Society for Endocrinology

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THE ENDOCRINOLOGIST

THE MAGAZINE OF THE SOCIETY FOR ENDOCRINOLOGY

Responding to RARE DISEASES

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A word from THE EDITOR...

In this final issue of 2023 we bring a focus to rare endocrine diseases, with articles covering aspects of clinical practice, innovation and funding. Patient registries are a vital resource for rare disease research, and you can read articles on new endocrine registries on pages 7 and 27.

On page 25 you'll find a fascinating feature on the variability of clinical assay set-ups; a must-read for anyone involved in patient management. And, on page 12, we present the first of a planned series of 'how to' articles, on a topic we all need to understand for our research to reach patients as rapidly as possible: commercialisation.

If, like me, you're drawn to human interest articles, you'll love this issue in which we interview five individuals making a difference in our discipline in a variety of ways. For instance, we hear from three people at the leading edge of changes at the Society: Kevin Murphy, the first ever Events and Training Officer-Elect, Ruth Andrew on changes to the way grant funding will be assessed and distributed, and her successor as General Secretary-Elect, Aled Rees.

We're all fresh from SfE BES 2023, and what a meeting it was! Craig Doig and I give a 'behind the scenes' look into how the schedule was put together by the Programme Committee on page 15, and discuss some of our personal highlights from the conference. One of the most rewarding things was seeing others enjoy the sessions that we painstakingly crafted. If you have a burning desire to see a particular themed session or speaker at our next SfE BES meeting, please do remember to submit your suggestions to the committee. It's your opportunity to have your say in shaping the meeting.

Wishing you all a peaceful, relaxing and enjoyable festive break and a healthy and prosperous 2024!

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Become a contributor... Contact the Editorial office at **endocrinologist@endocrinology.org**

The Society welcomes news items, contributions, article suggestions and letters to the Editor. We would also like to hear your feedback on this issue of the magazine.

Deadline for news items for the SPRING 2024 issue: **10 January 2024**.

Front cover image ©Shutterstock

Season's greetings and a happy new year to all our readers!

OUR STRATEGY FOR A THRIVING SOCIETY

In our summer issue, we shared the Society's draft strategy for 2024–2027, which has been developed by Council, the Trustee–Directors and the Chairs of all of our committees. Following a consultation process with members, this strategy has now been formally adopted. Our new strategy will provide an important framework to help us effectively support the UK endocrinology community, and ensure that our discipline remains vibrant. You can read it here: **www.endocrinology.org/about-us/society-strategy-2024-2027**.

COUNCIL AND COMMITTEE UPDATES

Following an open call for applications to join our governance team this summer, we welcome everyone who is taking up a new role within the Society after our 2023 Annual General Meeting. You can see your new Council and Committee Chairs on page 17.

SUCCESS FOR SfE BES 2023

It was great to welcome so many of you to Glasgow for this year's Society for Endocrinology BES conference. The event was a resounding success, with more than 1,100 attendees, submission of 495 abstracts and presentation of 365 posters. You can read more later in this issue.

Thank you to everyone who made this one of our best conferences yet. We hope to see you all in October 2024 for our special joint meeting with the Irish Endocrine Society.

SOCIETY CALENDAR

2 February 2024
WOMEN'S HEALTH SUMMIT
Birmingham, UK

29 February–1 March 2024
NET MODELS
Oxford, UK

24 March 2024
THYROID ULTRASOUND
Birmingham, UK

ENDOCRINE ACADEMY
25–27 March 2024
Clinical Update
26–27 March 2024
Endocrine Nurse Update
Birmingham, UK

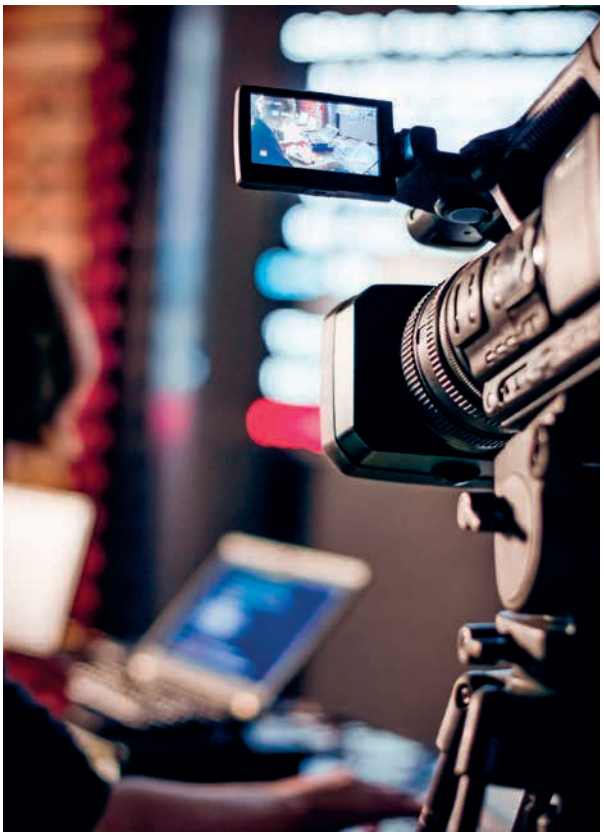
JOINT IRISH–UK ENDOCRINE MEETING
14–15 October 2024
Belfast, UK

SfE BES CONFERENCE
10–12 March 2025
Harrogate, UK

www.endocrinology.org/events for full details

HELP IMPROVE SCIENCE REPORTING IN THE MEDIA

Become a Society Media Ambassador to share your expertise with journalists. Help them to report more responsibly and accurately on endocrinology-related topics in the news. Find out more at **www.endocrinology.org/engaging-with-the-media**.



CHANGES TO THE SOCIETY'S GRANTS

As part of the Society for Endocrinology's 2023 strategic review, we have adapted our grants portfolio to ensure that we effectively meet the funding needs of our members, post-pandemic. We want to support members at all career stages, and operate a transparent application and award process.

Our new grants portfolio comprises four grant types:

- **Research:** support for members' research and audit activities
- **Meeting, Travel and Learning:** funding for members to organise meetings, and to travel to foster collaborations, disseminate research, or learn new skills
- **Teaching:** to support teaching and learning in endocrinology at all stages
- **Outreach:** funding for members and patient support groups for outreach activities.

There will be three deadlines per year and applications for all four grant types will be accepted at each deadline. The first deadline is **17 January 2024**. Find out more, and submit your grant applications. See **www.endocrinology.org/grants-and-awards**.

ADVERTISE YOUR VACANCIES TO OUR COMMUNITY

Attract the best talent by sharing your job, studentship and grant opportunities with our membership.

Check current vacancies at **www.endocrinology.org/careers/jobs**.

HOT TOPICS

SOCIETY FOR ENDOCRINOLOGY OFFICIAL JOURNALS

Society members have free access to the current content of *Journal of Endocrinology*, *Journal of Molecular Endocrinology*, *Endocrine-Related Cancer* and *Clinical Endocrinology* via the Members' Area of the Society website, **www.endocrinology.org**. *Endocrine Connections*, *Endocrinology, Diabetes & Metabolism Case Reports* and *Endocrine Oncology* are open access and free to all. Publishing in *Endocrine Oncology* is currently free.

JOURNAL OF ENDOCRINOLOGY

Sex-based impact of pancreatic islet stressors in Glu^{CreERT2}/Rosa26-eYFP mice

Tanday *et al.* examined variations in metabolic responses and pancreatic islets following the administration of streptozotocin (STZ) and hydrocortisone (HC) in male and female transgenic Glu^{CreERT2}/Rosa26-eYFP mice. Both male and female mice displayed STZ-induced hyperglycaemia, impaired glucose tolerance and reduced insulin concentrations. The metabolic effects of HC were also similar in the two sexes, leading to the classic rise in circulating insulin levels, indicative of insulin resistance.

Following HC administration, female mouse islets contained a higher proportion of α-cells compared with males. In all HC-treated mice, there were relatively comparable increases in β- and α-cell turnover rates, with female mice displaying a slight increase in HC-induced β-cell apoptosis susceptibility. Interestingly, healthy control female mice demonstrated an inherently higher rate of α- to β-cell transdifferentiation, which was reduced by HC treatment. Moreover, the number of glucagon-positive α-cells transitioning into insulin-positive β-cells increased in male STZ mice, but not in females.

In summary, while there were no overt sex-specific alterations in metabolic profiles in STZ or HC mice, subtle differences in pancreatic islet morphology underscore the influence of sex hormones on islets. These findings emphasise the importance of consideration when interpreting observations between male and female subjects.

Read the full article in *Journal of Endocrinology* **259** e230174

JOURNAL OF MOLECULAR ENDOCRINOLOGY

Inhibiting mitochondrial fission and protein kinase R improves progesterone in placental stress

The placenta is essential for human existence, yet remains one of the biggest physiological mysteries. Researchers have attempted to understand the molecular functioning of placental tissue for decades and have struggled to do so, particularly when it comes to shining a spotlight on changes that may proceed disease states and, ultimately, the successful growth of a fetus.

This new research study by Kolaç begins to unravel the fundamental mechanism of placental cell stress, with the goal of improving the release of a key steroid hormone, progesterone. The study's overall aim was to determine the roles of the mitochondrial division inhibitor mdivi1 and the protein kinase R (PKR) inhibitor 2-aminopurine in countering the decrease in progesterone synthesis which is seen as a result of lipopolysaccharide (LPS)- and polyinosinic:polycytidylic acid (Poly I:C)-induced stress in the mitochondria of cultured BeWo trophoblast cells.

This study clearly demonstrates that the upregulation of mitochondrial fission under LPS- and Poly I:C-induced stress is accompanied by a downregulation of progesterone biosynthesis in the placental trophoblast. Furthermore, it suggests that both mdivi1 treatment and inhibition of PKR (a kinase located at the intersection of many signalling pathways) is effective in elevating progesterone levels.

The negative impact of inflammatory stress-induced mitochondrial fission on progesterone synthesis may lead to complications in placental function and the progression of pregnancy, and may be an underlying molecular change in many pregnancy-related pathologies. This study opens up thoughts of whether big stress events are the trigger, or whether smaller stress insults over a longer period may be influential. Regardless, effects on the production of progesterone have huge ramifications for the control of the maternal immune system and placental growth. If this molecular stress is the cause, we can begin to incorporate therapeutic options for pregnancy complications, which have long been left wanting.

Read the full article in *Journal of Molecular Endocrinology* **71** e230059

ENDOCRINE-RELATED CANCER

Lymphangioleiomyomatosis: where endocrinology, immunology and tumour biology meet

A new review by Gibbons *et al.* showcases why multidisciplinary approaches are crucial in furthering our understanding of endocrine conditions. They highlight lymphangioleiomyomatosis (LAM), a rare chronic disease where the lungs of affected individuals (almost exclusively genetically female) will progressively develop large cysts that replace normal alveolar airspace. This results in an inevitable decline in lung function that, in some extreme circumstances, can result in a need for lung transplantation.

Despite recent advances in understanding the pathogenesis, there remains only one viable treatment option to delay the loss of function. This involves inhibition of mTORC1 (mechanistic target of rapamycin complex 1) with medications such as sirolimus, but this is not curative, only preventative.

The article provides the background of LAM; it links the disease and its progression to oestrogen, concisely describes the melanocytic markers and introduces the role of the immune environment in LAM disease progression. It then brings all the strands together and pushes forward to what we need to know in order to attempt to successfully treat this disease and give patients much better outcomes.

Ultimately, this review highlights why lateral and collaborative thinking are essential in tackling some of endocrinology's biggest issues.

Read the full article in *Endocrine-Related Cancer* **30** e230102

ENDOCRINE CONNECTIONS

Optimal LDL-cholesterol for secondary prevention of CVD differs between young and old patients with type 2 diabetes

There is a scarcity of real-world population data to determine the ideal low density lipoprotein–cholesterol (LDL-C) level for preventing cardiovascular disease (CVD) in extremely high risk populations. To address this, Jeong *et al.* analysed data between 2009 and 2012, from 26,922 individuals aged 40 years or older with type 2 diabetes mellitus, who had previously undergone percutaneous coronary intervention (PCI). All participants were categorised based on their LDL-C levels: <55mg/dl, 55–69mg/dl, 70–99mg/dl, 100–129mg/dl, 130–159mg/dl and ≥160mg/dl.

In individuals under 65 years of age, there was a linear increase in the hazard ratios (HRs) for recurrent PCI and stroke with rising LDL-C levels, compared with those whose LDL-C levels were below 55mg/dl. However, for individuals aged 65 and older, the HRs for recurrent PCI and stroke in the 55–69mg/dl LDL-C range were 0.97 (95% CI: 0.85–1.11) and 0.96 (95% CI: 0.79–2.23) respectively. The most favourable range, associated with the lowest HR for heart failure, was an LDL-C level of 70–99mg/dl, while for all-cause mortality, it was an LDL-C level of 55–69mg/dl, irrespective of age (HR: 0.99, 95% CI: 0.91–1.08 and HR: 0.91, 95% CI: 0.81–1.01).

For individuals with type 2 diabetes and established CVD who are under 65 years of age, maintaining an LDL-C level below 55mg/dl seems to be optimal. In contrast, individuals aged 65 and older may benefit from an LDL-C level of 55–69mg/dl in preventing recurrent PCI and stroke.

Read the full article in *Endocrine Connections* **12** e230142

Hot Topics is written by Sophie Clarke, Craig Doig, Louise Hunter, Kim Jonas and Gareth Nye.

ENDOCRINOLOGY, DIABETES & METABOLISM CASE REPORTS

Acute adrenal crisis precipitated by thyroid storm in undiagnosed autoimmune polyglandular syndrome type 2

Autoimmune polyendocrine (polyglandular) syndrome type 2 is characterised by autoimmune adrenal failure accompanied by autoimmune thyroid disease and/or type 1 diabetes. Other autoimmune conditions may also be present. Its aetiology is incompletely understood.

Lassoued and colleagues report the case of a young woman who presented acutely with fever, shock and worsening abdominal pain. She reported a 2-month history of weight loss, and of missing her period. Initial biochemistry demonstrated hyponatraemia, hyperkalaemia, acute kidney injury, elevated liver enzymes, and a serum calcium at the upper end of the normal range. She was resuscitated and treated with parenteral hydrocortisone, but also underwent exploratory laparotomy, given her acute abdominal pain, shock and recent amenorrhoea. This did not detect any pathology, but endocrine biochemistry showed a free thyroxine level of 65pmol/l (reference range 10–20pmol/l), suppressed thyrotrophin (TSH), and low baseline cortisol.

Thyroid storm (Burch–Wartofsky score 70) and adrenal failure were diagnosed, and the patient was treated with methimazole, propranolol and glucocorticoids to good effect. Adrenocorticotrophin was 70pg/ml, indicating primary adrenal failure. TSH receptor antibody titre was normal, but thyroid peroxidase antibody titre was grossly elevated. The patient became hypothyroid in the months after presentation, and was treated with levothyroxine. She required long term hydrocortisone and fludrocortisone replacement.

The authors diagnosed autoimmune polyglandular syndrome type 2 (Schmidt's syndrome) given the co-occurrence of autoimmune adrenal failure and autoimmune thyroid disease. They propose that thyroid storm precipitated an acute adrenal crisis in their patient. The authors discuss management of thyroid storm in the acute setting, and also highlight how important it is to consider co-existence of autoimmune conditions at presentation, to ensure that correct treatment is initiated promptly and misdiagnosis is avoided.

Read the full article in *Endocrinology, Diabetes & Metabolism Case Reports* 2023 EDM 21-0152

ENDOCRINE HIGHLIGHTS

A summary of papers from around the endocrine community that have got you talking.

Age, but not menopausal status, is linked to lower resting energy expenditure

Resting energy expenditure (REE) is assumed to decline with age. The menopause is also thought to be associated with reducing REE. However, variable data exist, with some reporting stable energy expenditure before the age of 60, whilst other studies report an earlier decline in adjusted REE.

To determine whether age and menopausal status influence REE, Karppinen and colleagues included 120 women aged 17–58 years, dividing them by age. Those aged 41–58 years were further subdivided by menopausal status. REE was quantified by indirect calorimetry and body composition using dual X-ray absorptiometry scanning.

Age was inversely associated with REE ($P<0.001$ across all comparisons). There was no difference in REE between those who were pre-/perimenopausal and those who were postmenopausal. Nor was there a difference between postmenopausal women who were on menopausal hormone treatment and those who were not. Additionally, no relationship was observed between basal oestradiol or follicle-stimulating hormone level and REE.

This study did include women on hormonal contraceptives, and is limited by its cross-sectional design. However, the data demonstrate declining REE with age, although they do not support the suggestion that menopause directly reduces REE. Further longitudinal data are required to determine whether changes in sex hormones impact REE.

Read the full article in *Journal of Clinical Endocrinology & Metabolism* **108** 2789–2797

Life expectancy associated with different ages at type 2 diabetes diagnosis in high income countries

Globally, the prevalence of type 2 diabetes is increasing, with 537 million adults estimated to have diabetes in 2021. There is an increasing trend for a lower age at type 2 diabetes diagnosis and, although previous work has estimated that adults with type 2 diabetes die on average six years younger than their counterparts, studies were not sufficiently powered to analyse age at diagnosis.

This study by the Emerging Risk Factors Collaboration aimed to estimate the associations of age at type 2 diabetes diagnosis with all-cause mortality, cause-specific mortality and reductions in life expectancy, in high income countries.

Individual records were analysed from 97 long term, prospective, UK, EU, Canadian and USA cohorts, with 1,515,718 participants followed up for a total of 23.1 million person-years.

They found a steep linear dose–response association between earlier age at diagnosis of diabetes and higher risk of all-cause mortality, with every decade of earlier diabetes diagnosis associated with a reduction in life expectancy of approximately 3–4 years. Interestingly, this reduction in life expectancy associated with diabetes was slightly greater for women than for men.

Read the full article in *Lancet Diabetes & Endocrinology* **11** 731–742

JEKYLL AND HYDE: LESSONS FROM SEVERE INSULIN RESISTANCE

WRITTEN BY ISABEL HUANG-DORAN AND ROBERT K SEMPLE

The centenary of insulin's isolation, and its seismic impact on the treatment of diabetes mellitus, have received worldwide commemoration. Such has the impact of insulin been in diabetes, however, and so potent is it at lowering blood glucose, that its complex additional metabolic growth-promoting effects are commonly under-appreciated. This glucocentric perspective on insulin action can lead us to overlook important aspects of the disorder we call 'insulin resistance' (IR).[1]

UNDERSTANDING IR

IR is defined by a decreased ability of insulin to lower blood glucose. Providing the pancreatic β-cells are fully functional, the response to IR is to make more insulin, until blood concentrations are high enough to return blood glucose to normal. If this simply compensated for reduced insulin responsiveness, and if all insulin's actions were blunted to a similar degree, then an affected person would be restored to normal, albeit with elevated blood insulin levels. However this is not what is seen.

IR is closely associated with non-alcoholic fatty liver disease, polycystic ovary syndrome, a velvety thickening of flexural skin called acanthosis nigricans, soft tissue overgrowth resembling acromegaly in severe cases, and increased risk of some cancers.[2] These are all likely consequences of high insulin levels, which appear capable of exerting growth and other effects, despite IR. In other words, the clinical syndrome of IR is actually a mixture of reduced insulin action, and likely secondary increased insulin action due to compensatory hyperinsulinaemia.[3]

The mechanisms which attenuate insulin's actions in some target tissues but not others are challenging to dissect in humans with common IR of unknown cause. Many common and important components of the IR syndrome are not seen in mice. A fruitful line of enquiry has thus been to evaluate people with rare syndromes of severe IR caused by single gene defects.

SEVERE IR SYNDROMES

Severe IR syndromes include primary disorders of the cellular insulin signalling pathway, for example genetic or acquired dysfunction of the insulin receptor itself, or of downstream signalling components, and lipodystrophy syndromes, defined by partial or complete absence of adipose (fat) tissue, with numerous causative genes.[2] Both groups exhibit reduced glucose lowering by insulin, polycystic ovaries and hyperandrogenism, acanthosis nigricans, and other soft tissue overgrowth depending on IR severity. These can be regarded as core features of the IR syndrome.

More surprisingly, while lipodystrophy is associated with severe dyslipidaemia and fatty liver – effectively a severe form of the obesity-associated metabolic syndrome – these are not seen in primary IR.[4] This underscores the critical role of adipose tissue as a buffer and regulator of inter-organ energy and substrate fluxes. Overloading adipose tissue – whether in lipodystrophy or unhealthy obesity – produces 'lipotoxicity' in distant organs such as the liver. This causes local and systemic inflammation, and fatty liver, among other problems, as well as causing IR. The converse is not true, however, and the absence of lipotoxicity in primary IR indicates that lipotoxicity is likely a consequence of 'adipose failure' itself.[5]

COMMON 'IR SYNDROME'

So, it appears that the common 'IR syndrome' may actually be explained by a combination of adipose failure and IR, combining to produce lipotoxic IR. But this still fails to explain how IR produces features of increased insulin-like action, especially on soft tissues.

It is theorised, with some supporting evidence, that certain tissues are more insulin-resistant than others, due to different local configurations of their insulin signalling pathways.[6] This means that they may 'see' compensatory hyperinsulinaemia differently. In some tissues, IR will be perfectly balanced by increased insulin concentrations, while other, less insulin-resistant tissues will show increased insulin action: a 'bystander' effect of correcting blood glucose levels. It is also plausible that highly increased insulin concentrations activate signalling via the insulin-like growth factor-1 (IGF-1) receptor in some tissues, a possibility supported by the soft tissue overgrowth seen in infants with extreme IR and no functional insulin receptor. This concept of partial or selective IR has been articulated since at least the 1980s, and may yet yield novel strategies to mitigate some IR-related diseases.[7] Much work remains to be done, probably in humans, to understand it fully.

DISEASE MANAGEMENT

In keeping with much rare disease, the evidence base for targeted treatment in monogenic IR is relatively thin, with no randomised clinical trials, but key principles and strategies have emerged.[8]

Management of lipodystrophy recognises it as a state of 'adipose failure', and prioritises adipose 'offloading', just as we would diurese to offload a failing heart. This means caloric restriction to reduce the burden of lipotoxicity, assisted in severe cases by recombinant human leptin, which lowers pathologically increased appetite. Bariatric surgery has shown promise in partial lipodystrophy, even where body mass index is below normal thresholds for surgery. In a complementary approach, pioglitazone can expand residual adipose depots and raise the threshold for lipotoxicity, though often at the expense of aesthetic distress.

Treatment for primary IR focuses on insulin-sensitising agents and suppressing hyperandrogenism in women. Recombinant human IGF-1 has been reported as helpful in extreme cases, whilst use of gonadotrophin-releasing hormone analogues can reduce even the most extreme levels of IR-associated hyperandrogenaemia.[9]

As endocrinologists, we face the consequences of IR every day, albeit in different guises. Thanks to our patients with severe IR, we can move towards a more nuanced understanding of insulin's pleiotropic actions, in which the tissue-specific consequences of both under- and over-insulinisation are appreciated. Not only do these insights guide current management strategies in our patients with monogenic IR, but they provide an important framework for developing new approaches to tackling common IR and its consequences.

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REGISTERING AN INTEREST: NATIONAL PATIENT REGISTRIES FOR ENDOCRINE DISEASES

WRITTEN BY RUTH T CASEY, JESSICA DAVIS AND KRISTIEN BOELAERT

Innovations in genetics, molecular and computational biology and basic research are rapidly evolving. However, translating this progress into clinic research, clinical trials or commissioned therapies in clinical practice remains challenging.

Some of these challenges relate to difficulties in pinpointing the greatest unmet clinical needs, and may be addressed through a systematic collection of data in the form of longitudinal patient registries. Patient registries can include data on patient demographics, diagnosis, treatment and outcomes. Prospective, well-co-ordinated, long term patient registries are an often under-recognised tool for building a comprehensive knowledge base for heterogeneous diseases.

The Society for Endocrinology has committed to promoting and supporting the development of national endocrine real-world data registries. An application for ethics approval for a UK Adrenal Tumour Registry has recently been submitted, with the Society's support, paving the way for this initiative. See page 27 for more details of your Society's work on registries.

MAKING USE OF REGISTRIES

Disease registries can serve a number of objectives and, as such, can benefit a variety of stakeholders. Such registries can provide data on the natural history and outcomes for a specific condition and inform disease guidelines, governmental policies and clinical service development. Registries can be utilised to innovate clinical trial design, particularly for rare disease, and can support the development of therapies by providing real-world evidence, which can be leveraged as an observational arm in a clinical trial setting. Furthermore, national registries can help identify patient populations suitable for recruitment to clinical trials, and can provide valuable clinical and molecular data for basic and clinical researchers.

Large scale data registries, such as the Surveillance, Epidemiology and End Results Program (SEER; **www.seer.cancer.gov**), have demonstrated the power of well-co-ordinated long term data collection. The SEER data registry has provided data on long term outcomes for cancer survivors,[1] temporal changes in cancer incidence and mortality,[2] and data supporting the risk of iatrogenic cancers,[3] and continues to play an advisory role for new cancer registry development.

'The Society for Endocrinology has committed to promoting and supporting the development of national endocrine real-world data registries.'

REGISTRIES FOR THE UK

The establishment of disease-specific national registries can facilitate annual auditing of standards and help identify discrepancies in resources and funding. Within the UK, it can contribute invaluable information for the commissioning of new therapies, biomarkers and technologies, through collaboration with organisations such as the National Institute for Health and Care Excellence (NICE) and NHS England. Furthermore, NHS Digital has set out strategic priorities for 2023–2034, which include a commitment to improving digital infrastructures and digital linkage within the UK, which will serve to improve the efficiency and accuracy of national data collection.

There are a number of exemplar UK disease registries, such as RaDaR (National Registry of Rare Kidney Diseases), which has recruited over 29,500 patients from 107 UK sites. It has contributed to over 30 peer research manuscripts between 2018 and 2023, and currently supports several national clinical research projects (**www.ukkidney.org/rare-renal/radar**).

The British Association of Endocrine and Thyroid Surgeons (BAETS; **www.baets.org.uk**) performs an annual audit of data returned to the UK Registry of Endocrine and Thyroid Surgery. This provides real-life data on quality performance indicators, which has prompted changes and innovations in thyroid surgical practices in the UK. Collection and submission of thyroid surgical data are mandatory requirements for BAETS members and contribute to the NHS Consultant Outcome Publication initiative, promoted initially by the Medical Director of NHS England.

PATIENT BENEFITS

Arguably the most important stakeholder for any disease registry is the patient. Enabling patient interaction in data registries can provide unique opportunities to study quality of life and patient-reported outcome measures.

The opportunity to involve patients in digital health registries has been pioneered by the patient-focused digital health platform PeopleWith (**www.peoplewith.com**). PeopleWith provides a secure digital platform to host anonymised data, which also enables patient interaction via an app. PeopleWith was developed to support better 'user' engagement with healthcare systems and to optimise the voice of the patient in the future of health.

A CO-ORDINATED EFFORT

Finally, national registries should be curated to ensure that data transfer can be easily facilitated to established international data registries or online disease catalogues, such as Online Mendelian Inheritance in Man (OMIM), and the Cancer Genome Atlas Program (TCGA), to name a couple.

Endocrine conditions are frequently heterogeneous and many have a strong hereditary basis, so co-ordinated efforts for national data collection in addition to international collaboration and data sharing will be crucial in ensuring the continued advancement of the specialty and improved patient outcomes.

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AN INTERVIEW WITH... PAUL STEWART

Paul Stewart is Emeritus Professor of Medicine at the University of Leeds. Until his recent retirement, Professor Stewart was a Consultant Endocrinologist at the Leeds Teaching Hospitals NHS Trust, with particular interest in endocrine hypertension, disorders of the pituitary–adrenal axis and reproductive endocrinology, although he was still also actively involved in acute medical admissions until six years before he retired.

The work of his research group spanned discovery science, early translation and patient-related outcomes, with a main focus on cortisol and its metabolism by the 11β-hydroxysteroid dehydrogenases (11β-HSDs), Cushing's syndrome and pituitary tumours.

Professor Stewart is also Editor-in-Chief of *Journal of Clinical Endocrinology & Metabolism*. Here, he tells us about his career and the source of his inspiration.

How did your career lead you to research into 11β-HSD/cortisol metabolism?

This can, in many ways, be summarised as 'serendipity'. After graduating from medical school in Edinburgh, I was destined for a clinical training rotation in cardiology. However, as a senior house officer in endocrinology/diabetes working for Chris Edwards, I became involved in the elucidation of a patient with a rare form of inherited hypertension: the syndrome of apparent mineralocorticoid excess (AME).

We went on to demonstrate that the offending mineralocorticoid was the 'glucocorticoid' hormone cortisol, and successfully treated the patient with suppressive doses of dexamethasone. We identified the enzyme responsible for the inactivation of cortisol to cortisone in the kidney (11β-HSD), showed how liquorice ingestion inhibited this pathway, replicating a milder form of AME, and identified mutations in the gene encoding 11β-HSD2.

This was a hugely exciting phase of my career – Chris was an amazing supervisor and remains a close friend.

What has kept you interested over the years you have worked in this area?

Perhaps not surprisingly, after my first four or five papers were published in *Journal of Clinical Investigation* or *The Lancet*, I was hooked on research and fascinated by the impact it could have on my patients.

AME became a paradigm for an emerging concept in endocrinology – 'intracrinology' – mediated by the pre-receptor metabolism of hormones in peripheral tissues. Thus, in all of us, 11β-HSD2 protects the mineralocorticoid receptor in our kidneys from cortisol excess and permits aldosterone to bind. The opposite-acting enzyme, 11β-HSD1, augments glucocorticoid action in key tissues such as liver, adipose, bone, muscle and skin, by activating cortisol from inactive cortisone. In 2011, it became one of the most patented biomedical targets worldwide, as numerous pharmaceutical companies embarked on selective 11β-HSD1 inhibitor programmes. The opportunity to work closely with industry/drug discovery pathways was enlightening.

Above all though, the main interest came from the people involved. I have had the pleasure to train 40 PhD/MD students in my career. To see their enthusiasm, their influence on our team's scientific approach and their onward personal career development has been immensely gratifying. They are still my extended family!

How have the clinical and research sides of your career intersected?

This was absolutely critical. Working in large tertiary referral centres meant there was no shortage of clinical material and living examples of the wonderful but also devastating effects that hormones can have on patients. Cushing's syndrome remains a fascinating disease and, on a daily basis, I was drawing on my clinical experience to inform and refine our research priorities and approach.

I had the good fortune to meet the Nobel Laureate and geneticist/biologist Sydney Brenner on a couple of occasions, and was always taken with his advice that 'the best (animal) model for human disease is man'. Thanks to

my training, I was privileged to be able to move from bench to bedside and back again, largely using clinical material as my disease models.

How have technological advances (e.g. the omics explosion) shaped your research?

They have had a very significant impact. The rationale for my move from Edinburgh to Birmingham in 1989 was to be trained in molecular biology. Michael Sheppard, Jayne Franklyn and Kevin Docherty in Birmingham were at the forefront of what was then a new technology, and embellishing this into my research was essential. This was endorsed through a further period of training with Ian Mason and Evan Simpson at UT Southwestern Medical Center in Dallas, TX, USA (funded as an MRC Senior Clinical Fellow).

Cedric Shackleton, based in Oakland, CA, USA, is the gas chromatography/mass spectrometry (GC/MS) guru when it comes to steroid hormones. We became close friends following our AME/liquorice work in the early 1980s. Through Wellcome Trust and European Research Council programmes, I was able to fund him to join the group in Birmingham and establish a GC/MS facility that could profile around 40 urinary corticosteroid metabolites, giving a direct read-out on individual cortisol metabolomes. This technology underpinned the clinical development of 11β-HSD1 inhibitors.

In addition, work with, and now led by, Wiebke Arlt has helped uncover new variants of congenital adrenal hyperplasia and alternative pathways for androgen secretion in the adrenal gland. It is leading to a novel diagnostic tool for patients with adrenocortical cancer. Omics certainly isn't just about genes and proteins!

'I have had the pleasure to train 40 PhD/MD students in my career. To see their enthusiasm, their influence on our team's scientific approach and their onward personal career development has been immensely gratifying.'

What have been your career highlights?

As above – the people I have worked with, and witnessing the impact that research has had on the care of my patients and others.

What paper in endocrinology has most inspired you?

There are so many – be they Harvey Cushing's original description of Cushing's disease in the 1930s to Hench, Kendall and Reichstein's marvellous description of the potent anti-inflammatory effects of cortisone in patients with rheumatoid arthritis in 1950. (Thanks to hepatic 11β-HSD1 expression, this resulted in the award of the Nobel Prize.)

However, my choice is as follows. I recall seeing a family with this rare hypertensive disorder in my clinic in Birmingham the week this was published. It is such a fascinating story and intricate unravelling of what was the very first monogenic example (AME being the second!):

Lifton RP, Dluhy RG, Powers M, Rich GM, Cook S, Ulick S & Lalouel JM 1992 A chimaeric 11β-hydroxylase/aldosterone synthase gene causes glucocorticoid-remediable aldosteronism and human hypertension *Nature* **355** 262–265.

'Thanks to my training, I was privileged to be able to move from bench to bedside and back again, largely using clinical material as my disease models.'

What do you consider your top three publications (impact factor/citation index aside)?

Publication 1: Stewart PM, Corrie JET, Shackleton CHL & Edwards CRW 1988 The syndrome of apparent mineralocorticoid excess: a defect in the cortisol–cortisone shuttle *Journal of Clinical Investigation* **82** 340–349. *n=1 but what a prismatic case!*

Publication 2: Bujalska I, Kumar S & Stewart PM 1997 Does central obesity reflect 'Cushing's disease of the omentum'? *Lancet* **349** 1210–1213. *The spark that ignited 11β-HSD1 as a potential therapeutic target for obesity–diabetes–metabolic syndrome.*

Publication 3: Tiganescu A, Tahrani AA, Morgan SA, Otranto M, Desmoulière A, Abrahams L, Hassan-Smith Z, Walker EA, Rabbitt EH, Cooper MS, Amrein K, Lavery GG & Stewart PM 2013 11β-hydroxysteroid dehydrogenase blockade prevents age-induced skin structure and function defects *Journal of Clinical Investigation* **123** 3051–3060. *With 11β-HSD1 inhibitors effective in metabolic syndrome – but not at a magnitude to drive larger phase III studies – the focus became looking for orphan indications, once more informed from patients with untreated and treated Cushing's syndrome. This a great example of how selective 11β-HSD1 inhibitors improve wound healing, work that is now led by Ana Tiganescu as an independent researcher.*

How important have the environment and community been in shaping your research?

The quality of supervisors and other colleagues has been of the utmost importance, as discussed above. Mentorship is another important aspect; it is good to seek out mentors (ideally not your supervisor). More widely, I have benefited from my networking across UK (a big shout out for the Society for Endocrinology), Europe (I was a founding member of the European Network for the Study of Adrenal Tumors in 2002), the USA (another big shout out, this time for the Endocrine Society) and the International Society of Endocrinology. This has enabled me to meet some excellent researchers and clinicians, many of whom are now close colleagues. Endocrinologists are really nice people!

What advice would you give endocrine trainees who are embarking on their careers?

Be inspired, this is an amazing discipline of medicine, where you can make a difference.

Society for Endocrinology

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by switching to direct debit

RENEWAL DEADLINE
31 December 2023

WHY SHOULD I SWITCH?

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HOW CAN I SET IT UP?

Setting up a direct debit is easy. Fill out the mandate from the Members' Area of the website, post it to the address listed and you're good to go!

Scan me to explore your member benefits

LOST IN TRANSLATION? BRINGING INNOVATIONS IN RARE DISEASE TO THE CLINIC

WRITTEN BY CATRIONA CROMBIE

Rare diseases – which include endocrine conditions that present with complex disease phenotypes and require care from multiple specialists – pose unique challenges, not only for the people affected by them, but also for researchers.

Researchers frequently tell us about the hurdles they face in translating and implementing their scientific discoveries. Having spent the last five years supporting rare disease research, we at LifeArc, a self-funded medical research charity, have been working on ways to tackle some of these challenges. We are hoping to address some of them through our Rare Disease Translational Challenge, committing up to £100 million to the rare disease ecosystem over the next few years.

LEVERAGING INVESTMENT

One thing we often hear is that there is limited access to funding, or challenges securing downstream investment. This can be especially difficult when trying to leverage investment from industry when patient numbers are low.

There are several things that can help. First, charities like us can often take risks that a commercial company might not, especially in early-stage research, de-risking projects and making commercial investment more likely.

Secondly, as a sector, there is a need to address market dynamics to ensure there are sustainable models for rare disease treatments, which not only get them to market, but also help keep them there and accessible to all. We'll be exploring options at LifeArc over the coming year.

'Research can happen more quickly when working with the right people at the right time, and with the right infrastructure in place. It's also a place where charities like us can play a key role.'

KNOWLEDGE AND ADVICE

Open access to advice alongside funding is also critical. Intellectual property, regulation, manufacturing and commercialisation are complex processes which many academics have not experienced before, and a lack of support can hold back promising innovations.

Funding streams and initiatives that offer academics support throughout the process can make a real difference.

For example, in 2021, we established three Innovation Hubs for Gene Therapy, along with the Medical Research Council and the Biotechnology and Biological Sciences Research Council. These offer academics access to facilities that are Good Manufacturing Practice (GMP)-compliant for clinical trials, alongside essential translational support and regulatory advice.

We also have £5 million available annually through our Gene Therapy Innovation Fund, which is open to all, and includes advice and support from the Hubs. Similarly, our Philanthropic Fund provides grant support to academics who have promising therapeutics, device or diagnostic projects for rare diseases, and we offer advice on intellectual property and commercialisation throughout the process.

'We've been delighted at the readiness of the community to work in this way, and it shows the potential for an even more joined up approach as we move forwards.'

INFRASTRUCTURE AND COLLABORATION

Research can happen more quickly when working with the right people at the right time, and with the right infrastructure in place. It's also a place where charities like us can play a key role.

For example, we have recently announced our intention to fund four Translational Rare Disease Centres (TRDCs), opening next year. They will serve as focal points for rare disease research translation, knowledge-sharing and engagement with the patient community in the UK.

As neutral partners, charities can often bring together research groups and institutions across specialties, and help challenge the status quo. And, as part of the TRDC process, we've encouraged collaborative applications where we've seen synergies between research groups and institutions.

'We're excited at the prospect of working with the wider community in order to get innovations to patients more quickly.'

We've been delighted at the readiness of the community to work in this way, and it shows the potential for an even more joined up approach as we move forwards.

While there are significant challenges facing rare disease researchers, that also means there are opportunities for real change. We're excited at the prospect of working with the wider community in order to get innovations to patients more quickly.

CATRIONA CROMBIE
Head of Rare Disease Translational Challenge, LifeArc

HOW DO I... COMMERCIALISE RESEARCH?

WRITTEN BY VEEMAL BHOWRUTH

Veemal Bhowruth made the transition from research to commercialisation, and now works at University of Birmingham Enterprise Ltd, the technology transfer company for the University of Birmingham, where he is the life science lead. Here, he answers some questions that are frequently posed by readers about technology transfer.

WHAT IS TECHNOLOGY TRANSFER?

Research commercialisation comes under the bracket of knowledge exchange, which, as the words suggest, brings together academic staff, users of research, and wider groups and communities.

Technology transfer is a subset of knowledge exchange and involves the transfer of innovative solutions that are protected by different intellectual property rights.

Universities and research institutions usually have a dedicated Technology Transfer Office (TTO), which is staffed by experts from a variety of disciplines. The focus of the TTO is not primarily on making money, but rather on finding and accessing the right avenues for translation or knowledge exchange.

WHAT ARE INTELLECTUAL PROPERTY (IP) RIGHTS?

In most medical fields, you can't commercialise if you don't have IP rights. For this reason, initial conversations with TTOs are usually about patents or IP.

'The TTO will give the best assistance if you engage with them early.'

IP rights are protected by law, and give the owner the right to benefit by providing them with control over how their property is used. This protection is territory-specific, and lasts for a set period of time, enabling the inventor or the owner of the patent to stop others from using, making or selling the invention without permission. Most medical innovations take several years to come to market, and this period of protection provides you with a monopoly to commercialise the technology and be the first to market, and to recoup R&D costs.[1]

IP rights include patents, copyright, trademarks and industrial designs (**www.wipo.int/about-ip**). For medical commercialisation, the relevant IP is usually a patent – and for an invention to qualify for patent protection, it must be novel, have an inventive step and be industrially applicable.[2] This last point is important – theories are not patentable in isolation but, if put into a practical context, the result could be patentable if it is also new and inventive.

WHAT DOES PATENTING INVOLVE?

Patenting is an expensive, lengthy, multistep process, and organisational budgets are limited, so you can expect your discovery or invention to be heavily scrutinised before filing.

There are two things that researchers need to be aware of at the outset.

First, disclosure to anyone, in any format, will jeopardise patentability, if this happens before the patent application is filed. This includes journal publication, posters or presentation at conferences, or even emails that inadvertently contain details of the invention. This creates an inevitable tension between research, which has the imperative of publishing or presenting results quickly, and filing a patent, which has the imperative of non-disclosure before filing a patent application, although most journals will defer publication if they are told a patent application is being filed.

Secondly, you need to prove that the inventive step was yours, and to be clear on what your research contract allows in terms of patenting, particularly if you are contracted to work with an external organisation. TTOs will ask to see both your lab notebooks and your research contracts, usually before they start on a patent search, to see whether the invention has already been patented. The TTO will give the best assistance if you engage with them early.

LICENCE OR SPINOUT?

If the discovery is patentable, there are two routes to market: licensing the IP to an external organisation to develop a product or service, or spinout, which involves setting up a company. They each have their own merits, and TTOs are well versed in the cases for both routes.

Good IP is 'necessary but not sufficient' for spinout success. Other factors – such as finding the right management team, having the right

UNDERSTANDING THE PATENTING PROCESS

The European patenting process is governed by the European Patent Office (EPO). It has immutable conditions and deadlines. It can take four years or more from filing the initial application to the patent being published in its final form.

Broadly speaking, the process is as follows:[3]

- The initial patent application is filed at your national patent office. This defines the 'priority date' – the date from which you believe your invention is new. Patent applications filed in other European countries in the 12 months after this date are treated as if they were filed on the priority date.
- The priority date defines the start of a 12-month period. Patent examiners search patent databases, technical and academic literature for similar inventions, and assess how these might impact upon your patent application. This search report is made available to the inventors who, as a result, may decide not to proceed beyond this stage.
- 18 months after the priority date, the application is published on patent databases. The patent is now 'pending' and its technical details are on public display.
- At this stage, the EPO can crowd-source evidence against the patent application, which may limit the scope of your application, or even block it.
- This evidence, together with the earlier search report, is presented as 'examiner's objections'.
- The patent application may need to be revised in response to these before it is granted.

'Spinout will be more time-consuming [than licensing] and is likely to require much greater input from you.'

business model, and securing sufficient capital to keep the company running before it brings in revenue – are necessary considerations.

What *you* want is equally important. Spinout will be more time-consuming and is likely to require much greater input from you, even if you want to stay in your current research or clinical role.

WHAT ELSE DOES A TTO DO?

It could be that your invention has applications in markets that you don't know about. TTOs will work with you to gain market knowledge and understanding, and they may support you or your research team through accelerator programmes such as ICURe (**www.icureprogramme.com**), which guides researchers through the process of refining and validating commercial potential.

TTOs can also help you find and apply for translational funds and, in some universities, they also run entrepreneurship training, which is worth considering.

Finally, patenting is not the only method of knowledge exchange. This covers a broad range of activities, including consultancy, collaborative research and Knowledge Transfer Partnerships (**www.ktp-uk.org**), which connect businesses that have an innovation idea with the academic expertise to help deliver it.

TTOs are exceptionally well-connected, and have access to these networks, which can help you commercialise in other ways.

VEEMAL BHOWRUTH
University of Birmingham Enterprise Ltd

*For further reading see the factsheet 'Knowledge exchange and commercialisation' at **www.praxisauril.org.uk/sites/praxisunico.org.uk/files/KEandCommercialisation.pdf**.*

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3. European Patent Office 2023 *What to Expect* www.epo.org/en/new-to-patents/what-to-expect.

Success at SfE BES 2023

Our annual SfE BES conference took place in Glasgow from 13 to 15 November 2023. More than 1,100 attendees joined us for an enriching conference which featured some of the best clinical and scientific research from across our field.

It was fantastic to return to Scotland to bring our community together and learn from each other, share our passion for endocrinology, and collectively work towards advancing research and improving patient care.

Thank you to all of our exhibitors and sponsors for supporting this amazing event.

Over 1,100 attendees

495 abstracts submitted

339 tweets used #SFEBES2023 during the event

365 posters presented

REWARDING EXCELLENCE

It's not just about the prestigious Medal Lectures at SfE BES, the best presentations on advances in research and clinical practice were also awarded a selection of prizes at the event.

ENDOCRINE NETWORK PRIZES

Adrenal and Cardiovascular
Best Oral – Lara Birch
Best Poster – Chris Smith, Ahmed Al-Salihi

Bone and Calcium
Best Oral – Catherine Lovegrove

Endocrine Cancer and Late Effects
Best Oral – Stephanie Agbana

Endocrine Cancer and RET
Best Poster – Courtney West

Metabolism, Obesity and Diabetes
Best Oral – T'ng Choong Kwok
Best Poster – Nikola Srni

Neuroendocrinology and Pituitary
Best Oral – Katie Sharrocks
Best Poster – James MacFarlane

Reproductive
Best Oral – Edouard G Mills
Best Poster – Marianne Watters, Jacqueline Maybin

Thyroid
Best Oral – Katie Brookes
Best Poster – Wei Yang

CLINICAL ENDOCRINOLOGY TRUST PRIZES

Best Basic Abstract –
Hassan Massalha
Best Clinical Abstract –
Benjamin Bakke Hansen
Best Nursing Practice Abstract –
Julie Lynch

ANNETTE LOUISE SEAL AWARD

Sponsored by the Addison's Disease Self-Help Group
Louise Breen

FEATURED CLINICAL CASES POSTER PRIZE

Supported by Endocrinology, Diabetes and Metabolism Case Reports
Yasir Elhassan

LATE BREAKING ABSTRACTS POSTER PRIZE

Nadia Chaudhury

SEE YOU NEXT YEAR!

With SfE BES moving to the spring from 2025, next year sees our joint meeting with the Irish Endocrine Society taking place in Belfast from 14 to 15 October.

More details will be available soon. In the meantime, we invite you to take part in our programme suggestions survey, via the QR code. The deadline for responses is **5 January 2024**.

A programme for everyone
INSIGHTS FROM THE ORGANISING COMMITTEE

Craig Doig (Nottingham) and Kim Jonas (London) were members of the Programme Committee for this year's SfE BES conference. Here, they share their perspectives on the process of making sure that everyone is catered for at the Society's leading annual endocrine event.

Crafting a good scientific programme for the SfE BES conference is no easy feat. There's considerable pressure to meet the interests of the Society's broad membership base. Despite this challenge, every year the Programme Committee fashions a tightly packed programme of outstanding content.

There's a finite amount of material that you can squeeze into three days. However, we manage: that's mostly through hard thinking, combined with exceptionally hard work. The Programme Committee's members who cover the breadth of endocrine specialties. We break into teams and give consideration to formulating each individual session in our specialist areas, as well as the Meet the Expert, How do I? and physiology workshops.

After we have thrashed out these sessions, we come together and discuss each symposium, including the rationale and the balance of speakers, selecting session Chairs and ensuring an overall balance with the other programme suggestions.

It takes an intense two days to put the programme together! After that, our work doesn't stop. We are all assigned sessions that we finesse. And, should speakers decline, we have to work to identify alternatives whilst still balancing the session. This year, we had a few speakers who were unable to join in person, and so we worked with Bioscientifica to ensure that they could either present remotely in real time, or pre-record their talk and join for live questions. Being a Programme Committee member is hard work but rewarding, especially when you see the fruits of your labour, and the enjoyment of attendees.

TAKING THE ROLE OF PROGRAMME CO-ORDINATOR

The Programme Committee Chair and two Programme Co-ordinators (one for basic science and one clinical) also put together the oral communications and oral poster presentations. This year Kim was the Basic Science Co-ordinator. About 500 abstracts were submitted across the standard and late breaking deadlines, so it was quite a task to go through the ranked abstracts and select the oral and oral poster presentations. We had a particularly good selection of neuroendocrinology and reproductive endocrinology abstracts, so we separated these two themes, though they have historically been combined in a single session.

Although the abstracts are marked and ranked by a panel, we still have the task of balancing the sessions and also have to take into account whether presenters have selected 'poster only' or 'either oral communication or poster' as a way of communicating their work. There were a few occasions where the abstracts had scored well but 'poster presentation' had been selected, so we would encourage you to be bold and select to present in either format. You never know – it could be you on the receiving end of an award!

Kim with Sumetha Sureshkumar and Ruijuan Xu (two members of her group) at the conference dinner.

CRAIG'S HIGHLIGHTS

This year's SfE BES conference saw the great and the good of UK and Irish endocrinology meet in Glasgow. As a Programme Committee member, it was gratifying to see our year-long plans turned into reality. Among the many excellent talks, a standout moment for me was John Speakman's Dale Medal Lecture, which offered a meticulous evaluation of weight gain in relation to amino acid dietary content. Grounded in solid basic science, the lecture presented a compelling hypothesis accompanied by a narrative that left the audience on the edge of their seats. In contrast to Netflix, where the next episode can be readily accessed, the science dictates that we must patiently await the next set of experimental results…

KIM'S HIGHLIGHTS

I agree with Craig that there were many (many!) excellent talks. One highlight was the workshop on what we should consider when selecting our experimental models and designing experiments. The session on reproductive ageing was truly excellent, with very considered presentations on basic, clinical, population-based and translational science, highlighting remarkable holes in our knowledge of this area. I was also impressed by the standard of presentations – oral, oral posters and posters – by our early career presenters. Of course, it would be remiss not to mention the social and networking side of the conference. It was great to see so many colleagues and friends, and catch up about science and life, as well as dancing at the notoriously fun SfE BES conference dinner!

Society for Endocrinology

Events and Training 2024

The Society for Endocrinology provides broad a range of events, designed to facilitate networking in our community, and to support your professional development.

NEW! WOMEN'S HEALTH SUMMIT

2 February 2024
Edgbaston Park Hotel and Conference Centre, Birmingham

This meeting will cover recent advances and best clinical practice in women's health. It is relevant to consultants, GPs, nurses and trainees.

NEW! NET MODELS

29 February–1 March 2024
Milton Hill House, Oxford

This event will bring together experts in neuroendocrine tumours (NETs) to pioneer change in NET research. The programme will feature presentations from leading voices in the field and participative sessions, where delegates can discuss their data and current model limitations.

THYROID ULTRASOUND

24 March 2024
Hilton Birmingham Metropole Hotel, Birmingham

A one-day course aimed at endocrine specialists who wish to enhance their thyroid ultrasound skills. The programme combines lectures, discussion of clinical cases, and hands-on experience of thyroid ultrasound.

CLINICAL UPDATE

25–27 March 2024
Hilton Birmingham Metropole Hotel, Birmingham

Clinical Update is an indispensable event for trainees and new consultants preparing to sit RCP's Specialty Certificate Examination in endocrinology and diabetes.

ENDOCRINE NURSE UPDATE

26–27 March 2024
Hilton Birmingham Metropole Hotel, Birmingham

This event is designed to support endocrine specialist nurses. The programme features two days of lectures, workshops a range of networking opportunities.

JOINT IRISH–UK ENDOCRINE MEETING

14–15 October 2024
Belfast

We're working with the Irish Endocrine Society to run this special joint meeting. Save the date for the largest gathering endocrine professionals in the UK and Ireland.

Find out more at **www.endocrinology.org/events**

Embracing new perspectives **AT THE SOCIETY**

We actively encourage members from all career levels, backgrounds and specialties to join our Council of Management and committees. This ensures that we are reflecting on the external challenges that our members face, supporting the field of endocrinology, and maximising the positive impact of our Society.

Following an open call for applications to join our governance team this summer, we welcome everyone who is taking up a new role within the Society after our 2023 Annual General Meeting.

NEW OFFICERS

Professor Aled Rees
Cardiff
General Secretary-Elect

Professor Kevin Murphy
London
Events and Training Officer-Elect

NEW COUNCIL MEMBERS

Professor Tim Cole
Clayton, Australia

Mr Sherwin Criseno
Birmingham

Dr Mark Turner
Coventry

NEW COMMITTEE CHAIRS

Dr Niamh Martin
London
Public Engagement Committee Chair

Dr Zoi Michailidou
Edinburgh
Science Committee Chair

Dr Anna Mitchell
Newcastle upon Tyne
Programme Committee Co-Chair

Professor Jeremy Tomlinson
Oxford
Grants Panel Chair

DO YOU WANT TO GET INVOLVED IN YOUR SOCIETY'S GOVERNANCE TEAM?

We'll be opening applications to join our Prizes and Awards working group and Events and Training Committee shortly, so keep an eye on the Society's website for more details.

Meet Aled Rees
OUR NEW GENERAL SECRETARY-ELECT

Aled Rees is Professor of Endocrinology and Consultant Endocrinologist at Cardiff University's School of Medicine. Aled's clinical practice spans all aspects of endocrinology, with a particular focus on neuroendocrinology. He is currently researching the impact of the hormonal environment in early life on cognition and neurodevelopment.

Professor Rees was chosen by the membership as the Society's new General Secretary-Elect, and began his term of office at the Annual General Meeting during this year's SfE BES conference. We took the opportunity to talk to him about his career and his perspective on our discipline.

What attracted you to endocrinology?

I enjoyed all my rotations as an undergraduate and junior doctor, but eventually settled on a career as a physician. I very nearly became a rheumatologist, but chose endocrinology when working as a senior house officer with Professor Maurice Scanlon. In those days, patients were brought into the ward for many dynamic tests, so we had the opportunity to see endocrine conditions first-hand. I liked the diversity of the presentations, the problem-solving element, and the academic nature of the discipline.

What are you proudest of in your career?

It's been a privilege to contribute in a small way to the development of young endocrinologists and scientists. I've enjoyed working with endocrine trainees and supervising undergraduate, PhD and MD projects. I've also been inspired by patients, and have really valued opportunities to work with patient support organisations, to help develop services and establish research priorities. On the academic side, I've been proud to take part in 'real-world' data projects and clinical trials which have led to changes in clinical practice and the development of new treatments.

How did you first get involved with the Society?

I was fortunate to secure funding for my PhD from a Society for Endocrinology Clinical Endocrinology Trust Fellowship (now known as the *Clinical Endocrinology* Journal Foundation). I was really grateful for this opportunity, and my career might have been very different without this support. I subsequently got involved in Society-supported initiatives (such as CaHASE (the Congenital Adrenal Hyperplasia Adult Study Executive) and the Acromegaly Project), and served on the Society's Clinical Committee, Finance Committee and Council.

What challenges face the Society and endocrinology in general?

There's no escaping the fact that we live in financially difficult times. The Society has the challenge of balancing financial prudence with the need to deliver on its numerous activities and its mission to enhance our discipline. However, I know from my previous experience of working on Council that it has strong leadership and expertise in place to deliver on these objectives.

The pressures on clinical services, training and science are also very real. We have to make sure that we work together as a community to share ideas, raise our profile and promote activity through collaboration.

> *'The recent governance review placed a great deal of emphasis on transparency, inclusivity and engagement.'*

What are the most exciting opportunities for the Society?

Our biggest strength is our collective ability. The breadth and quality of work presented by our scientists, young endocrinologists, nurses and healthcare professionals at the recent SfE BES conference were impressive and inspiring. If we can get better at working collaboratively, there is real opportunity in the UK to take advantage of some our 'unique selling points' such as the NHS, big data, the NIHR Clinical Research Network, and genomic initiatives, to enhance our position as a leading endocrine community on the world stage.

What do you hope to achieve during your term as General Secretary?

First and foremost, I'd like to pay tribute to my predecessor, Professor Ruth Andrew, who has been a superb General Secretary over the last few years. I'm looking forward to working with her in an initial 'shadow' role. We already have a large, thriving community, but I would like to help drive a continued expansion of our membership. I'm also keen to see the great work that has been undertaken in recent years on the Society's new governance structure, on equality, diversity and inclusion, and on revised grants schemes, delivered and developed further.

Why should members get involved with the Society's governance?

I had the privilege of seeing the work that the Society undertook in delivering meetings such as the SfE BES conference and Endocrine Academy, and I felt the need to contribute in some way. I have learnt a great deal from working with highly skilled colleagues at the Society in various roles. I enjoyed helping contribute to many national initiatives but also benefited from gaining new knowledge, which I have used to help shape endocrine services in my own practice. The recent governance review placed a great deal of emphasis on transparency, inclusivity and engagement. I would strongly encourage others to apply for committee vacancies, so that they can benefit in the same ways that I have done, and so that the Society can maximise representation from the diversity of its membership.

Meet Kevin Murphy
OUR NEW EVENTS AND TRAINING OFFICER-ELECT

Kevin Murphy is Professor of Endocrinology and Metabolism at Imperial College London. His research focuses on how nutrient sensing in the gut regulates appetite and glucose homeostasis. Professor Murphy has been chosen by members as the Society's first Events and Training Officer-Elect, to chair our new Events, Training and Skills Committee. He will work with Robert Semple, the Programme Secretary, until Professor Semple stands down at the SfE BES conference in March 2025.

What attracted you to endocrinology?
The glamour, mostly… Well, I suppose it crept up on me. After my undergraduate degree, I ended up working as a technician in a department full of endocrinologists. I got interested in the regulation of energy and glucose homeostasis, which are controlled by hormones. After a while, you start to realise that hormones pretty much do everything: any kind of physiological system or medical specialty, there's a hormone for that (usually there are several).

What have been your career highlights so far?
The science is fun, but I also like the supervisory and support aspects of the job. It's been nice seeing early career members from my lab go on to bigger and better things. And I enjoyed working in the team who reviewed gender inclusion at the SfE BES conference and came up with some practical approaches to improve it.[1]

How did you first get involved with the Society?
I joined as a PhD student, because most of my department went to the SfE BES conference every year. I found the conference provided a very helpful introduction to the field (and the Society was very generous with travel funding for students). Later, I applied for a position on the Science Committee, and I seem to have been involved in some shape or form ever since.

Tell us about your role as Events and Training Officer – why is this new position needed?
We are trying to ensure that the Society offers its diverse membership what they want and need. Our aim is to provide training and organise events for our members in the NHS (doctors, nurses and other healthcare professionals) and scientists in academia and industry. And we want to do this across a range of roles and levels of experience, from seasoned consultants to undergraduate students. The Society's previous committee structure wasn't well-suited to co-ordinating all these different potential offerings, so that's what this new role is designed to do.

'It's nice to listen to people's ideas about how the Society can better serve its members and to work with the Society and the committees to think about how we can make this work.'

What do you think are members' key training challenges?
For scientists, it is helpful to have opportunities to learn about new techniques and then to go and be taught how to actually do them by other researchers. In the case of early career scientists in particular, the transition to academic positions is always challenging. Any support we can provide for people at that stage will be useful.

For those in healthcare, how we deliver good care is always changing, and we need to help our members keep up with that, and to be responsive to the opportunities for professional development that they want.

Really, I'm hoping our members will tell us what they most value, so we can try to provide it.

What do you hope to achieve during your term?
I want us to offer courses and events that mean all Society members feel included and that their Society membership is valuable to them. I think the Society has made great progress with equality, diversity and inclusion in recent years, but I'd like to do what I can to improve that further, at flagship events like the SfE BES conference, and across the whole range of support we can offer to all of our members. And hopefully not to break anything valuable.

Why did you get involved with the Society governance, and why should other members do the same?
Governance is a very dry-sounding word, but really it is just about helping to run stuff. It's nice to listen to people's ideas about how the Society can better serve its members, and to work with the Society and the committees to think about how we can make this work – and then to help put those ideas into practice.

Also, I wanted the opportunity to become crazed with power!

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An interview with…
RUTH ANDREW
MEETING OUR MEMBERS' FUNDING NEEDS

Ruth Andrew is Professor of Pharmaceutical Endocrinology at the University of Edinburgh, and directs the Clinical Research Facility Mass Spectrometry Core. She sits on the Society for Endocrinology's Council as General Secretary, and is the incoming Editor-in-Chief for two Society journals: *Journal of Endocrinology* and *Journal of Molecular Endocrinology*.

We caught up with Ruth, who has also been part of the team modernising the Society's grants portfolio. We asked her why the time was right to review our grants, and how the new portfolio will better meet our members' funding needs.

Ruth, how did you become involved with the Society, and how has that relationship progressed?
I was guided to join the Society when I started at the Endocrinology Department at the University of Edinburgh during my first post doc. My first Society event was the 1995 Meeting of the Society in London just before Christmas, where I was selected for a talk. This was very exciting and, at the time, I had to get my slides printed. I remember carefully packing them like gold dust! Since then, I've attended every SfE BES conference, and now bring my own team with me.

I became involved with Society activities, first as a local co-ordinator, and then joined the Science Committee. During that time, I was part of the team that developed the Society's Career Development Workshop with Rob Fowkes and Derek Renshaw. It is really rewarding to see so many of those delegates still attending the SfE BES conference and progressing in their careers.

I spent time on the Society's Programme Organising Committee, then on Council and, more recently, the Finance Committee. I've also been involved in several Society working groups. I've found that broad experience has been highly valuable in my current role as General Secretary, where you need a holistic overview to join the jigsaw of the 'Society group' together, and make sure we find opportunities to link the right people up.

How much have grants had an impact on the course of your career?
Hugely – the Society's grants are enabling, and we probably don't capture well enough the significant good we've done as an organisation.

As a junior researcher, my first Society grants were for travel, both to the SfE BES conferences and internationally, usually to ENDO. Presenting at these meetings enabled me to gain exposure to international experts and build skills in answering unexpected questions.

Later on, I gained one of the first research grants, and that facilitated an important clinical arm to complement the preclinical studies of one of my PhD students, Alison McNeilly (now a lecturer in Dundee, and an Academy of Medical Sciences Springboard Fellow). That translational element really boosted the impact of her work, and opened doors to a more impactful publication.

Further students of mine have similarly benefited, gaining their own small grants. Some of them, for instance Mark Nixon, have gone on to join the Society's Leadership and Development Awards Programme. These funds often provide the keys to unlock the full potential of research and researchers.

My team has also been able to gain Practical Skills Grants to learn from world experts, which not only helps their individual careers, but also enables us to grow as a team through shared knowledge.

In addition, I've gained grants to support undergraduates, and I think the grant that gives me the greatest pleasure is the smallest one: the Undergraduate Achievement Award. I've held this with Edinburgh colleagues since 2007, to promote endocrinology in Honours years, benefiting both scientists and intercalating medics. It is just £300 per annum and, even then, we split it between several courses and across several activities. We've awarded a small part of this award to an undergraduate performing an abstracting task, and the best performing student is often not the one who might shine in the end of term exam. It is hard to express how rewarding it is to see their reaction when their previously untapped skills are unexpectedly recognised.

How did our new strategy highlight the need for an updated grants portfolio?
The Society's grants portfolio had grown iteratively over a number of years, with the best intentions, and resulted in a complicated array of grants, largely focused on junior researchers. The system had become unwieldy, with some disparities in criteria and also no possibility of veering between grant pots to best utilise the available funds. It had been a long time since we'd taken a holistic view of the grants portfolio, and it made sense to do this alongside the Society's strategic review.

At the time, the Society's Council was executing a review of equality, diversity and inclusion, and we wanted to ensure the benefits of membership were clearly available to all. Feedback from our Science and Clinical Committees also highlighted that that it would be valuable to support a larger proportion of our members' activities, including teaching, clinical audit, and patient and public involvement.

Overall, a more flexible grants structure was proposed, linked to the pillars of our new strategy. This was guided by a working group including representatives from all our member categories. We're really grateful to Professor Jeremy Tomlinson for stepping forward to lead the new Grants Panel, and the next year will allow us to embed and shape the new portfolio, to provide the maximum benefit to members.

How will our new grants support the changes in members' funding needs, post-pandemic?

Speaking as a researcher, I find there has been a move to greater integration of data science and support from expert technology facilities. Going forward, training in computer programming, such as R, is becoming an essential research skill.

Although not pandemic-related, another evolving change is the participation of patients and the public in research design and execution. The UK is one of the world leaders in this area; integrating these constituencies is now essential for a successful grant application, even for basic science.

The Society can help with this through linking to patient groups, and also by providing essential funds for an initial scoping, to satisfy the larger funders of feasibility, as well as evaluating population numbers in database resources.

Who can apply for the new grants?

Everyone (subject to being a member for the appropriate amount of time). Even student members can be part of a team application. Our governance body still has a strong desire to support early career researchers, but the new portfolio allows other members to apply on merit. The proportions of junior to senior members supported is something that Council and the new Grants Panel will be monitoring closely, until we get it right.

Why did the Society decide that grant applications should now be marked by a Grants Panel?

This arose through recommendations from our Science Committee, where the Chair, Kevin Murphy, scoped best practice. Having a dedicated Grants Panel will also bring us in line with guidance from the Association of Medical Research Charities. All the Society's grants will now be reviewed on merit, by the same committee, to allow equity across the portfolio. And, although our Council has provided guidance on how, roughly, the funds should be split amongst different grant types, evaluation of all grants by one panel will bring greater flexibility about how funds are distributed, ensuring that we spend every penny on members!

The Society is also going to offer 25% of the spaces on the Grants Panel to more junior members who want to gain experience of grant-awarding panels. This will allow us to develop our members, so that the Society can be highly represented in the larger UK funding bodies. We are a small Society, but we already punch above our weight nationally, so we need to keep that up by developing a sustainable stream of leaders in all career types.

What does this mean for our members?

Well, first, please check out the opportunities and read the new guidance on the website; become familiar with what is on offer and the deadlines. Grants will be judged by the panel three times annually and, wherever possible, feedback will be given. All the opportunities that were there previously are still there now, but they may be 'wearing a different hat' and require more justification.

Some of our previous grants were awarded on a capacity basis; that is no longer the case. All will be judged on merit, so justification is now more important. If you have a need and a reason, and can express the value and impact that the grant will have, please apply.

Do you see this having a big effect on endocrinology?

I probably need to reflect on the impacts I have seen. These grants had a large impact on me at a junior stage, and enabled me to improve the impacts of my research outcomes. My team has also benefited from access to funds for skills training or supporting a summer student. These benefits don't just help the student, they help train the young academic in supervision, and provide evidence of their leadership skills for their own progress reviews. For me, being on the Society's Science Committee offered me my first experiences of grant reviewing, and helped me gain roles on national and international panels.

The Society's Meeting Support Grants also have a significant impact. I've been lucky to have been involved with teams in Edinburgh delivering small conferences with the help of these awards. These have led to highly stimulating events, fostering ongoing collaborations and developing younger colleagues. Two of the Society's Leadership and Development Awardees were on the programme committees for these events, which gave them their first taste of how to develop stimulating programmes, with opportunities for networking and student development. At least one, Zoi Michailidou (our incoming Science Committee Chair), has gone on to work on the Programme Committee for the SfE BES conference.

So, I believe these awards help us to promote excellent endocrine science and clinical medicine but, importantly, they also enable our members to rise to the top in their own arena as champions of endocrinology.

What is your advice to members who are considering applying for grants?

Well, first of all, please do so! We want to support you. The process is competitive, so make it easy for us to award the grant. We've also got useful resources on the careers pages of our website, which explain what a good grant application looks like: **www.endocrinology.org/careers/career-resources-and-information**, so make sure you take time to think about that, and also take advice from your peers who have been successful in the field.

If you have a specific question, ask us. As with any process, read the guidance and try to answer all aspects. If we can't award a grant to you the first time, please take on board the feedback and, if it encourages you to reapply, please do. That type of feedback is genuinely trying to encourage you, because we think – with some tweaks – you can succeed.

Lastly, please help us by telling us how the grants have helped you, so that we can engage others.

Find out more at **www.endocrinology.org/grants-and-awards**

Corporate liaison: THE BENEFITS OF ENGAGING WITH INDUSTRY

In our second article highlighting the crucial work of the Society's Corporate Liaison Committee, Tijana Mitić gives her perspective as a committee member.

Building relationships with industry can offer numerous benefits and opportunities, both for societies and academic institutions to fulfil their charitable aims, and for individuals to advance their careers. As a university lecturer, networking with industry partners enables me to stay current with industry trends, technologies and best practice.

At the University of Edinburgh's Centre for Cardiovascular Science (CVS), we have invited several guest speakers from industry to the CVS External Seminar Series (**www.linkedin.com/feed/hashtag/?keywords=cvsexternalseminars**). Representatives from AstraZeneca, Synthego, Takeda and GenScript have presented their latest innovative developments. We have also hosted industry partners and arranged table-top displays for them to showcase their products and resources. Some of our industry partners have sponsored CVS seminars, helping to enhance the reputation of the series.

I have seen first-hand how engagement with industry can be pivotal for the professional development of early career researchers, inspiring them to undertake internships and work placements within industry. Several fruitful collaborations in this regard saw industry partners join CVS principal investigators as applicants on Medical Research Scotland PhD studentships. Beyond funding and grants, students have also been inspired to take extra courses during their PhD programmes, to better align with industry needs. In all, engaging with industry offers a myriad of advantages and avenues for professional growth.

TIJANA MITIĆ
University of Edinburgh

Getting to know… FAISAL AHMED

Professor S Faisal Ahmed will become Editor-in-Chief of the Society for Endocrinology's open access journal, *Endocrine Connections*, from 1 January 2024, taking over from Professor Adrian Clark.

Professor Ahmed is a consultant at the Royal Hospital for Sick Children, Yorkhill, Glasgow and holds the Samson Gemmell Chair of Child Health at the University of Glasgow. We caught up with him to find out more about his career in endocrinology, and what this new role means to him.

What inspired you to choose a career in endocrinology?

I was always interested in paediatrics as a career, even when I was a medical student. As far as endocrinology goes, I was inspired purely by chance, being in the right place at the right time. I had energy, enthusiasm and an appetite for inquiry, so I pursued a wide range of research, supported by some leading figures in endocrinology, including Chris Kelnar, Raj Thakker and Ieuan Hughes.

I was convinced that paediatric endocrinology was the right choice when another leading light in endocrinology, Stephen Shalet (the external examiner for my MD), later explained that paediatricians were nice people and so were endocrinologists, so paediatric endocrinologists had to be the nicest!

What motivated you to join the Editorial Board of *Endocrine Connections*?

I have served on the editorial boards of other journals and have followed the progress of *Endocrine Connections* for a few years. I have worked with Bioscientifica, the publisher, in other areas and have a great deal of respect for Adrian Clark, the outgoing Editor-in-Chief. So, when the opportunity arose, I didn't have to think twice before throwing my hat in the ring.

What are you looking forward to most in your new role as Editor-in-Chief? And what are you looking for in submissions to *Endocrine Connections*?

As the incoming Editor-in-Chief, I believe we need to build on the word 'connections', whether that be connections with other sciences, connections between the different clinical professions within endocrinology, connections between the bench and the lab, connections between centres, or connections between data sets. These are the qualities I hope to see in future submissions to the journal.

I am often asked what is the best paper I have ever published, and my usual answer is my first one, which was a methodology paper in the journal *Annals of Human Biology*. I would also like future endocrinologists to remember *Endocrine Connections* as the journal where they published their first paper, and which connected them to endocrinology.

Scan the QR code to read the full interview in *Endocrine Connections*

At the core of your Society
EQUALITY, DIVERSITY AND INCLUSION

In 2020–2021, the Society for Endocrinology undertook a review of its governance structures and processes, to ensure that we continue to operate in line with current best practice, and are able to fulfil our mission as effectively as possible.

Equality, diversity and inclusion (EDI) emerged as an important theme in this review and, to ensure that this issue could be given sufficient attention, the Society established a limited working group to investigate how EDI practices could be better embedded throughout the Society's membership, governance and activities.

Channa Jayasena, an ex-officio member of Council, agreed to Chair the EDI Working Group. Members were recruited in the summer of 2022 via an open call to the whole membership.

The EDI Working Group focused on three main themes:

- increasing participation in Society governance
- overcoming barriers to membership
- embedding a culture of EDI (relating specifically to EDI questions from the 2020–2021 Governance Review).

EDI WORKING GROUP MEMBERS

Dr Channa Jayasena Chair, Clinical Academic, London
Ms Leanne Delbene Nurse, Taunton
Dr Taha Elajnaf Early Career Scientist, Oxford
Dr Anneke Graf Early Career Clinician in Practice, Harlow
Dr Kagabo Hirwa Early Career Clinician in Practice, Plymouth
Dr Nauman Jadoon Early Career Clinician in Practice, Kilmarnock
Dr Mamta Joshi Clinician in Practice, Sutton
Dr Li Kang Scientist, Dundee
Dr Ashutosh Kapoor Clinician in Practice, London
Dr George Lam Early Career Clinician in Practice, Frimley
Dr Sath Nag Clinician in Practice, Middlesbrough
Dr Cristina Perez Ternero Early Career Scientist, London
Dr Kiserah Philip Student Clinical Academic, London

The EDI Working Group reported to Council with a list of recommendations, which you can read at **www.endocrinology.org/about-us/diversity-and-inclusion/equality-diversity-and-inclusion-working-group**. Council voted on the recommendations, and all bar one were approved. The one that was not approved was deferred to a new group, which is going to review the complete portfolio of Society prizes and awards.

Importantly, Council has approved a new set of guiding principles for the Society (see panel). These principles will form the basis of the Society's EDI policy and act as a framework for all Society activities moving forward. Council will also actively monitor progress in EDI on an annual basis.

GUIDING PRINCIPLES

- The Society must demonstrate that every person professionally interested in endocrinology is welcome as an equal, and adopt a clear set of values that include equality, diversity and inclusion.
- All members must have equal opportunities to hold a position within the Society's structure – including governance – regardless of their location in the UK, career stage or protected characteristic. Where specific knowledge or experience is needed to fulfil a role, this will be clearly communicated through a detailed job description.
- The Society will aim to have equitable representation from across the membership within its Council, as far as is practical.
- All governance vacancies and opportunities to be involved in Society activities will be advertised openly to the whole membership and selection will be based on having the necessary skills, experience and motivation for the role, as set out in the formal job description.
- If any member who is involved in a committee or other Society activities takes a career break for any reason, the Society will endeavour, where possible, to ensure that they are still able to take full advantage of the opportunity.
- All efforts will be made to ensure that the overall provision of support, in the form of grants, prizes and awards, benefits the membership equally. Selection of members for support will be made through a fair and equitable process, with clear criteria for success.

UNDERSTANDING THE LIMITATIONS OF YOUR LAB RESULTS

WRITTEN BY RACHEL MARRINGTON AND FINLAY MACKENZIE

How much do you know about your local laboratory? Do you know the limitations regarding your biochemistry endocrine results? Do you know which assay system is used to determine each result? Is it an immunoassay or mass spectrometry method? If it's immunoassay, do you know which equipment is used?

Do you know which tests are performed in-house and which are sent away? Do you know the current assay performance? Do you have patients whose samples are analysed at a different laboratory, either prior to referral or as part of their management pathway?

You are probably thinking that you don't need to know the answers to these questions, as all assays should give you the same result. They don't. You can't assume that you will get the same result on different assay systems. Likewise, you can't assume that assay performance is, and will always be, stable over time. This is not new; it has always been the case.[1–3]

This article highlights some of the key areas that you, as a clinician, should consider and question with any analytical result.

HOW A ROUTINE LABORATORY OPERATES

Automation has been universal in clinical laboratories over the last two decades. The advantages are clear to see with regard to processing power and workflow. However, one of the main limitations is that laboratories are usually restricted to a single equipment provider for all their assays.

The majority of endocrine results will have been determined by an immunoassay. However, some laboratories do have access to mass spectrometers for some analytes, such as steroids. Mass spectrometry methods provide greater specificity for the analyte in question, whereas immunoassays are inherently non-specific and show wider variability, as is shown in the examples below.

The number of tests processed by a laboratory has rapidly increased over the years, in terms of both repertoire and volume of work. This means that a laboratory may now have multiple analysers performing the same assay. Laboratories increasingly form 'networks' with neighbouring laboratories. This is beneficial in terms of resilience, but the equipment, reference ranges, etc., may be different. All of these factors contribute to the analytical variation.

Workforce requirements have also changed over time. When assays were more manual and in-house, the scientist would have had a greater understanding of their architecture and limitations. The 'black box' effect of automation has removed the need for this knowledge, but the patient complexities have not changed.

'Just because there is a commercially available assay, it should not be assumed that it is, indeed, fit for the purpose for which you intend to use it.'

MANUFACTURER DIFFERENCES

An example is shown here of external quality assessment (EQA) data for free thyroxine (fT4) from pooled human serum (Figure 1). The two most common methods in the UK at present are (a) Abbott Alinity and (b) Roche Cobas, which give very different results. This isn't a unique case for fT4; it has been the position for a number of years. Variation is also observed for thyrotrophin, which may make the diagnosis and monitoring of thyroid disorders more challenging if guidelines are used which have single, method-independent cut-offs. Significant progress has been made towards global standardisation of fT4 assays, but there are still several challenges.[4]

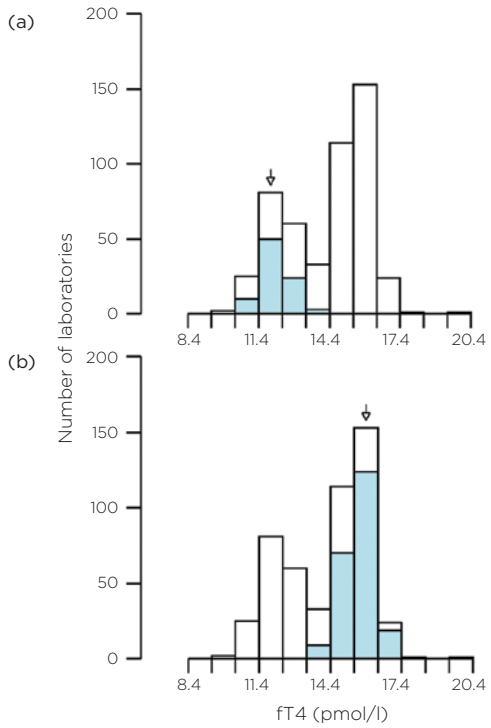


Figure 1. EQA data for fT4 in 2023 on an unmanipulated, native, euthyroid, pooled human serum. The histogram shows all data, but the blue-coloured sections are for (a) Abbott Alinity and (b) Roche Cobas respectively.

Cortisol is another example. It is well known that there are method- and sex-related differences and, as such, there are method-dependent cut-offs for short synacthen tests[5] and sex-related, method-specific, reference ranges are given by manufacturers. Cortisol is an analyte for which there is a reference method, and so the exact amount can be quantified by mass spectrometry assays. A number of UK laboratories do, in fact, use this more specific method of analysis for a few of the steroid hormones, but we lag behind some countries in this area. Figure 2 shows the sex- and method-related biases for cortisol, compared with mass spectrometry, as determined by EQA data for two manufacturers (one with no bias and one with sex-related biases). Cortisol assays are different.

EQA data provide a good means of seeing how a method–manufacturer combination performs over a period of time.[2,6] Some methods, for some manufacturers, are very stable over time and there is very little deviation in

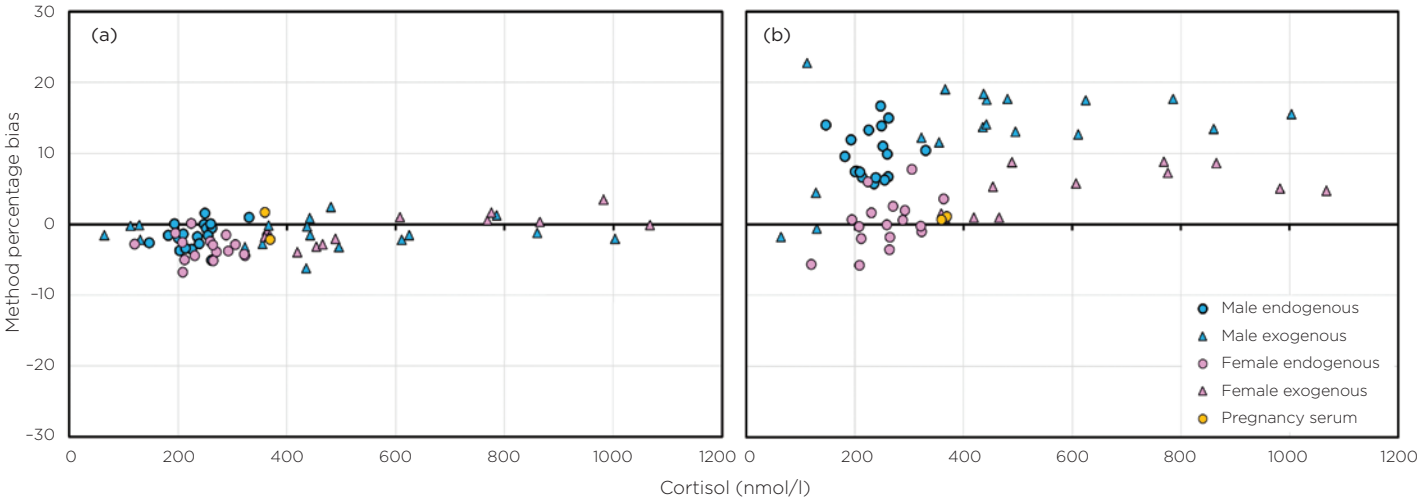


Figure 2. Sex- and method-related biases for cortisol, compared with mass spectrometry, as determined by EQA data for two manufacturers: (a) Roche (no bias) and (b) Siemens Centaur (sex-related biases). Data are from 2021–2022 using both endogenous serum and serum with exogenous cortisol added.

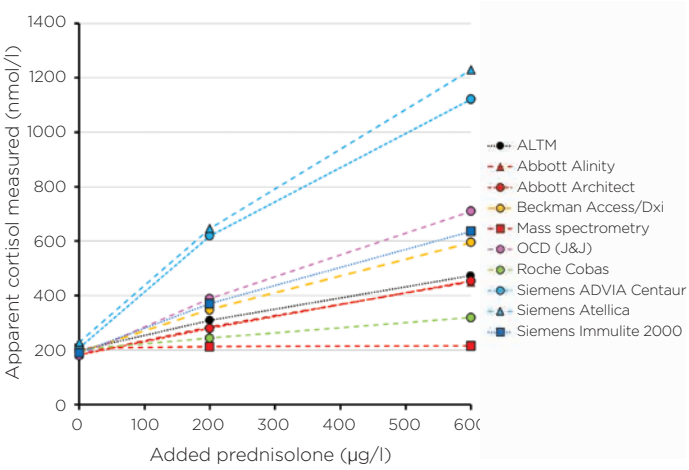


Figure 3. Apparent cortisol measurement for different manufacturers with increasing amounts of prednisolone, a structural homologue of cortisol, widely used for steroid replacement.

their biases. However, other method–manufacturer combinations can be highly variable. Formal, product-wide, recalibration is infrequent. When it occurs, clinicians should be informed by their laboratory. However, the far more frequent lot-to-lot variation changes in reagent formulation can cause significant differences in results. Your laboratory will be able to look at seismograph plots on their UK National External Quality Assessment Service (NEQAS) reports to probe trend data.

INTERFERENCE

Every immunoassay is prone to interference, and the degree of interference may be manufacturer-specific. Interference could be due to specificity issues from closely related homologues. Examples include prednisolone (Figure 3) and 11-deoxycortisol interference in cortisol immunoassays[7] (11-deoxycortisol levels increase with use of metyrapone in the treatment of Cushing's syndrome), and norethisterone in testosterone immunoassays,[8] to name a few. Once again, these are detailed in specific manufacturer kit inserts, but is this information always communicated to the requesting clinician? Probably not. Other interferences include haemolysis, icterus and lipaemia, as well as proteins or antibody effects.[9]

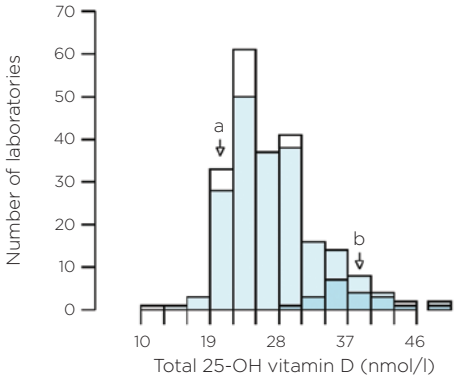
USE OF ASSAY

Just because there is a commercially available assay, it should not be assumed that it is, indeed, fit for the purpose for which you intend to use it. The manufacturer will always detail the intended use and limitations in their kit insert. It is the responsibility of the laboratory to verify that all assays are suitable for their use.

TAKE HOME MESSAGES

- Laboratory tests are crucial in helping you in your clinical practice, and are generally performed to a very high standard.
- Not all manufacturers' assay kits behave in the same way, and they don't all give the same results for the same test.
- Immunoassays, by their very nature, are non-specific, as they measure different parts of similarly structured molecules. They are therefore prone to potential interference. Some laboratories may use mass spectrometry, which is more specific.
- Sometimes primary and secondary care specimens go to different laboratories and these laboratories may use different methods.
- Good regular dialogue between you and your local laboratory is imperative, so you know which manufacturer's assays are being used and how they are performing. Ask to see EQA summaries and long term trend data at your multidisciplinary team or similar meetings with the laboratory.
- Research studies regularly span several years, and it is important to be aware that assays can change over time, due to calibrator or reagent lot number shifts.

Figure 4. EQA data on pooled human serum. The histogram shows all data, but darker blue sections relate to the Siemens Atellica, light blue sections are all immunoassays, and the white sections are mass spectrometry. The reference method total vitamin D value of 22.8nmol/l is shown by arrow a and the method mean for Siemens Atellica is shown by arrow b.



One notable example are the immunoassays for total vitamin D. A number of kit inserts state that the assay should be used in the assessment of vitamin D sufficiency, whereas in reality the test is predominantly, if not exclusively, used to aid diagnosis of deficiency. Performance at low vitamin D concentrations is important. However, this is not always accurate or consistent between manufacturers, even when assays are performing 'within their specifications'. Figure 4 shows EQA results on pooled human serum, with a reference method total vitamin D value of 22.8nmol/l, but some laboratories reported results >35nmol/l.

DOES IT MATTER?

Only you can answer this. If you use guidelines with hard cut-offs that don't take into account method differences, or if you have patients who have their specimens analysed by a different laboratory, or if you monitor results over a long period of time, or if you are involved in multicentre research studies, then yes – it probably does!

You can find out the impact for your patients by asking your local laboratory probing questions about their assay systems. Simply asking if all assays have acceptable performance may not be sufficient, as it may be that not everyone in the laboratory fully appreciates the limitations of the service that they are offering.

RACHEL MARRINGTON AND FINLAY MACKENZIE
Consultant Clinical Scientists, Birmingham Quality (UK NEQAS), University Hospitals Birmingham NHS Foundation Trust

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Optimising patient outcomes with REAL-WORLD DATA REGISTRIES

As part of the Society for Endocrinology's 2022 Research Strategy, the Clinical Committee identified an opportunity to expand our existing data registries.

We have now joined forces with PeopleWith, an app provider, to develop the next generation of real-world data registries to advance clinical understanding of endocrine-related conditions and optimise patient care.

Our new data registries will serve as comprehensive repositories of patient information. They will provide valuable insights into prevalence, historical data, clinical manifestations, better concordance and suggested treatment outcomes for patients with endocrine-related diseases. This will enhance our understanding of patient outcomes, facilitate improvements in clinical care, and enable personalised treatment for each patient.

HOW DATA REGISTRIES WILL SUPPORT YOUR CLINICAL PRACTICE

1. Access comprehensive national databases of endocrine conditions
Draw from a wealth of holistic patient data to make well-informed decisions about your patients' health. Think of it as having a global network of patient insights to inform your clinical judgments.

2. Empower your patients to manage their health
Your patients can actively monitor their symptoms, track diagnoses and manage medications. This means you will have a more comprehensive overview of patient histories, resulting in more effective treatment plans.

3. Access enhanced reporting with patient-reported outcome measures (PROMs)
Patient-reported outcomes put the patient front and centre. Gaining insights into your patients' experiences will aid your clinical assessments and help you tailor treatments.

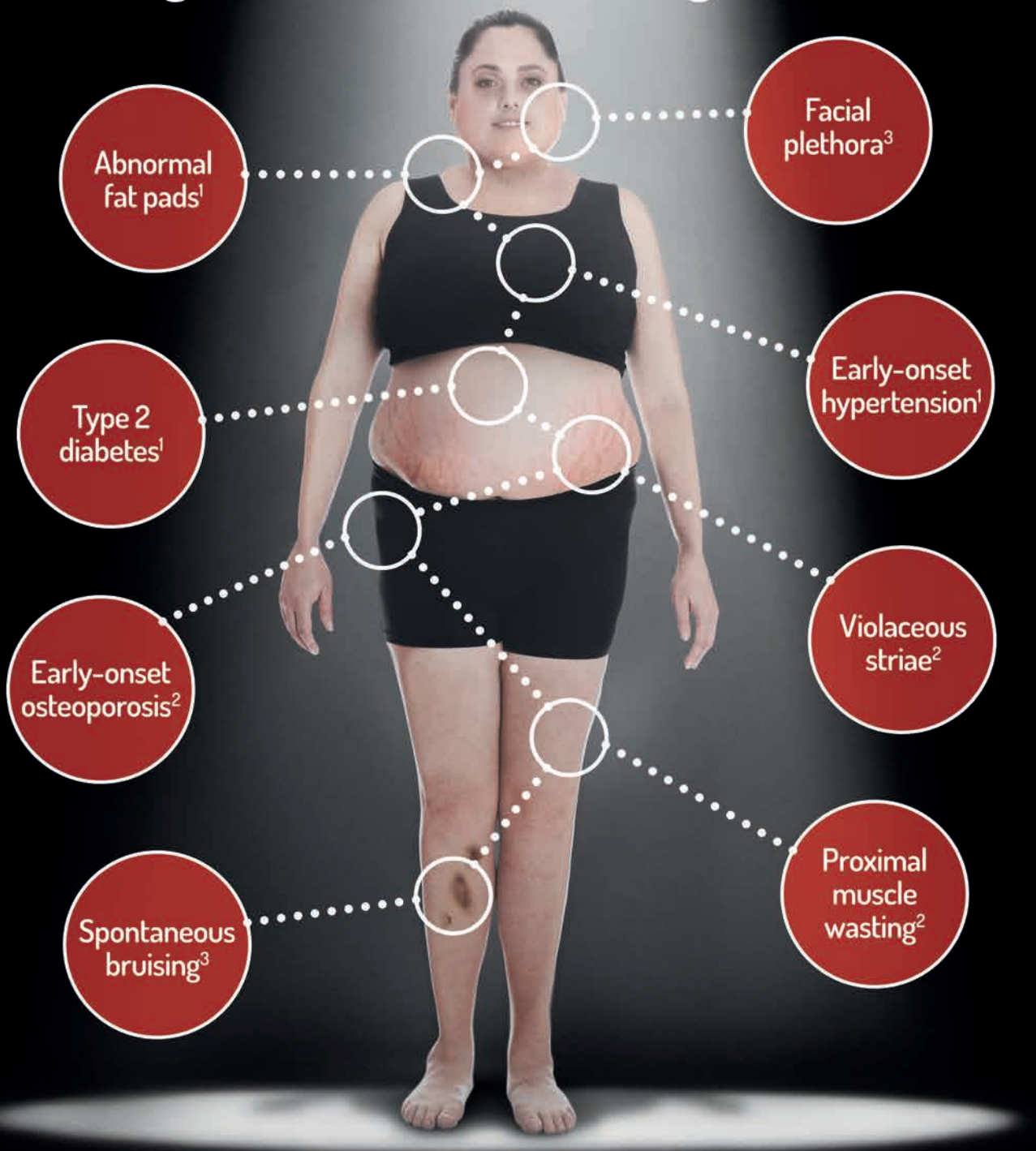
4. Advance research in endocrine care
Our data registries will foster collaboration among healthcare professionals, researchers and patients. They will help to identify trends, support evidence-based practices and provide new insights into endocrine care.

HOW YOU CAN GET INVOLVED

You can empower your patients to start tracking their health by downloading the PeopleWith app (**www.peoplewith.com**).

To find out more about data registries and how you can get involved, contact Jessica Davis, the Society's Clinical Practice Manager, at **clinical@endocrinology.org**.

Although the condition might be rare...



...the features are common

Perhaps it's Cushing's syndrome, perhaps it's something else? If you connect any of these dots within a patient, consider referring them to a specialist endocrinologist.

For a clinician's guide to recognising Cushing's syndrome's signs and features, email **cushings@connectthedots.health** and help shine a light on this rare condition.

HRA Pharma
Rare Diseases

Connect the dots

References: 1. Pappachan JM *et al. J Clin Pathol.* 2017;70:350–359. doi:10.1136/jclinpath-2016-203933
2. Nieman LK. *Endocrinol Metab.* 2018;33:139–146. 3. Yorke E *et al. Int J Endocrinol.* 2017; 1547358.

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