durham, UK, 5-8 July 2005

The scientific content of the meeting covered a wide spectrum and included sessions on proteomics, stem cells, management of thyroid, adrenal and pituitary diseases, management of gut neuroendocrine tumours and differentiated thyroid cancer, and a session on paediatric endocrinology. The speakers were generally excellent and included both regional experts and invited speakers. The meeting was punctuated by discussion of illuminating and clinically relevant case presentations.

It was well organised, well balanced and delivered by an impressive array of speakers. I would rate the educational value of this meeting highly and would recommend the Summer School to any endocrine SpR wishing to gain further insight into and understanding of the clinical and research aspects of this speciality.

TOM BARBER



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Central image supplied by Dr Elaine Huston, Glasgow, UK

Leptin and neonatal mitochondria

Leptin is thought to mediate some of the dramatic changes in mitochondrial protein function that occur immediately following birth. It modulates the amount of uncoupling protein-1 (UCP1) in brown adipose tissue. However, its effects on UCP2, common in pancreas, lung and skeletal muscle tissue, are less well understood. In this study, Gnanalingham and colleagues have investigated neonatal leptin's potential tissue-specific programming effects on mitochondrial protein in sheep.

The amounts of UCP and other mitochondrial proteins show a peak immediately after birth, followed by a gradual decline. This pattern is thought to be conducive to normal tissue function. Leptin administration after birth reduced the amount of UCP2 specifically in pancreatic β -cells, so influencing insulin secretion and possibly improving resistance to the detrimental effects of exposure to non-esterified fatty acid.

The authors conclude that the effects of leptin are potentially important in regulating neonatal tissue development, and in optimising metabolic control mechanisms in older individuals. **VN**

(See the full article in *Journal of Endocrinology* 187(1), October 2005)

Thyroid hormone in health and disease

The effects of thyroid hormones in normal physiology and disease clearly show that thyroid dysfunction is associated with significant morbidity and mortality. Boelaert and Franklyn continue the Starling review series with this detailed examination of the clinical effects of thyroid hormone in health and illness.

They examine the epidemiological evidence for the effects of thyroid hormone in cardiovascular morbidity and mortality, bone formation and resorption, the developing fetal brain and the neuropsychiatric morbidity associated with thyroid dysfunction. But the review also goes beyond these best known effects and looks at other tissues and organ systems. It

HOT TOPICS

Vicki Norton, Gawain Lagnado, Jayanthi Mondi and Andrew Lowe bring you highlights of the latest research from the Society's journals.

provides an intriguing view of the role of thyroid disease and treatment in the development of malignancy, particularly the use of ^{131}I for the treatment of hyperthyroidism.

Much progress remains to be made in understanding the effects of thyroid hormone. However, better knowledge of its local regulation and modulation should follow the recent characterisation of the MCT8 thyroid hormone transporter. The authors conclude by describing the significant role of thyroid hormones in the morbidity and mortality related to other illnesses, particularly in the critically ill, the elderly, infants and those undergoing extreme surgery, like bone marrow transplantation. **GL**

(See the full article in *Journal of Endocrinology* 187(1), October 2005)

Molecular prostatic imaging in vivo

Investigations into prostate carcinogenesis have not previously used a model that allowed imaging of the prostate gland in live animals.

In this article, Hsieh and co-workers report development of a transgenic mouse model that enables non-invasive bioluminescent imaging of prostate gland development and involution, as well as the androgen-induced restoration of prostate growth in adult transgenic mice. The model uses a firefly luciferase enzyme under the control of a specific supra-prostate-specific antigen (sPSA) promoter. The luciferase reporter gene expression was measured in live animals using a CCD (cooled charge-coupled device) imaging technique. This helped to follow prostate development and the effects of androgen in activating the sPSA promoter quantitatively in living animals.

The sPSA-Luc mouse model could potentially be applied as a founder strain in the study of prostate carcinogenesis or to evaluate prostate-targeted pharmacotherapeutics. The results also suggest that the sPSA promoter could have broad application in developing prostate-specific transgenic mouse strains. **JM**

(See full article in *Journal of Molecular Endocrinology* 35(2), October 2005)

A p53 homologue in thyroid cancer progression

While loss of p53 function has traditionally been perceived as the major factor in thyroid tumour progression, several studies have reported inactivity of the p53 protein in certain thyroid tumours and cell lines. This suggests that other mechanisms may cause p53 inactivation in these tumour cells.

p63 and p73 are members of the p53 family that exhibit remarkable functional and structural homology with p53. Following their previous work on p73, Malaguarna and others have shown in this study that most human thyroid cancers express transcriptionally active p63 α (one of three transcriptionally active p63 isoforms). Furthermore, they have demonstrated that TAp63 α differs from p53, as it does not activate p21Cip1, Bax or Mdm2, which would normally induce cell cycle arrest and apoptosis.

The results suggest that TAp63 α antagonises p53-mediated tumour suppression, through occupancy of the DNA binding sites of p53 responsive elements, and may therefore have an oncogenic role. **AL**

(See the full article in *Endocrine-Related Cancer* 12(4), December 2005)



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Indication: Treatment of facial hirsutism in women. **Dosage and Administration:** Apply a thin layer of the cream to clean and dry affected areas of face and under chin twice daily, at least eight hours apart. Rub in thoroughly. For maximal efficacy, the treated area should not be cleansed within four hours of application. Cosmetics (including sunscreens) can be applied over the treated areas, but no sooner than five minutes after application. Improvement in the condition may be noticed within eight weeks of starting treatment. Continued treatment may result in further improvement and is necessary to maintain beneficial effects. The condition may return to pre-treatment levels within eight weeks following discontinuation of treatment. Use should be discontinued if no beneficial effects are noticed within four months of commencing therapy. Patients may need to continue to use a hair removal method (e.g. shaving or plucking) in conjunction with Vaniqa. In that case, the cream should be applied no sooner than five minutes after shaving or use of other hair

removal methods, as increased stinging or burning may otherwise occur. **Elderly:** (> 65 years) no dosage adjustment is necessary. **Children and Adolescents:** (< 12 years) safety and efficacy of Vaniqa have not been established. **Hepatic/renal impairment:** the safety and efficacy of Vaniqa in women with hepatic or renal impairment have not been established. **Pregnancy and Lactation:** Pregnant or breast-feeding women should not use Vaniqa. **Contra-indications:** Hypersensitivity to eflornithine or to any of the excipients. **Special Warnings and Precautions:** Excessive hair growth may be as a result of serious underlying disorders (e.g. polycystic ovary syndrome, androgen secreting neoplasm) or certain medications (e.g. cyclosporin, glucocorticoids, minoxidil, phenobarbitone, phenytoin, combined oestrogen-androgen hormone replacement therapy). These factors should be considered in the overall medical treatment of patients who might be prescribed Vaniqa. Contact with eyes or mucous membranes (e.g. nose or mouth) should be avoided. Transient stinging or burning may occur when the cream is applied to abraded or broken skin. If skin irritation or intolerance develops, the frequency of application should be reduced temporarily to once a day. If irritation continues, treatment should be discontinued and the physician consulted. It is recommended that hands are washed following use. **Undesirable Effects:** The mostly skin related adverse reactions reported were

primarily mild in intensity and resolved without discontinuation of Vaniqa or initiation of medical treatment. Most events were reported at similar rates between Vaniqa and vehicle. * denotes when higher levels in Vaniqa treated patients were reported: Very common (> 10%); acne. Common (> 1% to < 10%); pseudofolliculitis barbae, alopecia, stinging skin*, burning skin*, dry skin, pruritus, erythema*, tingling skin*, irritated skin, rash*, folliculitis. Uncommon (> 0.1% to < 1%): ingrown hair, oedema face, dermatitis, oedema mouth, papular rash, bleeding skin, herpes simplex, eczema, cheilitis, furunculosis, contact dermatitis, hair disorder, hypopigmentation, flushing skin, lip numbness, skin soreness. Rare (> 0.01% to < 0.1%): rosacea, seborrhoeic dermatitis, skin neoplasm, maculopapular rash, skin cysts, vesiculobullous rash, skin disorder, hirsutism, skin tightness. **Legal Category:** POM. **Price:** 1 x 30g tube £26.04. **Marketing Authorisation Holder:** Shire Pharmaceutical Contracts Ltd., Hampshire International Business Park, Chineham, Basingstoke, Hampshire RG24 8EP, UK. **Marketing Authorisation Number:** EU/1/01/173/002. **Date of Preparation:** July 2004. **Further Information is Available from:** Shire Pharmaceuticals Ltd., Hampshire International Business Park, Chineham, Basingstoke, Hampshire RG24 8EP. Code: 039/0086 Date of item: November 2004

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