Society for Endocrinology

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THE ENDOCRINOLOGIST

THE MAGAZINE OF THE SOCIETY FOR ENDOCRINOLOGY

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A word from THE EDITOR...

Welcome to the autumn issue of *The Endocrinologist*, which has been dedicated to diabetes mellitus. We now have a myriad of diagnostic and therapeutic tools in our armamentarium for managing diabetes, which did not exist when most of us were training. Despite remarkable scientific advances, diabetes continues to present inordinate clinical and economic challenges to healthcare providers. In this issue we are looking to the future with several feature articles giving insight into the direction of travel.

Patha Kar's article welcomes the greater recognition about insulin safety and asks a number of key questions that need to be addressed to reduce insulin errors. Wilma Leslie writes about the role of low energy formula diets in achieving the benefits of weight loss and remission of type 2 diabetes. Wui Hang Cheung gives an account of some of the admirable initiatives undertaken by the Young Diabetologists and Endocrinologists' Forum to improve the training in diabetes and endocrinology.

Rochan Agha-Jaffar summarises our current understanding of the pathophysiology of gestational diabetes and highlights the importance of prevention strategies. Erika Vainieri and Prash Vas outline the steps to better management of diabetic foot disease as a multi-system, cross-specialty disorder.

James Johnson and Jake Kushner discuss parallels in the complex relationship between insulin and both major forms of diabetes. Sarita Naik reminds us, with some practical tips, that language used in diabetes healthcare can have a profound effect on people with diabetes. Finally, Nick Oliver describes some of the latest advances in diabetes technology, including glucose monitoring and closed loop systems.

I hope this issue goes some way towards answering the question of 'where are we going' in the world of diabetes education, research and care.

With warmest good wishes

AMIR SAM

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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 Winter 2018 issue: **5 October 2018**.

Front cover image ©Shutterstock

Julia Buckingham

CONGRATULATIONS

Julia Buckingham, Vice-Chancellor at Brunel University, London, and former President of the Society for Endocrinology, has been awarded a CBE.

The award recognises her services to biology and education during her distinguished career as a pharmacologist and academic leader.

LET US BOOST YOUR CAREER

Don't miss the approaching deadlines for Society grants, which are available to help fund your research, travel or lab equipment.

- A **Practical Skills Grant** will allow you to forge new collaborations or learn skills by funding a visit to another lab or attendance at a workshop. Apply by **31 October**.
- Society **Early Career Grants** provide financial support to boost your research. Apply by **28 November.**
- An **Equipment Grant** could buy vital equipment for your laboratory. Apply by **28 November**.
- **Endocrine Nurse Grants** help fund projects that enhance nursing clinical practice. Apply by **28 November**.
- A **Travel Grant** will help you meet and engage with the endocrine community worldwide. Apply by **5 December.**

Visit **www.endocrinology.org/grants-and-awards** for full details of how to apply, and for more Society funding opportunities.

REWARD YOUR BEST STUDENTS

The Undergraduate Achievement Award allows teaching departments to encourage excellence in endocrinology by rewarding outstanding endocrine-related work from undergraduate students. Applications deadline **12 October**.

Visit **www.endocrinology.org/grants-and-awards/prizes-and-awards/undergraduate-achievement-award** for more details.

LAST CHANCE TO NOMINATE CONVENORS

Applications to fill the Endocrine Network Convenor vacancies must be received by **28 September**. Don't miss this opportunity to nominate your candidates to drive collaboration in your endocrine areas of interest. Full details and a nomination form can be found at **www.endocrinology.org/membership/endocrine-networks**.

INSPIRE THE NEXT GENERATION

Volunteer to help at our SfE BES 2018 public engagement event. Hone your outreach skills by bringing your own activity or inspire others at the careers Q&A. Register your interest before **25 September** by emailing **media@endocrinology.org**.

LEARN ABOUT YOUR SOCIETY'S ACHIEVEMENTS IN 2017

Download the 2017 *Year in Review* to find out more about last year's journey to advance endocrinology, and to discover opportunities for you to become more involved. **www.endocrinology.org/about-us/governance/year-in-review-2017**

NEW SOCIETY CLINICAL GUIDANCE

The Society's Clinical Committee has published the following new clinical guidance documents. These will help health professionals assess and manage patients more safely.

Acute management of the endocrine complications of checkpoint inhibitor therapy
Higham CE *et al.* 2018 *Endocrine Connections* **7** G1–G7

In-patient management of cranial diabetes insipidus
Baldeweg SE *et al.* 2018 *Endocrine Connections* **7** G8–G11

HELP SHAPE THE FUTURE OF YOUR SOCIETY

Apply for Society committee vacancies and help guide the Society's work, while developing your own career.

Visit **www.endocrinology.org/about-us/governance/call-for-nominations** for more information and to apply, or nominate a colleague, online. Application deadline is **28 September**.

SOCIETY CALENDAR

19–21 November 2018
SfE BES CONFERENCE
Glasgow

www.endocrinology.org/events for full details

SOCIETY SUPPORTED EVENTS

24 September 2018
PITUITARY MASTERCLASS 2018
London

25–30 August 2019
SPETSES SUMMER SCHOOL – NUCLEAR RECEPTORS, EPIGENOMICS, AND DISEASE
Spetses, Greece

GRANT AND PRIZE DEADLINES

26 September 2018
PUBLIC ENGAGEMENT GRANTS

12 October 2018
UNDERGRADUATE ACHIEVEMENT AWARDS

31 October 2018
PRACTICAL SKILLS GRANTS

28 November 2018
EARLY CAREER GRANTS

28 November 2018
EQUIPMENT GRANTS

28 November 2018
ENDOCRINE NURSE GRANTS

5 December 2018
TRAVEL GRANTS

www.endocrinology.org/grants for full details of all Society grants and prizes

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 on the Society home page, **www.endocrinology.org**. *Endocrine Connections* and *Endocrinology, Diabetes & Metabolism Case Reports*, the Society-endorsed case reports publication, are open access (OA) and free to all.

JOURNAL OF ENDOCRINOLOGY

A role for miR-876-3p in metabolic health

The role of microRNAs in regulating important metabolic processes continues to gain prominence.

Rajan and colleagues highlighted the significance of miR-876-3p, found in adipose tissue, in maintaining glucose homeostasis. Importantly, inhibition of miR-876-3p expression was able to improve insulin resistance in adipocytes both *in vitro* (in human mesenchymal stem cells) and *in vivo* (in high fat diet fed mice). The authors found adiponectin, a hormone that plays a very important role in carbohydrate and lipid metabolism, to be a direct target of miR-876-3p.

Consequently, modulation of miR-876-3p expression has an impact on crosstalk between adiponectin and insulin signalling in adipose tissue.

In the past few years, microRNAs have emerged as an important biopharmaceutical for future medicines. Studies such as this, which interrogate the roles of specific microRNAs, are important for our continued understanding of their impact in health and disease.

Read the full article in *Journal of Endocrinology* doi:10.1530/JOE-17-0387

JOURNAL OF MOLECULAR ENDOCRINOLOGY

Cholesterol signalling in single cells

Cholesterol is an essential component of cell membranes and an essential substrate for the synthesis of biologically active signalling molecules, including steroids. Activation of cholesterol requires transport within cells which can have a significant local effect on cellular activity.

In this review, Jefcoate and Lee reframe the perspective of cholesterol trafficking via steroidogenic acute regulatory protein (StAR) by summarising how a new imaging approach can provide an insight into local cell signalling by imaging gene expression in single cells.

Single molecule fluorescence *in situ* hybridisation of mRNA (sm-FISH) has been developed to complement single cell RNA sequencing (sc-RNASeq) to determine precise 3D positioning of individual cells based on mRNA markers. Use of sm-FISH delivers novel insights into single cell signalling by resolving single RNA molecules as mRNA and by quantifying pre-mRNA at gene loci. The sm-FISH technique allows the spatial relationship of individual cells to be identified by their distinctive expression profiles, and it can be utilised to provide novel insights into cholesterol signalling.

Read the full article in *Journal of Molecular Endocrinology* **60** R213–R235

ENDOCRINE-RELATED CANCER

How does obesity affect PSA?

Men with obesity have been found to have lower serum levels of prostate specific antigen (PSA) than non-obese men of the same age. This has potential implications for the use of PSA for prostate cancer detection in obese men.

Aref and colleagues examined the cause of this difference, with pre-existing theories suggesting the role of haemodilution, or of lower serum testosterone. They used data from the Florey Adelaide Male Ageing Study (FAMAS) cohort, which included more than 1,000 adult men. They excluded data from subjects with known prostate cancer, or with persistently abnormal PSA elevation.

In agreement with previous studies, PSA was found to increase with age, and to decrease with obesity. Using mixed-effects models on the anthropometric, biochemical and haematological data collected, the authors suggest that reduced PSA in obese men can be explained by an elevated oestradiol/testosterone ratio, with a lesser contribution of haemodilution. They also suggest that this hormonal imbalance seen in obesity may contribute to the higher grade and more advanced stage of prostate cancer found in obese men.

Read the full article in *Endocrine-Related Cancer* doi:10.1530/ERC-17-0438

ENDOCRINE HIGHLIGHTS

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

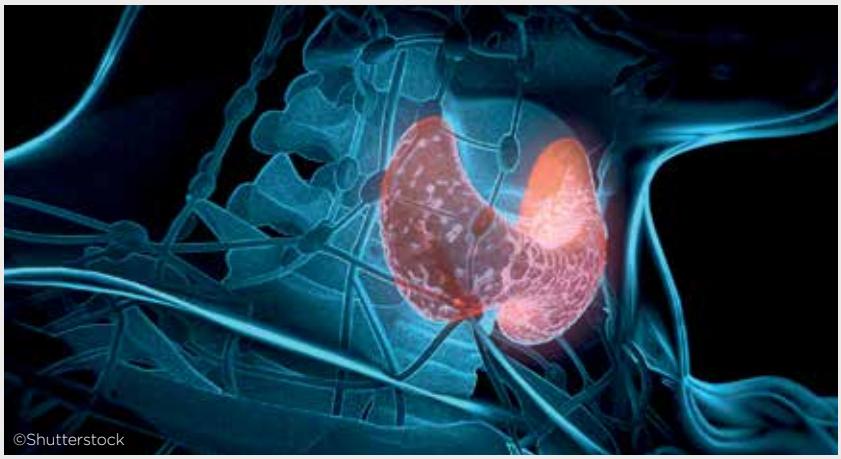
TH's contrasting β-cell roles and stem cell protocols

Thyroid hormone (TH) has contrasting actions in different tissues, with roles in both the development and the ageing processes.

Aguayo-Mazzucato *et al.* showed that, in addition to driving the maturation of pancreatic β-cells, TH also has a dichotomous effect on β-cell ageing. Both processes can occur simultaneously via different TH receptor (THR) isoforms: THRB1 for maturation via *Mafa* and THRA via the *Cdkn2a* gene.

These findings are key in light of recent protocols for human embryonic stem cell-derived insulin-positive cells, which use TH to induce maturation. Importantly, initial findings from the authors suggest that specific THR agonists could be used to optimise the final functional maturation step without compromising the ability of these cells to respond to the necessary growth factors.

Read the full article in *Diabetes* **67** 1322–1331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Hot Topics is written by Douglas Gibson, Louise Hunter, Lisa Nicholas and Helen Simpson.

HT

CLINICAL ENDOCRINOLOGY

Bone fragility in Turner syndrome

Wasserman *et al.* report increased fracture prevalence in older patients with Turner syndrome (TS).

They conducted a patient-based survey (771 patients, 231 controls), performed in association with national patient advocacy groups in the USA. During childhood, adolescence and young adulthood, there was no difference in fracture prevalence between individuals with TS and controls, whereas older women (>45 years) with TS were more likely to experience fractures than controls without TS (P=0.01). Balance problems were more common in individuals with TS than in controls (26.5 vs 14.8%, P=0.0006).

Oestrogen replacement was started at an older age in the group of patients >25 years of age. The mean age at discontinuation of oestrogen replacement was 36.5±12.5 years, and in the older age group those women discontinuing oestrogen replacement had a higher fracture rate. There was no difference in time of puberty between those who did and did not fracture.

Whilst this paper is a self-reported questionnaire, and not cross-checked with medical notes, its relatively large number of patients provides us with useful information, and supports the continued use of oestrogen replacement in adult life. It also describes an association with balance issues and falls in TS which may be worthy of further investigation.

Read the full article in *Clinical Endocrinology* **89** 46–55

ENDOCRINOLOGY, DIABETES & METABOLISM CASE REPORTS

Post-partum diabetes insipidus

Gestational diabetes insipidus (DI) is an extremely rare complication of pregnancy, and is even rarer in the post-partum period. It is thought to be related to excessive activity of vasopressinase, an enzyme expressed by placental trophoblasts during pregnancy, which degrades arginine vasopressin (AVP) and therefore increases AVP clearance.

Rodrigo and Hockin report a 48-year-old woman with headache, polyuria, polydipsia and nocturia associated with post-partum pre-eclampsia and hepatic dysfunction. A water deprivation test was stopped after 4 hours, as it was thought to confirm DI (although full results were not reported) due to the residual action of placental vasopressinase. She required desmopressin for a few days to control the polyuria and polydipsia, and sodium normalised. The patient stopped taking the medication after a few days and polyuria, polydipsia, nocturia resolved spontaneously; no hyponatraemia was reported.

This must be a very hard diagnosis to make. Water metabolism changes during pregnancy, as plasma volume is expanded 1.5-fold, and the post-partum period is associated with polyuria as the increased plasma volume from pregnancy is lost. However, it is an important diagnosis to consider, especially during pregnancy, and this article serves as a reminder.

Read the full article in *Endocrinology, Diabetes & Metabolism Case Reports* EDM180052

ENDOCRINE CONNECTIONS

Vitamin D status in pregnancy

The prevalence of 25-hydroxyvitamin D (25OHD) deficiency in pregnancy is high and may be associated with adverse pregnancy outcomes such as pre-eclampsia.

In this nested, case-controlled, longitudinal study, Agudelo-Zapata *et al.* assessed serum concentrations of 25OHD in 29 non-pregnant women, 61 healthy pregnant women and 20 pre-eclamptic pregnant women. 25OHD was measured across pregnancy and at 3 and 6 months post-partum, and correlated with anthropometric, biochemical and hormonal parameters. In non-pregnant women, 25OHD was measured across the menstrual cycle, and concentrations were found to be significantly lower during the follicular phase (31.9 ng/ml) compared with the luteal phase (34.9 ng/ml).

Serum concentrations of 25OHD in pregnant women were measured in the first, second and third trimesters of pregnancy and increased as pregnancy progressed. Interestingly, 25OHD concentrations were lower in the first trimester than in samples from non-pregnant women. Postpartum, 25OHD concentrations were significantly decreased compared with non-pregnant levels after both 3 and 6 months. However, no statistically significant differences in serum 25OHD concentrations were found between pre-eclamptic pregnant women and healthy pregnant women.

These results shed light on potential cross-talk between oestrogens and progesterone, which vary across the menstrual cycle and in pregnancy, and 25OHD concentrations.

Read the full article in *Endocrine Connections* **7** 698–707

'Artificial pancreas' benefits in-patients with type 2 diabetes

Closed-loop systems, whereby continuous glucose sensing works in tandem with an insulin pump, can be used to improve glycaemic control in patients with type 1 diabetes mellitus. In this randomised trial, Bally *et al.* compared the use of standard subcutaneous insulin regimes (control group, n=66) with the use of closed-loop technology (experimental group, n=70) in non-critical adult hospital in-patients with type 2 diabetes.

The two groups had similar values for body mass index, glycated haemoglobin and daily insulin requirement before the trial. Patients' food intake and activity were unrestricted for the duration of the study (either 15 days or until discharge from hospital).

Closed-loop patients spent significantly more time than the control group with glucose levels in the target range of 5.6–10mmol/l (mean 65.8% of the time, compared with 41.5%). Glucose variability was significantly reduced in the closed-loop group too. There were no differences in insulin requirement or incidence of hypoglycaemia. Closed-loop patients reported high levels of satisfaction with both their glycaemic control and the technology.

The authors propose that closed-loop systems could improve the safety of in-patient diabetes care, without increasing demands on hospital staff.

Read the full article in *New England Journal of Medicine* doi:10.1056/NEJMoa1805233

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INSULIN ERRORS: WHERE NEXT?

WRITTEN BY PARTHA KAR

Gillian Astbury. I am not sure if the name rings a bell, but it should. Not just in the world of endocrinology and diabetes, but to anyone involved in healthcare who believes in the basic mantra of 'Do no harm'.

Gillian was the woman who died in 2007 during the low point of the Mid Staffs scandal. An inquest into her death ruled that low staffing levels and other systemic failures at Stafford Hospital were contributing factors, and that a failure to administer insulin to the 66-year-old amounted to a gross failure to provide basic care. The Mid Staffordshire NHS Foundation Trust was subsequently prosecuted by the Health & Safety Executive. The Trust was fined £200,000 and ordered to pay more than £27,000 in costs over what the judge described as 'the wholly avoidable and tragic death of a vulnerable patient'.

So, roughly 11 years later, how have things changed?

THE CURRENT SITUATION

National audits suggest 1 in 25 patients with type 1 diabetes go into diabetic ketoacidosis in a hospital (a harm rate of 4%) while insulin errors continue to be a consistent feature, albeit dropping over the years. With the population incidence of diabetes increasing, the incidence of those with diabetes in a hospital – at any given time – continues to increase, and so does the number of people on insulin.

'With up to 20% of in-patients having diabetes, should training for all staff involved in handling insulin be compulsory? Or is it less important than, say, fire safety?'

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However, things have also changed, to an extent for the better. Ten years ago, in-patient diabetes teams were unheard of, but now they form a core part of the diabetes team in most hospitals. However, about 28% of hospitals still do not have a dedicated in-patient diabetes nurse specialist.

However, there is no question that the importance of this has continued to rise in the eyes of national bodies, especially with regard to the safety aspect. 2017/18 saw a fresh injection of money into diabetes care. One of the main areas of focus was improving in-patient safety, with specific emphasis on nursing staff. Approximately £5 million has been invested into recruiting nearly 100 whole-time equivalent nurses across the country, which can only be viewed positively when looking ahead. The national diabetes in-patient audit, performed annually, provides an opportunity to look at improvements (or their absence) while also focusing on areas that need tackling, such as e-prescribing or training.

GIRFT
GETTING IT RIGHT FIRST TIME

In addition, a national programme called GIRFT (Getting It Right First Time) has been designed to look at variation in diabetes care across all hospitals in England, with insulin safety being a key focus of this exercise.

LOOKING FORWARD

The question is 'where next?'. The investment has come, as has the process of benchmarking. Is the next step for some aspects to be mandatory?

With up to 20% of in-patients having diabetes, should training for all staff involved in handling insulin be compulsory? Or is it less important than, say, fire safety? Should all hospitals have a specific panel reviewing diabetes and insulin errors? These are musings which may appear too specialist-centric, but the volume of patients, the rapid turnover of staff, and new insulin of different concentrations perhaps make a case to consider this.

Or is it sometimes about the basics too? Why would a healthcare professional who rarely deals with insulin know more about it than the person who lives with it day in and day out? Why shouldn't there be self-management protocols for those who can? After all, safety is paramount, and we have at our fingertips the ability to ask someone who is the actual expert: the person living with diabetes.

In summary, there is indeed greater recognition at all levels about the importance of insulin safety, and there are some great examples in places such as Derby, Southampton and Leicester of initiatives which have been helpful in improving care. It's now a question of how we adapt these good practices, use the money wisely, and tackle issues of general education amongst fellow healthcare professionals.

Beyond all, much of the answer will probably also sit with those we try to look after. It feels as though things are moving in the right direction, with patient charities such as Diabetes UK also focusing on this as a matter of importance. Hopefully with greater awareness, we will, as a system, reach a place where insulin errors are a rarity and a distant memory, in place of an environment where people living with diabetes fear their time in hospital.

PARTHA KAR
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MANAGING TYPE 2 DIABETES: A ROLE FOR LOW ENERGY FORMULA DIETS

WRITTEN BY WILMA LESLIE

Excess weight gain is a key risk factor responsible for the development of around 90% of cases of type 2 diabetes. A majority of people with type 2 diabetes have a body mass index (BMI) >25kg/m^2 and about half have a BMI >30kg/m^2. Among those with a BMI >35kg/m^2, 20% of all men and 11% of women have been diagnosed with diabetes.

Weight management is a fundamental element in the management of type 2 diabetes. While modest sustained weight loss of 5–10% can prevent its onset, obesity guidelines in Scotland, in recognition of the increases in the prevalence of obesity, recommend a weight loss target of >15–20% for those with a BMI >35kg/m^2 with obesity-related complications such as type 2 diabetes.

THE CHALLENGE OF WEIGHT LOSS

In routine diabetes care, it is very challenging to achieve weight loss. With conventional dietary advice, average weight loss is usually only in the region of 3–5%, and many of the older medications used to manage diabetes (sulphonylureas and insulin) favour further weight gain. Hence, few individuals achieve a weight loss of ≥15kg (or ≥15%).

Bariatric surgery, which results in substantial weight loss and remission of diabetes, is one treatment option and is indeed recommended by UK guidelines for those who are obese and have type 2 diabetes. However, surgery is unattractive to many who are fit enough to undergo the procedure, side effects are common, and it is unlikely to be feasible within the already constrained resources of the NHS. There is therefore little prospect of it being offered to the majority of people with type 2 diabetes.

FORMULA DIETS

An alternative approach is the use of liquid formula diets as a total diet replacement (TDR). This can achieve substantial weight loss, up to 15% or more. A non-surgical approach is more attractive to the general public. The diets are popular and widely used outside healthcare settings. But historical reluctance by medical staff to support their use means that they have seldom been offered as part of diabetes care.

There is already considerable evidence regarding the safety and efficacy of low energy formula diets for achieving weight loss in the management of type 2 diabetes. Safe, nutritionally complete, formula diets were first introduced in the 1980s and, since then, many studies have consistently found that they can achieve weight loss of about 15kg. This does not seem to be dependent on the calorie content, as similar weight loss is achieved with 820kcal/day, which may be more palatable, and 300–400kcal/day. Importantly, results for people with type 2 diabetes are equally good.

PROVING EFFECTIVENESS

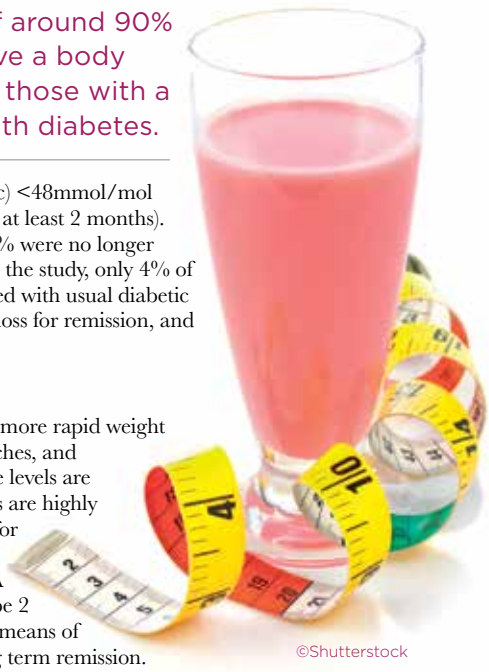
While providing proof of concept, these studies were small and undertaken in a research setting. The question remained whether this approach would be equally effective when delivered on a larger scale and within primary care, where the majority of people with type 2 diabetes are managed.

The Diabetes Remission Clinical Trial (DiRECT), was carried out in primary care, to discover if the use of a structured weight management programme that included a low energy formula diet (825–853kcal/day) could be a practical option for achieving ≥15kg weight loss and remission of type 2 diabetes of less than 6 years' duration. An initial 12–20 weeks of TDR (soups and shakes) were followed by carefully managed food reintroduction and then long term weight loss maintenance. The intervention was delivered at GP practices by either a specially trained practice nurse or a community dietician.

A mean weight loss of 10kg was maintained after 1 year with striking effects on remission of type 2 diabetes: 46% overall achieved remission (glycated haemoglobin (HbA1c) <48mmol/mol off antidiabetic medication for at least 2 months). With weight loss of >15kg, 86% were no longer diabetic. In the control arm of the study, only 4% of participants (who had continued with usual diabetic care) achieved enough weight loss for remission, and none lost 15kg.

IN SUMMARY

Use of formula diets results in more rapid weight loss than conventional approaches, and improvements in blood glucose levels are seen quickly. Both these factors are highly motivating, as is the potential for remission and remaining free of diabetes medications. A top priority for people with type 2 diabetes is finding a cure, or a means of putting their diabetes into long term remission.



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'Use of formula diets results in more rapid weight loss than conventional approaches, and improvements in blood glucose levels are seen quickly.'

Formula diets, used for a period as a TDR, allow the individual to step away from food for a period of time. This is often welcomed, since decisions over what and how much to eat are removed. Formula diets are reasonably palatable and, in DiRECT, many people chose to continue with the TDR for longer than the minimum required period.

Some side effects can be experienced. In DiRECT, the most common were constipation, feeling cold, dizziness and headache. In the main, these were described as mild-to-moderate and transient. It is important to reintroduce meals gradually and provide ongoing support for weight loss maintenance. Weight loss maintenance is crucial in sustaining remission.

Concerns that rapid weight loss will lead to greater weight regain are not supported by evidence. There was no difference in weight regained at 144 weeks of follow-up between people who had followed a 12-week rapid weight loss programme and those who had undertaken a 36-week gradual programme. Supportive follow-up is important to maximise long term weight stability.

While they will not appeal to everyone, formula diets are an acceptable, safe and effective option which can achieve the benefits of substantial weight loss and remission of type 2 diabetes seen following bariatric surgery.

WILMA LESLIE
Research Associate, University of Glasgow

THE YDEF: STRIVING FOR A BETTER DIABETES FUTURE

WRITTEN BY WUI HANG CHEUNG

YOUNG DiABETOLOGISTS & ENDOCRINOLOGISTS
EDUCATION • REPRESENTATION • COMMUNICATION

The Young Diabetologists and Endocrinologists' Forum (YDEF) is the trainee and young consultants' wing of Diabetes UK. It serves three core functions: education, communication and representation. Our work is also supported by the Society for Endocrinology and the Association of British Clinical Diabetologists. Our mission is to enable high quality care for people with diabetes by delivering excellence in diabetes specialist education, and providing an effective voice for young diabetologists and endocrinologists.

The YDEF Committee is made up of specialist trainees from a diverse background of clinical, academic, education and management experience, to comprehensively represent our trainees' needs and viewpoints. This has been our principle since the inception of the YDEF. For instance, our team members currently include dedicated research fellows, chief registrars, quality and improvement fellows, specialist educationists, experts in patient, public and social media engagement, and advocates for trainees' well-being.

FOCUSING ON QUALITY TRAINING

Each year, the YDEF provides established events across the country to support our trainees' educational needs, complementing our national specialist training curriculum.

The YDEF Annual Day, our main event during the Diabetes UK Professional Conference, continues to be a popular, resourceful experience for our trainees. The theme this year was diabetes healthcare transformation and variation, with the aim of inspiring and empowering trainees to reduce inequalities in care.

Our other educational events remain consistently in demand:

- the Insulin Pump Course offers practical hands-on experience, with the opportunity to try and become comfortable with a range of different insulin pumps
- the Retinopathy Course offers the invaluable experience of participating in one of the country's most renowned retinopathy screening centres
- others include the Diabetic Foot Course and the Motivational Interview Course, to name a few.

We also collaborate with the DAFNE (Dose Adjustment for Normal Eating; **www.dafne.uk.com**) Central Office, offering yearly scholarships to support trainees to attain qualifications in structural education for patients with type 1 diabetes.

ENCOURAGING AND SUPPORTING RESEARCH

The YDEF proactively encourages research training. With the generous support of charities and pharmaceutical organisations, we regularly sponsor trainees to attend major conferences such as the Diabetes UK Professional Conference and the European Association for the Study of Diabetes Annual Meetings, to present their work, exchange ideas, and acquire knowledge at the forefront of diabetic care.

Another regular feature of the YDEF is our North Europe Young Diabetologists research meeting. This brings together young researchers from Denmark, the Netherlands and the UK to present and discuss their research in a relaxed setting, to showcase their projects and gain feedback, as well as to develop international collaborations.

CREATING A GOOD FOUNDATION

The YDEF has recognised that building a good foundation based on knowledge, motivation and aspiration is of paramount importance for continuing professional development. In June this year, we launched our ABC of D&E Course, designed to be a foundation course for all new specialist trainees in diabetes and endocrinology. The course provides a supportive, non-judgmental, relaxed environment for trainees early in their careers to identify and discuss the gaps in their current knowledge, to receive mentoring from our faculty consultants either formally (in group sessions) or informally (over coffee, beer and wine!), and to explore their potential subspecialty interest for the later part of their training.

We have also relentlessly strived for better national training provision for our specialist trainees. Over the last year, we have undertaken two important surveys: our Trainee Well-being Survey, and our Variations in Training Survey.

The Trainee Well-being Survey demonstrated that many of our specialist trainees experience physical and psychological burnout. An over-burdening workload in general medicine service provision and lack of exposure to diabetes specialty training opportunities were identified as the key contributory factors.

The Variations in Training Survey identified significant variations in specialty training programme structures across the country. Some regions offer their trainees up to 2 years of training dedicated to the diabetes and endocrinology subspecialty, whereas trainees in other regions did not have any such tailored and protected training opportunities.

ENDOCRINOLOGY AND DIABETOLOGY TOGETHER

In recent years, the YDEF has collaborated closely with the Society for Endocrinology's Early Career Steering Group in recognising the importance of reintegrating diabetology and endocrinology right from the beginning of our early career paths.

We have jointly taken part in many of our successful education events, including our YDEF Annual Day during Diabetes UK Professional Conferences, Society for Endocrinology specialist registrar training events, and our 'Keep your career sweet' first National Diabetes and Endocrinology Taster Day.

In addition, we also work hand-in-hand in developing, shaping and reshaping our national specialist training curriculum and education framework, contributing to decision-making processes with stakeholders including Health Education England, the Royal College of Physicians (and its Specialty Advisory Committee in Diabetes and Endocrinology) and the British Medical Association, representing our diabetologist and endocrinologist trainees' needs and viewpoints in a united front.

If you would like to learn more about the YDEF and our work, to find out about becoming a member, or are interested in joining our committee, please visit our website at **www.youngdiabetologists.org.uk**.

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GESTATIONAL DIABETES MELLITUS

WRITTEN BY ROCHAN AGHA-JAFFAR

BACKGROUND

Gestational diabetes mellitus is defined as 'hyperglycaemia first detected in the second or third trimester that is not clearly overt diabetes'.[1] It is a common complication of pregnancy and is associated with increased risks to the mother and developing baby. For the former, this includes an increased risk of developing pre-eclampsia and later development of type 2 diabetes and for the latter, birth-related injuries, metabolic and physiological sequelae including fetal macrosomia, neonatal hypoglycaemia and in adolescence, insulin resistance and obesity.

The term 'gestational diabetes' was initially introduced to describe women with poor obstetric outcomes who had high glucose levels in subsequent pregnancies. Early diagnostic criteria were based on values that best predicted later development of maternal type 2 diabetes mellitus. Since then, understanding of the implications of developing hyperglycaemia in pregnancy has evolved considerably and diagnostic criteria are now based on the thresholds that best predict risk of adverse outcomes, in particular, fetal overgrowth.

EPIDEMIOLOGY

The historic absence of universally agreed screening strategies and diagnostic criteria has rendered it difficult to accurately establish the incidence of gestational diabetes. Furthermore, prevalence varies according to ethnicity and mirrors variations in prevalence of type 2 diabetes across the world. Rates are thought to be highest in the Middle Eastern and North African region with a median estimate of 12.9% (range 8.4–24.5%) of pregnancies affected by the condition and lowest in Europe, where the proportion of pregnancies affected is estimated at 5.8% (range 1.8–22.3%).[2]

PATHOPHYSIOLOGY

Pregnancy is characterised by an insulin resistance that increases with advancing gestation. The feto-placental unit is primarily responsible for driving this and, while the mechanisms are not fully understood, placental production of tumour necrosis factor α, placental lactogen, growth hormone, and increased cortisol and progesterone levels are all thought to contribute (Figure). To maintain maternal normoglycaemia, β-cell production of insulin increases. The resultant changes in maternal carbohydrate and lipid metabolism ensure the continuous and adequate delivery of substrate required for fetal development.

Women unable to adapt to these pregnancy-induced physiological changes develop gestational diabetes. A significant overlap exists in the pathophysiology of gestational diabetes and type 2 diabetes, such that gestational diabetes could be seen to reflect an early stage of type 2 diabetes expressed under the conditions of pregnancy. Consistent with this is the observed increased rate of progression to type 2 diabetes in those with a history of gestational diabetes, with one meta-analysis demonstrating a cumulative incidence of type 2 diabetes ranging from 2.6% to over 70% in women who were assessed between 6 weeks and 28 years postpartum.[3]

'Gestational diabetes is associated with a significant economic burden, with one model indicating a 34% increase in the cost of care for a woman whose pregnancy is complicated by hyperglycaemia.'

THE CLINICAL PROBLEM AND PREVENTION STRATEGIES

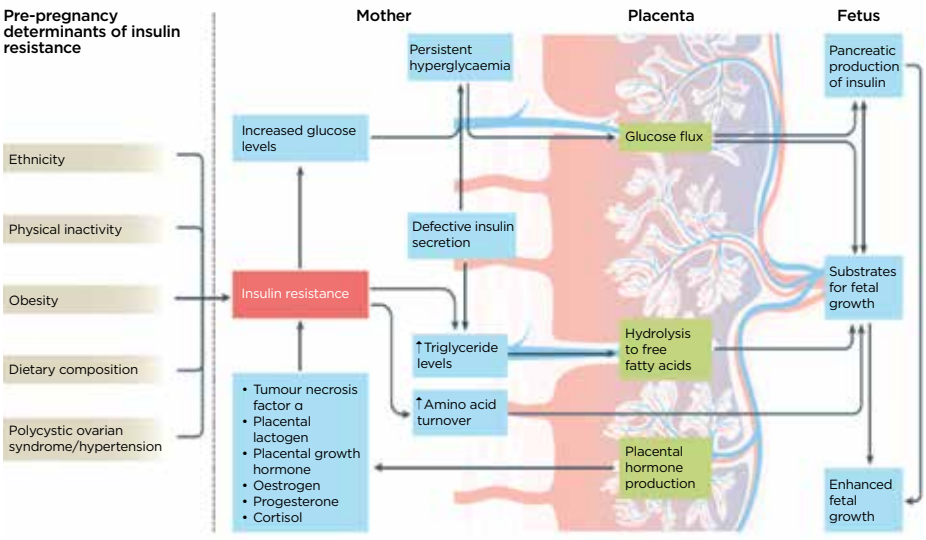
The incidence of gestational diabetes and its complications are increasing, reflecting changing pre-gravid female demographics. Gestational diabetes is associated with a significant economic burden, with one model indicating a 34% increase in the cost of care for a woman whose pregnancy is complicated by hyperglycaemia.[4] Although treatment has consistently been shown to reduce this, it nonetheless remains substantial. Furthermore, long term follow-up of infants born to mothers whose pregnancies are complicated by hyperglycaemia suggests that adiposity remains a significant problem despite effective treatment and management.[5]

Therefore, preventing pathological hyperglycaemia during pregnancy has several theoretical benefits: reduction in associated immediate maternal and fetal adverse outcomes, potential for improvements in the risk of long term sequelae and reductions in the economic burden to healthcare systems worldwide.

The randomised control trials investigating the impact of lifestyle interventions in preventing gestational diabetes have yielded conflicting results. This, in part, relates to the large degree of heterogeneity across the trials both in terms of the recruited cohort baseline demographics and the screening strategies and diagnostic criteria used to define the condition. However, despite the absence of identifying a clear preventive strategy, important signals from these trials have emerged, such as the benefits of interventions

continued on page 10…

Factors contributing to maternal resistance and fetal growth. Reprinted by permission from Springer *Nature, Nature Reviews Endocrinology* 12(9) Gestational diabetes mellitus: does an effective prevention strategy exist? Rochan Agha-Jaffar, Nick Oliver, Desmond Johnston, Stephen Robinson @Springer Nature 2016



DIABETIC FOOT DISEASE: CONTEMPORARY DEVELOPMENTS IN MANAGEMENT

WRITTEN BY ERIKA VAINIERI & PRASH VAS

The convergence of two unique, individually devastating complications – diabetic neuropathy (DN) and peripheral vascular disease – in addition to abnormal local host immune responses, a tendency to develop infections and the impact of ambulatory biomechanics in the foot makes diabetic foot disease (DFD) one of the most complex conditions to manage.

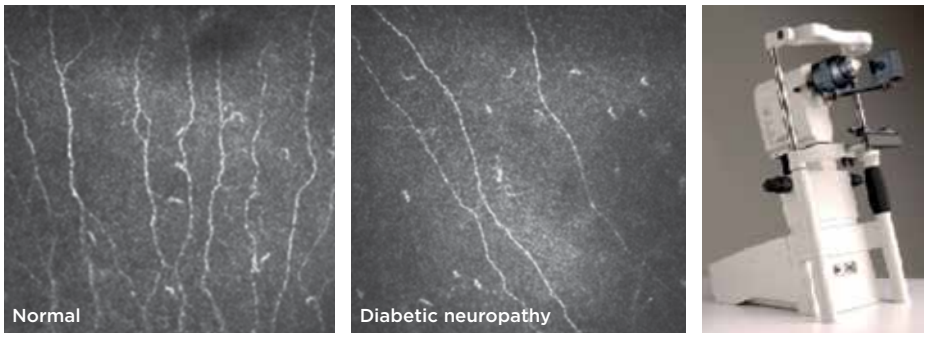


Figure 1. Corneal confocal microscopy in healthy normoglycaemic volunteer (left panel) and in an individual with established diabetic neuropathy (middle panel). A Heidelburg HRT3 corneal confocal microscope with corneal module (right panel). ©Sanjeev Sharma, Ipswich Hospital

Coupled with a lifetime incidence risk of 19–35% for the development of DFD and a 3-year recurrence rate of 60%, individuals with DFD are at high risk for amputation. Mortality is also unusually high in those with DFD; recent estimates suggest a rate in excess of 50% over 5 years, higher than many common cancers.

The modern management of a diabetic foot encompasses the early recognition and treatment of ischaemia, high quality wound care, prompt treatment of infection, off-loading and the correction of any underlying biomechanical anomalies, provided in a multidisciplinary setting.[1] Alongside this, most individuals with DFD will require a spectrum of supportive medical and psychological care.

DIABETIC NEUROPATHY

The development of DN (sensory, autonomic and, in later stages, motor), in particular the distal symmetrical phenotype, is perhaps the most important predisposing factor for diabetic foot ulceration (DFU). DN may also lead to neuropathic pain and development of Charcot neuroarthropathy.

While the precise sequence of neuropathic damage is unclear, recent studies have suggested that the small nerve fibres (Aδ and C fibres) which mediate pain, temperature and autonomic functions are perhaps the earliest to be involved, even prior to the development of large fibre changes.[2] This recognition has been made possible due to the development of modern neuropathy assessment techniques.

Corneal confocal microscopy (Figure 1) can accurately quantify corneal innervation in the human sub-basal plexus. It has been shown that reductions in corneal innervation occur early in the course of type 2 diabetes and worsen with increasing severity of DN, and that such changes run parallel to decrements in intraepidermal nerve fibre density at the distal leg.[3]

The laser Doppler flare technique (LDIflare) is another emerging sensitive technique to assess small nerve fibre function which, in addition to picking up early small fibre abnormalities, is able to demonstrate improvements in neural function, for example after correction of hypothyroidism.[4]

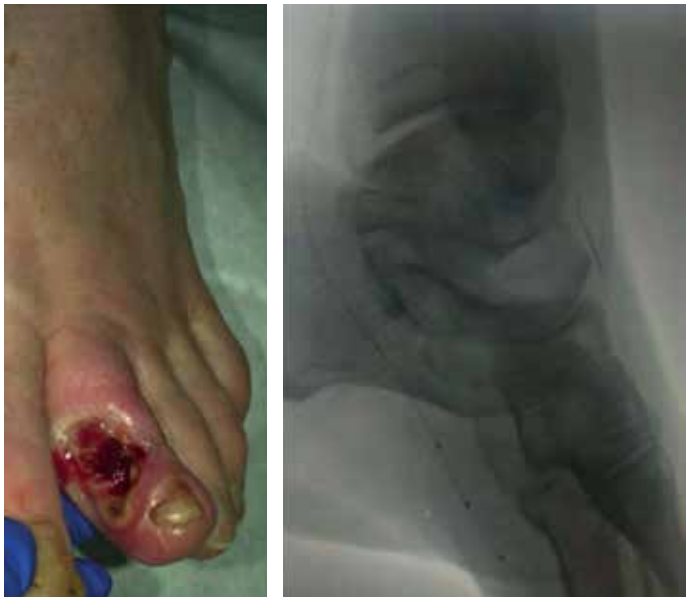
Sudoscan® can quantitatively assess sudomotor function, a marker of cutaneous autonomic neuropathy, in a clinic setting. The novel Vagus™ device allows for bedside assessment of cardiovascular autonomic neuropathy, once the domain of the neurophysiology lab. Sadly, despite extensive research, apart from good glucose control, there are no licensed disease-modifying agents for DN.

PERIPHERAL ARTERIAL DISEASE (PAD)

Peripheral obliterative arteriopathy is present in 50–60% of patients with DFU. This is classically distal and bilateral, involving most commonly the below knee and pedal vessels. It has been an area of significant advance – current technology allows for better characterisation of the PAD and there have been significant advances in both endovascular and surgical techniques of revascularisation.[5] Transcutaneous oxygen measurements and laser Doppler perfusion assessment allow for objective assessment of the functional impact of any vascular insufficiency and may predict healing or the risk of amputation.

One important development has been the ability of modern percutaneous endovascular techniques to summarily revascularise the distal crural, pedal and, if necessary, even the digital vessels (Figure 2). When used effectively with a high quality foot service, remarkable outcomes have been reported.[6] Even the traditional surgical approach has evolved, thanks to

Figure 2. Left pedal artery loop angioplasty in a patient with second toe osteomyelitis. ©KingsDFC



new techniques of ultra-distal bypass and hybrid procedures, whereby, in the latter, both a surgical bypass and endovascular revascularisation are undertaken concurrently.[5] It is crucial as part of the medical management to evaluate the conditions of the other vascular regions such as the coronary and carotid arteries.

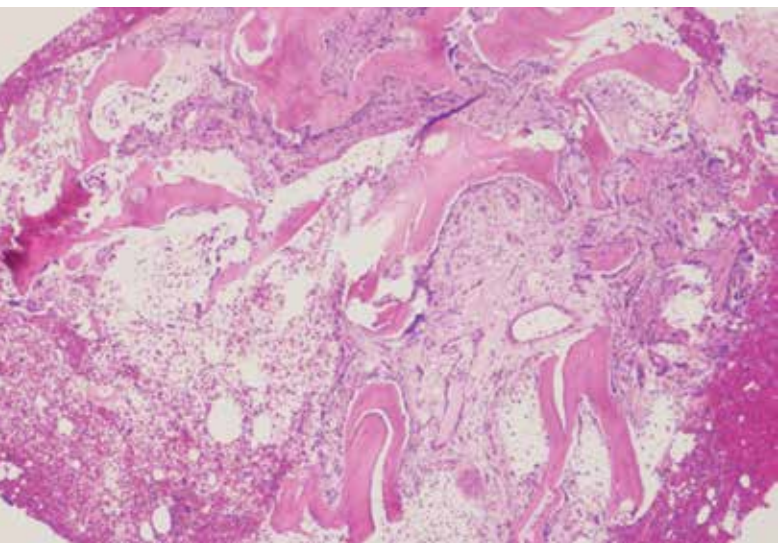
INFECTION: DIAGNOSIS AND MANAGEMENT

Infection frequently complicates DFU, increasing the risk of amputation. While the index infection in western Europe is classically caused by gram-positive cocci, in particular *Staphylococcus aureus*, the milieu in chronic DFU is often polymicrobial. How we evaluate the presence of infection is crucial.

The recently published CODIFI (Concordance in Diabetic Foot Ulcer Infection) study reported that 58% of pathogens differed between wound swab and tissue specimens.[7] Pathogens (as compared to non-pathogens) were more frequently identified in tissue specimens, with the additional observation that clinicians were more inclined to make changes to antibiotic therapy based on tissue specimen results. 16S rRNA quantitative polymerase chain reaction (qPCR) and metagenomic sequencing techniques are being increasingly deployed to determine specimen biodiversity, allowing faster and arguably more reliable identification of culture-hardy bacteria.[8]

For the diagnosis of diabetic foot osteomyelitis (DFO), in addition to the traditionally utilised probe-to-bone test (a clinical indicator) and plain radiography, hybrid imaging techniques such as ^{99m}Tc WBC-SPECT/CT (^{99m}Tc-white blood cell single-photon emission computed tomography/computed tomography) and [^{18}F]FDG-PET ([^{18}F]fluorodeoxyglucose-positron emission tomography) have been validated to evaluate the location and extent, and to distinguish bone from soft tissue infections.[9] However, the gold standard for the diagnosis of DFO is a bone biopsy (surgical or percutaneous) which provides histological evidence (acute and/or chronic inflammatory cells, necrosis) alongside microbiological information to target antimicrobial therapy (Figure 3). In forefoot predominant DFO with *viable* bone, remission may be achieved with antibiotics and podiatric wound care only.

Figure 3. Bone biopsy showing core of cancellous bone trabeculae forming a mixture of viable bone and new reactive woven bone. There is a patchy infiltrate of neutrophils and plasma cells. The features are of subacute bacterial osteomyelitis. ©Dr John Salisbury, King's College Hospital



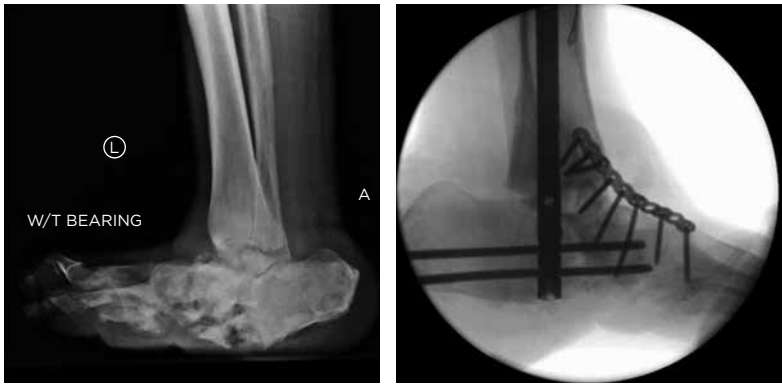


Figure 4. Left foot hind-foot and mid-foot reconstruction (right panel) for severe Charcot deformity (left panel). L, left; W/T, weight. ©KingsDFC

CHARCOT NEUROARTHROPATHY (CN)

Injury to the diabetic neuropathic foot can trigger inflammation and aggressive osteolysis resulting in multiple fractures and bone fragmentations. Ongoing research has focused on understanding the pathogenic mechanisms driving such activity, such as the osteoclastogenic cytokine receptor activator of nuclear factor-κβ ligand RANKL, and on exploring the role of proinflammatory cytokines such as tumour necrosis factor-α. This raises the potential of future putative pharmacologic therapeutic options, something we lack currently. Contemporary orthopaedic reconstruction techniques offer a new hope to those with gross deformities and facing amputation (Figure 4).

WOUND CARE AND OTHER DEVELOPMENTS

We have not discussed the contemporary thoughts on high quality wound care (which cannot be over-emphasised) and dressing choice (no dressing is singularly advantageous) in DFU prevention and, importantly, the emerging focus on tackling the variation in clinical outcomes within and between healthcare systems.

For interested colleagues, the NICE NG19 guideline provides an overview of frontline DFD care in the UK.[10] The International Working Group on the Diabetic Foot (IWGDF; **www.iwgdf.org**) produces consensus guidelines every 4 years on the management and prevention of the diabetic foot and is another useful resource.

Perhaps the one biggest development is the recognition that the diabetic foot is a multi-system, cross-specialty disorder. It is developing into a sub-specialty in its own right, providing its practitioners with a stimulating balance between clinical practice and fast-moving research.

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ENDOGENOUS INSULIN:
ITS ROLE IN THE INITIATION, PROGRESSION AND MANAGEMENT OF DIABETES

WRITTEN BY JAMES D JOHNSON & JAKE A KUSHNER

We think of diabetes pathophysiology as primarily driven by insulin insufficiency. However, long before diagnosis of type 2 diabetes, a profound excess of insulin predicts the people with obesity and pre-diabetes who will progress to disease.[1] Moreover, genetic evidence suggests a very early excess of insulin production prior to type 1 diabetes.[2,3] Non-trivial persistent endogenous insulin secretion may shape the course of type 1 diabetes,[4] a disease we used to define by the complete absence of endogenous insulin.

Here, we discuss parallels in the complex relationship between insulin and both major forms of diabetes. We describe pharmacological and non-pharmaceutical methods, including dietary modifications, by which insulin can be modulated for the prevention and improved management of diabetes.

OBESITY, INSULIN RESISTANCE AND TYPE 2 DIABETES

The coincidental timing of hyperinsulinaemia, insulin resistance and obesity has led to a tripartite 'chicken and egg and egg salad' problem. One cannot assign causality from correlational clinical studies, even ones with very sensitive measures aimed at determining which of these features can be detected first.

Pharmacological reduction of insulin with diazoxide or octreotide caused weight loss in some clinical trials, suggesting that excess insulin plays a causal role in human obesity,[5,6] but both drugs have multiple effects besides insulin inhibition. Animal models wherein insulin production can be suppressed without impairing long term glucose homeostasis provide robust evidence that hyperinsulinaemia is a biological requirement for diet-induced obesity[7] and a partial driver of age-dependent insulin sensitivity.[8] Modest hyperinsulinaemia is also sufficient for adipose tissue inflammation.[9] Thus, factors that contribute to excess insulin production may predispose individuals to later type 2 diabetes.

In the majority of people, dietary carbohydrates are the major stimulus for insulin secretion. Diets that are high in refined carbohydrates are now globally ubiquitous from a very young age. Epidemiological studies aimed at determining whether high carbohydrate diets promote obesity, insulin resistance and diabetes are fraught with confounders, but the rise in consumption of sugars and other carbohydrates is hard to ignore. Long term interventional diet studies, especially in children, will be required to determine the impact of dietary macronutrients on obesity and the progressions to pre-diabetes and diabetes.

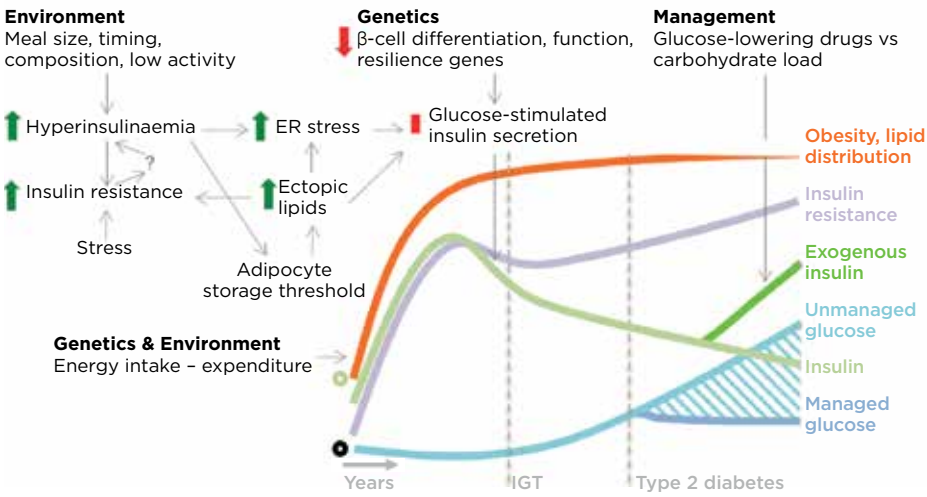
Similarly, fetal and early childhood environmental programming due to excess β-cell stimulation may lead to β-cell dysfunction and increased β-cell mass,[7] an initially adaptive feature that eventually promotes hyperinsulinaemia and then insulin resistance. In addition, genome-wide association studies indicate that genes regulating the development of functional β-cell mass mediate susceptibility to type 2 diabetes.[10] Collectively, a picture is emerging wherein abnormal β-cell function, first with an excess insulin release and then via impaired β-cell responsiveness, plays a key role in the progression from obesity, through impaired glucose tolerance, and into frank type 2 diabetes (Figure 1).

MANAGEMENT OF TYPE 2 DIABETES

At current rates, a majority of patients with type 2 diabetes will eventually be prescribed exogenous insulin. Recombinant insulin drugs have increasingly sophisticated pharmacokinetics but they cannot permanently reverse the course of the disease, even when administered early to promote 'β-cell rest'.[11] We speculate that this is probably because prolonged elevation of exogenous insulin causes modest but consistent weight gain,[12] or is weight neutral at best. Some glucose transport inhibitors or GLP-1 (glucagon-like peptide-1) agonists (both of which may alter macronutrient metabolism and lower fasting insulin) appear to have superior cardiovascular benefits compared with long-acting insulins.[12–14]

'Balanced' diet and other lifestyle modifications continue to be advanced as first-line therapies for type 2 diabetes, despite evidence that traditional lifestyle approaches do not reliably or robustly alter the course of disease.[15] People are encouraged by government agencies to achieve a negative

Figure 1. Roles for insulin in insulin resistance, obesity and type 2 diabetes. On a background of genetic and environmental factors that increase food intake, we propose that meal size, timing and macronutrient composition stimulate excess insulin production/secretion in fasting and fed states. Hyperinsulinaemia may contribute to insulin resistance through receptor and post-receptor desensitisation, possibly further promoting hyperinsulinaemia via unknown mechanisms. Hyperinsulinaemia drives lipid storage in adipocytes, which eventually leads to adipocyte dysfunction and lipid spillover into other tissues. Ectopic lipids are deposited in many tissues including the pancreas where, together with the increased insulin demand, they produce endoplasmic reticulum (ER) stress and metabolic dysfunction, resulting in impaired glucose-stimulated insulin secretion. Impaired insulin secretion in response to glucose begets impaired glucose tolerance (IGT) and eventually type 2 diabetes. The late stages of type 2 diabetes are associated with more severe changes in β-cell differentiation state and cell death. Type 2 diabetes management is a balance between glucose-lowering drugs, including insulin, and glucose load, which can be modified by diet. Green circle denotes normal insulin; black circle represents the norm for other features.



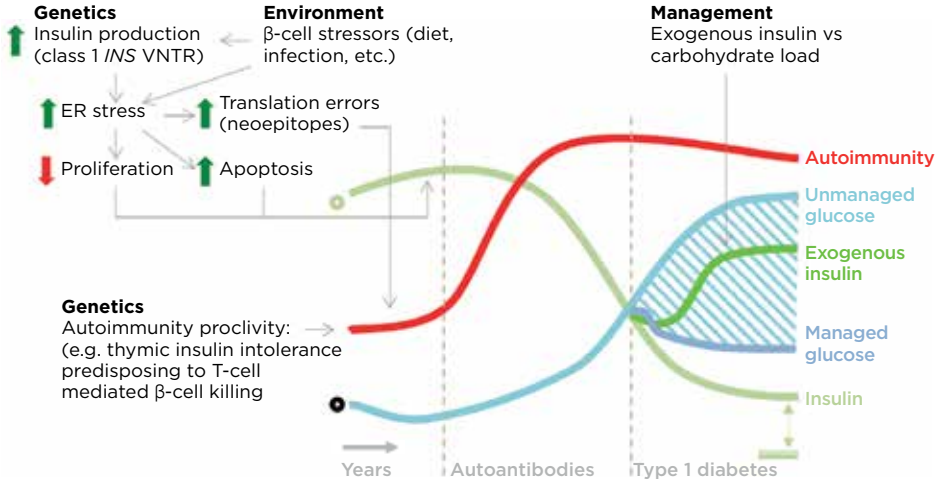


Figure 2. Potential role of insulin in autoimmunity and type 1 diabetes. On a background of genetic autoimmunity susceptibility, increased insulin production driven in part by at-risk VNTR (variable number tandem repeat) alleles and, we speculate, in part by diet leads to a cell autonomous stress on β-cell insulin production capacity that increases the chances of errors and decreases β-cell proliferation in a critical window for the development of thymic tolerance and insulin secretion capacity respectively. Type 1 diabetes management should consider carbohydrate load, exogenous insulin and residual endogenous insulin (indicated by double-headed arrow to double line, bottom right). ER, endoplasmic reticulum; green circle denotes normal insulin; black circle represents the norm for other features.

energy balance by increasing exercise and reducing calorie intake, but the environment in which we live makes this nearly impossible for most, and clinical evidence in favour of this approach is lacking.

Yet, we know from recently published work that type 2 diabetes remission is possible with extreme caloric restriction (below 850kcal/day).[16] Similarly, new research is continuing to provide evidence of ways to tailor eating habits that do not involve such stringent calorie restriction. For example, maintaining food intake within a shorter than normal window can reduce insulin secretion and improve apparent insulin sensitivity in men with pre-diabetes.[17]

The scientific literature and the public sphere remain unsettled as to which dietary modifications are best for healthy populations or people with diabetes. Dietary guidelines have stressed a reduction in saturated fat consumption (**www.diabetes.org**), while others have argued from a biological standpoint that people with diabetes are carbohydrate-intolerant, which has led to efforts to prevent and treat type 2 diabetes with low carbohydrate diets.[18]

Though not a randomised trial, impressive results including 12% weight loss and diabetes remission were found in a cohort of patients consuming a low carbohydrate, ketogenic diet with supportive coaching.[19] Similarly, a small randomised trial recently found that low carbohydrate, high fat nutrition was associated with reduced medication use and improved secondary outcome measures in patients with type 2 diabetes.[20]

Together, these results support the hypothesis of low carbohydrate nutrition for type 2 diabetes and reinforce the need for well-funded, highly powered randomised trials in large populations.

INITIATION AND PROGRESSION OF TYPE 1 DIABETES

While the genetics of type 1 diabetes point squarely at the immune system as the largest arbiter of risk, variation upstream of the human insulin gene is the second most important genetic factor. At-risk *INS* alleles decrease insulin production in the thymus, potentially impairing immune tolerance to insulin,[21] but simultaneously increase insulin production in β-cells by approximately 30%.[2,21] Increased insulin production would be predicted to increase β-cell stress and decrease β-cell proliferation.[22] Similarly, mutations in *GATA4*, a transcription factor required for normal insulin processing, predispose to type 1 diabetes.[23] An early increase in β-cell stress, perhaps in combination with β-cell agitations from diet,[24] obesity,[25] or other environmental factors, could promote the production of disease initiating neoepitopes[26] (Figure 2).

Studies are underway to test the hypothesis that an early increase in insulin production contributes to the triggering and/or progression or type 1 diabetes in immunologically susceptible mice. Controlled human trials of diets meant to minimise β-cell stress are warranted in children at risk for type 1 diabetes.

EXOGENOUS AND ENDOGENOUS INSULIN IN TYPE 1 DIABETES

People with type 1 diabetes have a fundamental inability to properly dispose of carbohydrates and therefore have uncontrolled fluctuations in blood glucose. Hyperglycaemia causes severe, but reversible, impairment of remaining β-cells[27] and promotes diabetes complications.[28]

There are essentially two ways to dampen harmful glucose excursions: (a) moderate glucose intake, or (b) enhance glucose disposal, either via the insulin system, or independently (e.g. SGLT (sodium–glucose co-transporter) inhibitors). A recent study has demonstrated the feasibility of using very low carbohydrate diets to prevent glucose excursions in children and adults.[29] We look forward to robust randomised trials to assess the generalisability of this approach to the wider population of people with type 1 diabetes.

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LANGUAGE MATTERS

WRITTEN BY SARITA NAIK

New treatments and new technologies are currently at the forefront of diabetes care. But sometimes it is the simple things, such as language, that can have a profound effect on the people with diabetes whom we support.

The language used in diabetes healthcare is key to building a relationship between people with diabetes and healthcare professionals which promotes trust and encourages self-management and shared decision making.[1] It is notable that many words in diabetes healthcare are likely to be negative and judgmental and, when used indiscriminately, are likely to stigmatise people with diabetes and contribute to shame and diabetes distress.[1]

Following position statements in both Australia and the USA, a collaboration between people with type 1 and type 2 diabetes, diabetes healthcare professionals and NHS England has resulted in guidelines which have helped to highlight this important issue.[2]

The guidelines have picked out several areas where the language chosen can have negative connotations. Some of these are summarised here, alongside possible alternatives that you could consider using instead.

AREA 1: DISCUSSING DIABETES CONTROL

'What's your control like?' might seem like a good way to start the discussion in a diabetes consultation, and I am sure many of us have used this approach. However, for many people with diabetes, it may feel quite challenging and suggest that that the focus is just on their control and not on their whole life and how their diabetes may fit into it.

The word 'control' seems quite innocuous, but may imply that diabetes can be controlled. The reality is somewhat different, and we know that there are many variables, such as insulin absorption, that can influence the outcome and result in unpredictability.

What can you say instead? Consider talking more about blood glucose levels rather than control, and try to discuss how diabetes is affecting the individual's life.

> *'Where possible, try to avoid "should", "can't", "must". Using words such as "could" or "consider" or "you could choose" can help.'*

AREA 2: COMPLIANCE

'Non-compliant' is commonly used to describe people with diabetes who are perceived not to be following advice given by healthcare professionals. Again, the implication is that if you are 'compliant', glycaemic targets will be achieved.

Yet we know that there is no linear relationship between good health and 'compliance', and the tools we have to manage diabetes are imperfect. It is also easy to assume that if you have diabetes you will be more 'compliant' than a person without diabetes, which is not the case.

Where possible try to be aware of talking about someone with diabetes in negative or judgmental terminology, even if it is well-intentioned.

AREA 3: FEELINGS OF SHAME

'I have been a bad diabetic – I know you're going to tell me off.' I am sure that many of you will have heard this in a diabetes clinic consultation.

Unfortunately, such comments probably stem from the individual's previous consultations during which they may have been told what to do and made to feel ashamed of not achieving 'good control'.

We advise people with diabetes to follow 'rules of self-management', but people can feel helpless and inadequate when it is unachievable. It can be good to explore what a person means when they say 'bad diabetic' rather than dismiss, or agree or reprimand. It might give you more insight into the difficulties the individual is facing.

Always try to respond to anything that can imply 'shame' with a comment such as 'there is no such thing as good or bad diabetes'. If you can, avoid 'diabetic' as it may imply that a person is only defined by their diabetes. Using 'suffering with' also has negative implications and it can be better just to say 'living with diabetes'.

Where possible try to avoid 'should', 'can't', 'must'. These words suggest we are giving instructions, when ideally we should aim to have a collaborative relationship. Using words such as 'could' or 'consider' or 'you could choose' can help with this.

> *'Everyone is doing their best, maybe not the same best as someone else, or even their best "best", but just the best they can at that moment.'*

PERSON-CENTRED LANGUAGE

To some people, this type of guidance may be considered to be about political correctness. However, we are supporting people with diabetes to achieve good clinical outcomes, and using more empathic, encouraging and person-centred language is important in that regard.

I would strongly encourage you to read the full guidelines, so that we can all aspire to use the most appropriate language possible. I'll leave you with a quote from an individual with type 1 diabetes, which will hopefully underline the importance of language and the impact it can have.

'Being described as "non-compliant" is awful, and does not reflect the fact that everyone is doing their best, maybe not the same best as someone else, or even their best 'best', but just the best they can at that moment. Life is way more than type 1 diabetes, and it isn't always given top priority. Life gets in the way.'

SARITA NAIK
Consultant Diabetologist, University College London Hospitals NHS Foundation Trust

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TOWARDS SELF-MANAGEMENT IN TYPE 1 DIABETES

WRITTEN BY NICK OLIVER

Banting House, the 'birthplace of insulin', in London, Ontario, Canada. Ken Lund. https://www.flickr.com/photos/kenlund/21650600540

I was recently fortunate enough to be able to visit the house in London, Ontario, Canada, where, in 1920, Fredrick Banting awoke from a dream and, in a notebook by his bedside, wrote 'Ligate pancreatic ducts of dog. Keep dogs alive till acini degenerate leaving islets. Try to isolate the internal secretion of these to relieve glycosuria.'

This simple recipe led to the isolation and use of insulin to treat type 1 diabetes. Nearly 100 years later, we have access to multiple analogues of the human insulin molecule, all engineered to optimise pharmacology. Alongside these, we have evidence-based education and specialist multidisciplinary teams supporting the 400,000 people with type 1 diabetes in the UK to self-manage as effectively as possible.

However, despite nearly a century of progress, self-management remains challenging, and fewer than one in three people with type 1 diabetes achieves a glycated haemoglobin (HbA1c) level less than, or equal to, 58mmol/mol. Hypoglycaemia, impaired awareness of hypoglycaemia and severe hypoglycaemia remain a major barrier to achieving targets and are associated with significant morbidity and mortality.

THE RISE OF GLUCOSE MONITORING TECHNOLOGY

Continuous glucose monitoring (CGM) has been available for more than 15 years, providing information on the direction, rate and magnitude of glucose changes in real time, with alerts and alarms for impending and established hypo- and hyperglycaemia. While not a recent technology, it has come of age in the last few years with a growing evidence base and inclusion in NICE guidelines for type 1 diabetes for adults and children.

The evidence base now encompasses reductions in HbA1c, minimising exposure to hypoglycaemia and mitigating fear of hypoglycaemia, while real world data suggest CGM can improve work absenteeism. These benefits are seen in people using multiple dose insulin injection regimens as well as in those using insulin pumps, and are seen even in the highest risk people with challenging hypoglycaemia. Next generation devices are being developed with improved accuracy, a longer duration of use and integrated decision support tools.

Flash glucose monitoring (GM) uses a reader or mobile phone to swipe a sensor and report 8 hours of retrospective data, along with a trend arrow. It does not have alerts and alarms, but is licensed to be used without calibration for up to 14 days, enabling people with type 1 diabetes to significantly reduce capillary blood glucose checks. The evidence base is, at present, limited, suggesting no impact on HbA1c and a reduction in time reported below a threshold of 3.9mmol/l in people with type 1 diabetes and an HbA1c less than or equal to 58mmol/mol.

Flash GM and CGM are different implementations of a continuous sensor, and important differences exist in how they may be used to benefit people with type 1 diabetes. Flash GM can act as a replacement for capillary blood glucose testing and CGM can enable optimised glucose outcomes where hypo- or hyperglycaemia is challenging. Cost effectiveness is uncertain for continuous sensors at present, but we are hopefully in a transition phase from routine capillary blood sampling to a blood-free monitoring future for people with type 1 diabetes.

THE QUEST FOR THE ARTIFICIAL PANCREAS

One of the long-stated goals of type 1 diabetes research has been to develop an artificial pancreas device, encompassing glucose sensing, a control algorithm and an insulin pump. This apparently simple task has been very challenging but, as sensor accuracy has improved and devices have become more usable, longer studies have been undertaken with impressive results.

In 2018, the first hybrid closed loop system has been licensed in Europe. The Medtronic 670G system has a safety algorithm which suspends insulin delivery if hypoglycaemia is predicted, and is able to dynamically adapt the insulin basal rate to increase time spent in the desired glucose range between meals. Users still have to check their capillary blood glucose several times a day and enter carbohydrate information at mealtimes but early data suggest an improvement in overall glucose.

Future systems with more automation and a smaller burden for users, which include additional features such as adaptation to manage day-to-day variability, are being assessed. In addition, more complex approaches, including glucagon to mitigate hypoglycaemia, have been developed.

Despite these exciting advances, people with type 1 diabetes will continue to benefit from education and support to understand their diabetes. Technology is an adjunct to effective self-management and education will remain key until we have a more lasting treatment for this disorder.

A 'perpetual flame' burns outside Banting's house in Ontario, and will only be extinguished when a cure for type 1 diabetes is developed. Until that time, technologies can support improvements in glucose outcomes and help to reduce the burden of living with the disease. Making technologies available and ensuring that people with type 1 diabetes have access to support and education to extract value from them remains a priority.

The 'perpetual flame' will burn outside Banting House until there is a cure for type 1 diabetes. Ken Lund. https://www.flickr.com/photos/kenlund/21838632935

NICK OLIVER
Wynn Professor of Human Metabolism, Consultant in Diabetes and Endocrinology, Imperial College London

Spotlight on SOCIETY JOURNALS

A FANTASTIC YEAR FOR IMPACT FACTORS!

The new impact factors for Society for Endocrinology journals have recently been announced, and we're delighted to say it's been another fantastic year.

Endocrine Connections' second impact factor has leapt up to **3.041**, reflecting the high quality of published articles. The journal now ranks 73/143 in the endocrinology and metabolism category.

Clinical Endocrinology has received a strong impact factor of **3.077**.

Journal of Endocrinology is ranked in the top quarter of the endocrinology and metabolism journal category, with an impact factor of **4.012** and a 5-year impact factor of **4.276**.

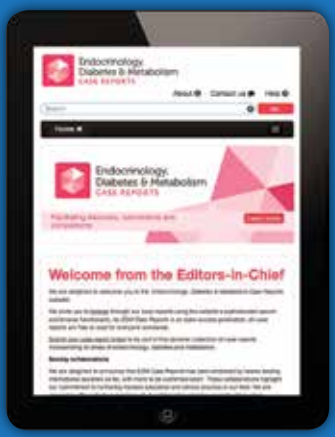
Our thanks go to the journals' Editorial Boards and publishing team for their commitment and to you for supporting the Society's journals.

Journal of Molecular Endocrinology's impact factor remains steady at **3.297,** with the 5-year measure increasing to **3.636**. The journal continues to be the leading journal dedicated to molecular endocrinology.

Endocrine-Related Cancer's impact factor of **5.331** is its highest impact factor since 2003. The journal ranks 21/143 in the endocrinology and metabolism category and 43/222 in the oncology category, strengthening its position as the leading journal linking the two.

Our member benefits include free online access to the Society's subscription journals through the members' area at **www.endocrinology.org** and reduced rates on print subscriptions. As well as a 40% discount on Open Access publishing in *Endocrine Connections*, and a 25% discount on Open Access publishing in *Endocrinology, Diabetes & Metabolism Case Reports*, you can benefit from waived colour or supplementary data charges for publishing when articles are accepted in *Journal of Endocrinology*, *Journal of Molecular Endocrinology* and *Endocrine-Related Cancer*.

NEW INSIGHTS ON DIABETIC KETOACIDOSIS



For this diabetes-themed issue of *The Endocrinologist*, I wanted to highlight the great work being published in *Endocrinology, Diabetes & Metabolism Case Reports* on the subject of diabetic ketoacidosis (DKA).

While DKA is typically associated with new-onset type 1 diabetes, insulin withdrawal and acute illness, there is increasing evidence that patients with type 2 diabetes are also vulnerable to DKA.

Five of the ten most-read cases in *Endocrinology, Diabetes & Metabolism Case Reports* in 2017 were on the subject of DKA. The most-read was 'Euglycemic diabetic ketoacidosis: a diagnostic and therapeutic dilemma' by Prashanth Rawla and colleagues. The report discusses two interesting cases that demonstrate the rare situation in which DKA presents with normal blood glucose levels.

These and other cases can all be found on the website. They involve DKA and complications or related diseases (Hamman's syndrome, Cushing's syndrome, pregnancy, hypocapnic seizure), as well as populations not typically associated with DKA (cases of type 2 diabetes), and DKA resulting from or being affected by medication (e.g. resperidone, nivolumab and canagliflozin).

Endocrinology, Diabetes & Metabolism Case Reports has become a home for cases reporting on the complications of DKA.

MARALYN DRUCE
Co-Editor-in-Chief, *Endocrinology, Diabetes & Metabolism Case Reports*

The Society for Endocrinology endorses *Endocrinology, Diabetes & Metabolism Case Reports*, along with eleven other learned societies. Browse the case reports at **www.edmcasereports.com**.

You and your Hormones

Get editorial experience

JOIN THE YOU AND YOUR HORMONES TEAM

Apply for our **CONTENT EDITOR** vacancies for the opportunity to contribute to our public facing website, **You and your Hormones**.

AS A CONTENT EDITOR YOU WILL:

- gain experience in an editorial role
- improve your writing skills for non-specialist audiences
- contribute to an endocrinology-related public engagement initiative.

You and your Hormones is written and reviewed by Society for Endocrinology experts and the Content Editors will support the Editorial Board to help ensure the latest research and clinical practice is included on the website across all areas of endocrinology.

MAIN RESPONSIBILITIES:

- Awareness of new developments in your field of endocrinology
- Identifying potential topics for articles to be produced
- Assisting in commissioning new articles
- Identifying candidates with relevant expertise to review new and existing articles
- Writing and reviewing approximately 10 articles per year, within your expertise
- Ensuring information is accurate, reliable and easy to understand
- Providing a short quarterly report updating the Editorial Board on progress

Visit **www.endocrinology.org/careers/jobs** for the full job description and to apply by **7 October 2018**.

Face to face WITH 'DR BUNHEAD'

WRITTEN BY NIGEL PAGE

We learned at our March Public Engagement Committee meeting that the Society had arranged for Dr Bunhead to come and run a 1-day public engagement training event, to coincide with the 2018 Endocrine Academy, held in April in Birmingham.

This news soon had Miles Levy and I frantically scrabbling for our phones for that inevitable Google search to identify 'Dr Bunhead'. It wasn't long before we were presented with images of a 'wacky' scientist in an orange jumpsuit with 3-foot plumes of pyrotechnics coming out of his ears; at that moment, we knew Society members were going to be in for something completely different!

The man behind the orange jumpsuit is in fact the showman Tom Pringle, a TV stunt scientist better known for his appearances on Sky One's *Brainiac: Science Abuse* and other shows such as *Blue Peter*. Tom, as well as being renowned as a pioneer of performance-science shows, also runs immersive training programmes in science communication and public engagement.

So I booked myself onto the training day partly out of curiosity about how Tom would bring a completely fresh perspective to public engagement, and partly to network with other Society members looking to develop new and exciting ways of communicating our passion for endocrinology to the wider public.

During the train journey to Birmingham International from Reading, I wondered what to expect. Had we let ourselves in for dressing up in orange jumpsuits, having our heads set on fire or breathing in strange gases (as witnessed in Tom's YouTube video antics, with the warning 'Do not try this at home')?

> *'We knew Society members were going to be in for something completely different!'*

As it turned out, we were greeted by a more casually dressed Tom, who cordially introduced himself simply as Tom rather than Dr Bunhead. And there were no orange jumpsuits in sight!

Nonetheless, something still told me that we were going to be in for a pretty immersive experience. I was right, and we were certainly kept on our toes throughout the rest of the day, with lots of opportunities to test out and practice a whole lot of new presentation techniques and approaches together.

Tom's background is in theatre, and we jumped straight in with some theatrical techniques. These may feel a little outside the comfort zone of many scientists, but in fact provided quite a refreshing outlook. We all need to communicate our research or get our message across to patients, which is all about engagement and ensuring understanding. We learned that what we say and how we say it are both important and are expressed and interpreted using whole-body communication, through our mind, body movements and feelings.

Therefore, making people feel comfortable, having the appropriate eye contact and acknowledging the response of your audience are essential skills to develop. Just as in theatre, we learnt to develop hooks to grab the attention of our audience.

We practised developing these by evolving simple language to express our own areas of endocrine interest, which remained factually accurate and could be placed in context with things we already know. For example, how would you explain 'ghrelin is a stomach hormone that has an orexigenic effect' to primary school children? Maybe 'a substance made in your tummy that makes you feel hungry', which could also be elaborated on using appropriate body visual movements of rubbing your tummy or demonstrating the feeling of being hungry: a bit like playing charades.

> *'The technique of having your audience raise their hands and make louder 'beeping' sounds when they felt you were no longer giving them the eye contact they deserved will still stick in my mind.'*

Likewise, using simple improvised everyday props found in the room were helpful in telling our stories: finding a pen to use as a hypodermic needle to demonstrate blood being taken or a plastic cup to represent the 'collection' of a urine sample.

I valued the one and half minute presentations we were asked to give about our work. It made us think hard about what we should include in our message and how we should express ourselves, particularly if we were talking to the media. However, in addition, imagine doing this in the form of a 'Chinese whisper', where the next person must recant your story, but in a much shorter timeframe. Contracting the description from 30 seconds, to 7 and then to 3 seconds was not only great for developing a final headline about our work, but also for demonstrating how our message was understood. Certainly, I thought this would be very useful for any PhD student and a great way to decide final thesis titles.

Even as a 'seasoned' lecturer, the technique of having your audience raise their hands and make louder 'beeping' sounds when they felt you were no longer giving them the appropriate attention or the eye contact they deserved will still stick in my mind, particularly when I give my next large class lecture!

All in all, I was very impressed with meeting Dr Bunhead face to face (even without the pyrotechnics) for what was an enlightening and thought-provoking insight into the world of public engagement. I would highly recommend members to sign up for any future public engagement events. There was something for everyone to take away, whether they had been feeling like a nervous novice or a seasoned presenter, in order to help develop life skills and your career.

NIGEL PAGE
Public Engagement Committee member and Endocrine Ambassador
Director of Learning and Teaching, School of Life Sciences, Pharmacy and Chemistry, Kingston University London

A sense of community: COLLECTING YOUR SfE BES STORIES

Our annual conference is shaped by you, our members. From early career endocrinologists taking their first steps in the field, to nurses presenting their work, to established scientists and clinicians keeping up-to-date with the latest endocrinology, we support our members at every stage of their career.

Now we're asking, what does the Society for Endocrinology BES conference mean to you? Share your experiences via our website: who you met, how you were inspired or what you learned. Here are a few brief quotes taken from your colleagues' stories…

"I'd only just started my first postdoc job and didn't have any idea what to expect, and to make it more nerve-racking my abstract was selected for an oral presentation. Thankfully after preparing myself with tea and cake at Betty's the talk went well.

Kate Lines
Radcliffe Department of Medicine, Oxford University

"Each time I have understood more and met more healthcare professionals, who are valuable sources of knowledge and information.

Lisa Shepherd
Birmingham Heartlands Hospital/ Diabetes & Endocrine Centre

"Attending SfE BES for me is like coming home, it has given me such pleasure over the years and I leave each meeting with a wealth of new knowledge and experiences, and a warm glow!

Annice Mukherjee
Salford Royal NHS Foundation Trust & University of Manchester

> *I remember listening to, and meeting throughout the conference, people whose papers I had read, and I was delighted to be a small part of it.*

Peter Taylor
Cardiff University

> *With each SfE BES I seem to become busier! I enjoy marking the posters as it is an opportunity to meet young endocrinologists – seeing their enthusiasm can inspire the "midult" generation.*

Helen Simpson
University College London

> *SfE BES always provides inspiration and I'm enthused by the knowledge and skill of others. It acts as a springboard for new ideas and revitalises my endocrine spirit.*

Antonia Brooke
Clinical Lead in Endocrinology in Exeter, Training Programme Director for Peninsula Endocrinology

Read your colleagues' stories in full and tell us your own at **www.endocrinology.org/sfe-bes-stories**

SfE BES 2018 JOIN US IN GLASGOW

The SfE BES conference is fast approaching. With another busy programme of the latest endocrine science and developments in clinical practice, we look forward to a packed 3 days in Scotland. Join us 19–21 November for workshops, lectures, meet the expert sessions and debates and be part of the SfE BES story.

Standard registration deadline: 18 NOVEMBER 2018

Be inspired

Medal Lectures:

- **Starling Medal** *Hepatic fatty acid metabolism: the effect of metabolic and nutritional state* Leanne Hodson (UK)
- **Transatlantic Medal** *Circadian clock genes and the transcriptional architecture of the clock mechanism* Joseph Takahashi (USA)
- **Dale Medal** *Disorders of thyroid hormone action: insights into diverse biological processes* Krishna Chatterjee (UK)
- **International Medal** Ursula Kaiser (USA)
- **Society for Endocrinology Medal** Stafford Lightman (UK)
- **European Medal** Maria-Christina, Zennaro (France)
- **Jubilee Medal** *Ups and downs of nuclear receptor action* Malcolm Parker (UK)

Specialist content for nurses

- *Pituitary adenomas – beyond surgery* Morag Middleton (UK), John Newell-Price (UK), Alison Milne (UK), Philip Rouse (UK)
- *Adrenal crisis and steroid education: raising the safety bar* - Gesine Meyer (Germany), Anne Marland (UK), Lisa Shepherd (UK)

Be part of the story

Join the debate:

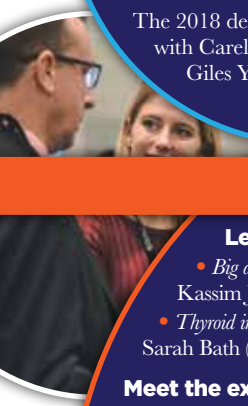
This house believes that the gut is the conductor of the endocrine orchestra – Brain vs Gut

The 2018 debate is a must-see event, with Carel Le Roux (For) and Giles Yeo (Against)

Endocrine Network Research Incubator Meetings

If you have an innovative research idea and are looking for collaborators to attract funding, or require resources to commence a project, why not apply for a slot presenting your ideas at a Research Incubator Meeting? All it takes is a brief description of your proposal.

Apply online at **www.endocrinology.org/research-incubators**



Stay up-to-date with the latest research

Lectures:

- *Big data and bone disease* Brent Richards (Canada), Duncan Bassett (UK), Kassim Javaid (UK)
- *Thyroid in pregnancy* Kristien Boelaert (UK), Peter Taylor (UK), Sarah Bath (UK)

Meet the expert sessions:

- *Brown adipose tissue* Jan Nedergaard (Sweden)
- *Gender dysphoria* Leighton Seal (UK)

Enhance your skills

Workshops:

- *Metabolites as hormones* Thue W. Schwartz (Denmark), Edward Chambers (UK), Sean F. Brady (USA)
- *Endocrine emergencies* Mark Sherlock (Ireland), Helen Simpson (UK), Carla Moran (UK)
- *How do I… manage endocrinopathies in HIV patients* Alison Wren (UK)

View the full programme online at **www.endocrinology.org/sfebes2018/programme**

Register today at **www.endocrinology.org/sfebes2018**
Be part of the conversation **#SfEBES2018**

Recognising and rewarding **EXCELLENCE**

The 2018 Society medal and award winners are selected to represent scientific excellence in endocrinology, across all career stages. They will be presented with their awards at the Society for Endocrinology BES conference in Glasgow.

EARLY CAREER PRIZE LECTURERS

SCIENCE LECTURER
Douglas Gibson Edinburgh, UK
The importance of local sex steroid action in the regulation of fertility

CLINICAL LECTURER
Julia Prague London, UK
Neurokinin 3 receptor antagonism – the magic bullet for hot flushes?

MEDAL LECTURERS

DALE MEDALLIST
Krish Chatterjee
Addenbrooke's Hospital, Cambridge

JUBILEE MEDALLIST
Malcolm Parker
Imperial College London

SOCIETY MEDALLIST
Stafford Lightman
University of Bristol

STARLING MEDALLIST
Leanne Hodson
University of Oxford

INTERNATIONAL MEDALLIST
Ursula Kaiser
Brigham and Women's Hospital, Boston, MA, USA

EUROPEAN MEDALLIST
Marie Christina Zennaro
Georges-Pompidou European Hospital, Paris, France

TRANSATLANTIC MEDALLIST
Joseph Takahashi
UT Southwestern Medical Center, Dallas, TX, USA

JOURNAL AWARD WINNERS

Five journal awards will be presented to the authors of the highest ranked papers selected by the Editorial Board, which contribute to excellence in endocrine research and practice.

Journal of Endocrinology
Laura E Pascal *et al.*
Pittsburgh, PA, USA
Conditional deletion of ELL2 induces murine prostate intraepithelial neoplasia (**235** 123–136 doi:10.1530/JOE-17-0112)

Journal of Molecular Endocrinology
Haoyong Yu *et al.*
Shanghai, China
5-ALA ameliorates hepatic steatosis through AMPK signaling pathway (**59** 121–128 doi:10.1530/JME-16-0260)

Endocrine-Related Cancer
Laura C Hernández-Ramírez *et al.* Bethesda, MD, USA
Loss-of-function mutations in the *CABLES1* gene are a novel cause of Cushing's disease (**24** 379–392 doi:10.1530/ERC-17-0131)

Endocrine Connections
Anne H van der Spek *et al.*
Amsterdam, The Netherlands
Increased circulating interleukin-8 in patients with resistance to thyroid hormone receptor α (**6** 731–740 doi:10.1530/EC-17-0213)

Clinical Endocrinology
Nicole Nigro *et al.* Basel, Switzerland
Evaluation of copeptin and commonly used laboratory parameters for the differential diagnosis of profound hyponatraemia in hospitalized patients: 'The Co-MED Study' (**86** 456462 doi:10.1111/cen.13243)

CORPORATE SUPPORTERS

The Society for Endocrinology operates a Corporate Supporters' scheme to strengthen our relationship with industry and further our charitable objectives.

We are delighted to highlight the activities of some of our Corporate Supporters here. We thank them for their support and contribution to scientific and clinical endocrinology. Corporate support is vital to the Society for Endocrinology, enabling us to further our charitable objectives and engage with endocrinologists, supporting their learning and advancing the science of endocrinology.

For further information, visit **www.endocrinology.org/corporate** or contact **amanda.helm@endocrinology.org**.

SOCIETY FOR ENDOCRINOLOGY PARTNER

Pfizer is one of the world's premier innovative biopharmaceutical companies, discovering, developing and providing over 100 different medicines, vaccines and consumer healthcare products that help save and transform the lives of millions of people in the UK and around the world every year.

For more than 25 years, Pfizer Endocrine Care has been committed to the advancement of endocrinology. This is demonstrated by our innovations in endocrine care: Pfizer UK was the first company to launch single-dose and multi-dose growth hormone (GH) delivery devices; it has built up the largest international databases of patients receiving GH therapy; and it produces the first and only GH receptor antagonist for the treatment of acromegaly.

The Society for Endocrinology has agreed a 2-year partnership with Pfizer. The agreement is the first of its kind for the Society, and aims to deliver maximum benefit to both organisations and the broader aim of advancing endocrinology.

Paul Carroll, Chair of the Society for Endocrinology Corporate Liaison Board, says
"*The partnership recognises the Society for Endocrinology's commitment to working with industry to achieve its objectives. It represents a true collaboration with an industry partner, working on joint projects for the benefit of endocrinology.***"**

James Steed, UK Lead for Endocrine Care at Pfizer, comments
"*The NHS is changing in response to various pressures, and the needs of our partners and the people they care for reflect this. We believe that, through working in partnership, combining our skills, experience and resources, together we can tackle some of the greatest challenges facing the NHS today. The new partnership will strengthen Pfizer's relationship with the Society, and ultimately improve patient care.***"**

To find out more about what Pfizer are doing to support the NHS and patients in the UK, please contact Endocrine Country Brand Lead on +44 (0)1304 616161.

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GOLD SUPPORTERS

HRA Pharma has been a significant presence in the niche area of adrenal cortical carcinoma since 2004, providing a standard therapy for this serious condition and a free of charge drug monitoring service to support clinicians in optimising its use.

HRA Pharma has more recently become a significant player in the field of Cushing's syndrome investing in two well-established but key treatment entities to further enhance its standing in the endocrine arena.

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Sandoz a Division of the Novartis Group, is a global leader in generic and biosimilar medicines. Sandoz contributes to society's ability to support growing healthcare needs by pioneering novel approaches to help people around the world access high quality medicine.

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SILVER SUPPORTERS

Hot out of the incubator: RESEARCH IDEAS RIPE FOR ADVANCEMENT

The Society's seven Endocrine Networks enable clinicians and scientists with common interests to come together and enhance progress in endocrinology.

During last year's Society for Endocrinology BES conference in Harrogate, the Adrenal and Cardiovascular Network took the opportunity to run a Research Incubator Meeting. We had issued a call for abstracts for research proposals, which had attracted two excellent presentations that concisely outlined specific plans and projects. The amassed expertise that gathered in the room for the session included some who had been specifically invited to provide all the knowledge and experience needed to facilitate proposal development. This meant we were able to ask all the relevant questions of the speakers and to offer constructive advice during the event.

As a Network Convenor, I felt that the session was a great success:

- Despite the early hour, it was well attended, attracting more than 50 people.
- We achieved our aim of a friendly, constructive and unintimidating atmosphere to help, not hinder, research. (The last thing we wanted was for enthusiastic young researchers to be shot down!)
- The session was bursting with relevant and helpful conversation.
- Plans were made and follow-up discussions held with key individuals, with the aim of submitting fellowship and grant applications to try and secure funding for the proposals.

Progress since has seen applications submitted which will hopefully be successful. Decisions are currently awaited. Certainly, I would like to think that the session at SfE BES 2017 helped to refine and improve the research ideas that were presented and to bring key people together.

Building on that success, we plan to run a similar session this year at SfE BES in Glasgow. We encourage as many people as possible to submit their research ideas for the Adrenal and Cardiovascular Network Research Incubator Meeting.

JEREMY TOMLINSON
Oxford Centre for Diabetes, Endocrinology & Metabolism

THE PROPOSER'S PERSPECTIVE

Amy Ronaldson is a Clinical Research Facilitator at the Centre for Endocrinology, Queen Mary University of London.

She presented a research proposal at the Adrenal and Cardiovascular Network's Research Incubator Meeting during SfE BES 2017, which she was developing for post-doctoral fellowship applications.

The proposal involves characterising the role of the hypothalamic-pituitary-adrenal axis in cardiovascular disease. So far, it has reached the second round of applications for the Sir Henry Wellcome Post-Doctoral Fellowship scheme. It is currently under review by the British Heart Foundation and will also be submitted to the MRC.

Amy reflects on her experience at the Research Incubator Meeting:

"I got to present the idea to a number of senior academics and clinicians in the field who provided really useful feedback. They were able to see the areas in the proposal that reviewers would potentially find problematic, and they suggested ways in which I could improve these problematic areas. The session was really helpful. It was a nice, casual environment where the feedback was more conversational than formal. I would recommend people to attend in Glasgow in order to support junior researchers and to get a chance to share expertise.

Do you have an innovative research idea?

Do you need access to resources, databases or collaborators to attract funding and get your research under way?

Apply for a presentation slot at the Research Incubator meetings during the SfE BES 2018 conference and you could be presenting your idea to an expert panel and audience of your peers.

Get constructive advice to help you get your ideas off the ground!

All are welcome to take part and only a short description of your proposal is needed to apply online at

www.endocrinology.org/events/sfe-bes-conference/sfe-bes-2018/endocrine-networks-research-incubator-meetings

MY JOURNEY TO BECOMING A 'NIGHTINGALE NURSE'
– AND HOW THE SOCIETY PLAYED A PART

WRITTEN BY LOUISE BREEN

Louise Breen with Jane Cummings, Chief Nursing Officer for England.

In September 2017, Guy's and St Thomas' NHS Foundation Trust launched the Trust's new professional award: the Nightingale Nurse Award.

Historically, nurses who trained at St Thomas' Hospital were known as 'Nightingales' and received a Nightingale badge on completion of their training. Prior to May 2018, the badge had last been awarded in 1996, before the Florence Nightingale School of Nursing moved to King's College London.[1]

THE NIGHTINGALE NURSE AWARD

The Nightingale Nurse Award is for nurses who are deemed outstanding and who meet the definition of a 'next generation Nightingale'. In summary, a Nightingale Nurse is an individual 'who is a dedicated pioneer, innovative with an enquiring mind, who inspires others and goes beyond the call of duty' and demonstrates the five Trust values in their everyday clinical practice:

- Put patients first
- Respect others
- Act with integrity.
- Take pride in what we do
- Strive to be the best

The key requirements and benefits of achieving the Nightingale Nurse Award are highlighted in the Table.

I have worked in the Trust since 1996, predominantly in endocrinology. For me, putting myself forward for the award was about strengthening my affiliation with the Trust and representing the outstanding nursing team we have in endocrinology. I am proud to say I was one of the 74 recipients of the Nightingale Nurse Award on International Nurses' Day 2018.

Table. The key requirements and benefits of achieving the Nightingale Nurse Award.

Application requirements:
• A personal statement on how the applicant meets the criteria for the award
• Two supporting statements from the Head of Nursing/line manager and a peer/colleague/team to support the individual's application
Course requirements:
• Work Based Learning Module (Level 6 or 7) comprising two reflective accounts demonstrating excellence in practice, underpinned by the Trust Values and Nightingale Pledge
• Minimum of two different sources of practice-based feedback
• Attendance at support sessions for the Nightingale Nurse Award
Benefits of the award
• Formal reflective practice, which can be used to support revalidation and make positive changes to current practice
• 15 credits at Level 6 or 7
• Next generation 'Nightingale Nurse' badge with award ceremony
• Title of 'Nightingale Nurse'
• Eligibility for full membership of the Nightingale Fellowship

WORKING WITH THE SOCIETY

A key part of the Nightingale Nurse Award is providing evidence of practice feedback, and I was able to demonstrate this via my role in the planning committee for the Nurse sessions for the Society for Endocrinology BES conference 2017.

I was tasked with chairing and designing a session, and suggested diabetes insipidus. This topic was on the revolving programme agenda and very topical, given the patient safety alert issued in February 2016: 'Stage one: warning. Risk of severe harm or death when desmopressin is omitted or delayed in patients with cranial diabetes insipidus'.[2]

When planning sessions for the Society for Endocrinology BES conference or the Endocrine Nurse Update, the Society's Nurse Committee jointly discusses the topics for presentation, the potential speakers and the chairs for the session. The programme is never put together in isolation and, once agreed, is ratified by the Society's Programme Planning Committee.

We were fortunate to secure excellent speakers for the diabetes insipidus session:

- expert consultants Miles Levy and Steve Ball
- co-Chair Pat McBride from The Pituitary Foundation
- a patient with the condition who has a background in healthcare.

For me, the speaker with the most impact was the patient representative, who eloquently described her journey with diabetes insipidus.

I felt the session went very well and, when reflecting on the practice feedback I could use for the Nightingale Nurse Award, this was at the top of the list. I was able to contact the Society for Endocrinology and get specific feedback from this session. I was delighted to find it was one of the more highly rated sessions. This demonstrates how we can use our contributions to Society meetings to support personal objectives and revalidation.

SUPPORTING OTHER NURSES

Going forward, I have asked the Society's Nurse Committee if it is possible to generate feedback for nurses who participate in the planning, presenting or chairing of Society sessions for their portfolios.

I am also happy to say that the next planning committee for Endocrine Nurse Update will comprise nurses drawn from the wider Society membership, rather than solely Nurse Committee members, thus widening our pool of contributors to Society for Endocrinology nurse events.

The Society's Nurse Committee offers members a great opportunity to be at the forefront of nursing care in endocrinology and to shape the future for endocrine nurses, importantly in recognition of our role, training and development needs. The more participation we have from the membership, the more progressive and diverse we become. I for one am excited by the fact our membership is growing and that we will see a lot of new faces in the future.

LOUISE BREEN
Advanced Nurse Practitioner–Endocrine, Diabetes & Endocrine Department, St Thomas' Hospital, London

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FLY THE FLAG THE ENDOCRINE NURSE COMMUNITY

Are you passionate about endocrine nursing? Do you take pride in being part of the Society's close-knit endocrine nurse community?

Then why not take a step further to drive the discipline forward, while supporting the people that make it what it is?

The Society for Endocrinology is recruiting Nurse Members to join their ranks in various capacities, offering unique opportunities to develop your leadership skills. The following are voluntary positions, however expenses to attend meetings will be reimbursed.

SOCIETY FOR ENDOCRINOLOGY NURSE COMMITTEE

Four vacancies are available for you to join your Nurse Committee, which helps to develop clinical practice, supports training and education, and raises the profile of endocrine nursing. Positions start from January 2019.

Apply online at **www.endocrinology.org/about-us/governance/call-for-nominations** before **28 September**.

SOCIETY FOR ENDOCRINOLOGY PEER REVIEW INITIATIVE

The Interdepartmental Peer Review initiative aims to improve the services offered to patients with endocrine pathologies, helping support requests for additional resources and lifting morale within the endocrine community. One vacancy is available for an Endocrine Nurse to join this project.

Contact **natasha.archer@endocrinology.org** for information on how to apply.

CONGRATULATIONS TO JULIE LYNCH ENDOCRINE NURSE GRANT AWARDEE

We are delighted to announce that the first-ever Endocrine Nurse Grant has been awarded to Julie Lynch, Senior Research Nurse at Leeds Teaching Hospitals NHS Trust, for her project 'Assessing the impact of residual adrenal function on adrenal crises and infections: can we direct educational resources?'

Do you have a project to improve nursing/clinical practice, or to gather preliminary data to be used in a PhD application? Apply for funding to take your career to the next level with the Endocrine Nurse Grant. **The next deadline is 28 November**. Find out how to apply at **www.endocrinology.org/grants-and-awards/prizes-and-awards/endocrine-nurse-award**.

LISA SHEPHERD

NURSE COMMITTEE CHAIR

It always gives me great pleasure sharing nurses' achievements with the endocrine community and I would like to congratulate two nurses in this autumn's edition of the Nurses' News.

First, I would like to congratulate Julie Lynch, who is our first Endocrine Nurse Grant awardee. Her research on 'Assessing the impact of residual adrenal function on adrenal crises and infections: can we direct educational resources?' will add to evidence in this area and inform practice. If you are interested in becoming our second awardee and in applying for this grant, further details can be found in the bottom panel to the left.

Second, I would like to congratulate Louise Breen, who works as an Advanced Nurse Practitioner at Guy's and St Thomas' NHS Foundation Trust on her wonderful achievement of receiving a 'Nightingale Nurse Award'. In her article on p. 27, Louise explains how she came to be awarded such a prestigious medal and how her work with the Society for Endocrinology played an important role in obtaining this.

These are two examples of how endocrine nurses highlight their important work. We have a number of vacancies on our Nurse Committee that commence January 2019. These are rewarding positions that allow you to be the voice of endocrine nurses, developing the role and training and development. If you are considering applying, see top left for further details.

I look forward to seeing you all in November in Glasgow at SfE BES 2018.

BEST WISHES

LISA SHEPHERD

WATCH THIS SPACE...

The Society for Endocrinology Competency Framework for Adult Endocrine Nursing was developed to enable Endocrine Nurses to evaluate their current practice, as well as to facilitate discussion leading to the provision of continuing career progression and service development. Documents used for the purpose of providing evidence for these competencies can also be used to support revalidation with the Nursing and Midwifery Council and local appraisal, or as part of your portfolio for the Endocrine Nurse Masters level module (see **www.endocrinology.org/careers/training-and-resources/courses/masters-level-module-in-endocrine-nursing**).

Providing evidence is always challenging and much uncertainty exists about what specific evidence is required or accepted. This addition to the competency framework will provide a selection of examples that can be used as evidence.

See **www.endocrinology.org/careers/training-and-resources/guides/society-for-endocrinology-competency-framework-for-adult-endocrine-nursing-2nd-edition** for further details.

SHARING AND CARING?

PERSPECTIVES OF MULTIDISCIPLINARY WORKING BETWEEN ENDOCRINOLOGISTS AND OPHTHALMOLOGISTS IN THYROID EYE DISEASE

WRITTEN BY PARIZAD AVARI, CLAIRE FEENEY, VASSILIKI BRAVIS, STEPHEN ROBINSON, KARIM MEERAN & VICKIE LEE

Thyroid eye disease (TED) is an autoimmune condition affecting the orbits[1] and is responsible for significant morbidity including, in rare cases, blindness.[2] Affecting up to 25% of patients with Graves' (autoimmune thyroid disease with thyrotoxicosis), TED is the most striking extra-thyroidal manifestation and can be extremely difficult to treat.[2,3] Yet, TED can often be undiagnosed for several months, or misdiagnosed, leading to significant delays in patient management.[4]

TEAMeD

In 2009, the European Group on Graves' Orbitopathy (EUGOGO) spearheaded an international drive to improve the care of patients with TED, with the Amsterdam Declaration signed by 84 national and international professional and patient-led organisations, including the British Thyroid Foundation. In the UK, TEAMeD (Thyroid Eye Disease Amsterdam Declaration Implementation Group) was formed to implement these objectives.[5] The most recent TEAMeD-5 guidelines recommend[6]:

1. Accurate diagnosis of Graves' disease
2. Screen all patients for Graves' disease
3. Alert all patients to the risk of TED
4. Prevent TED
5. Refer patients with moderate or severe TED, or TED which affects their quality of life, to a specialist multidisciplinary joint thyroid eye clinic

SURVEY OF ENDOCRINOLOGISTS

To assess awareness of these new guidelines among those managing thyroid conditions on a routine basis, we surveyed 86 endocrinologists, including consultants and registrars, as well as endocrine surgeons (Figure 1). Three-quarters (76%) of respondents were not aware of TEAMeD/TED guidelines. Only 13% currently work in a multidisciplinary setting; with 68% opting they would like to work within one.

One-third of respondents rated their current department's relationship with local ophthalmology services as good, with the remaining two-thirds stating either just 'average', 'poor' or 'did not know'. When questioned about using a screening tool for thyroid eye disease, 20% use NOSPECS, 7% use DIAGO and 5% use the Vancouver Orbitopathy Rule. Sixty-eight per cent do not use a routine tool for screening for TED.

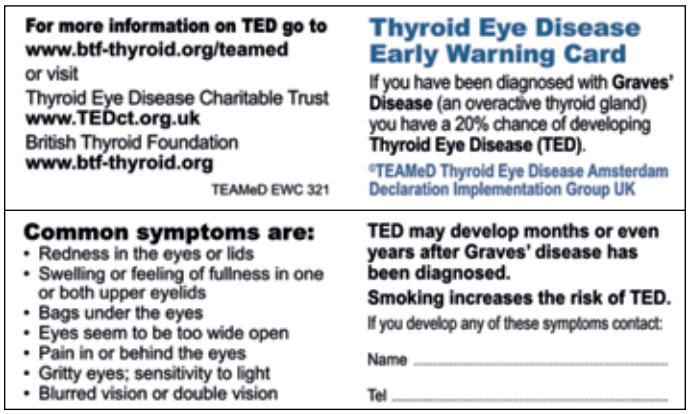


Figure 2. Thyroid eye disease early warning card.

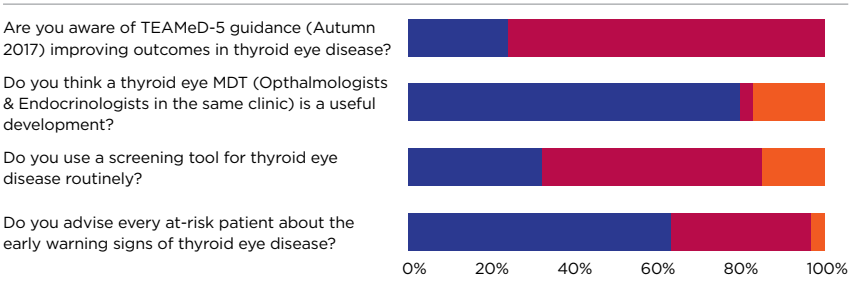
One of the key objectives of TEAMeD includes empowering patients with Graves' to recognise early symptoms of TED with an early warning card (Figure 2). Of total respondents, almost two-thirds provide written/verbal advice, with the remaining one-third not routinely advising every at-risk patient about the early warning signs of thyroid eye disease.

Our survey indicates the need for increased awareness and addressing the short-fall of specialised multidisciplinary thyroid-eye clinics. There is a growing amount of evidence to show that when patients are assessed in a combined thyroid-eye clinic, they have a favourable outcome compared with patients who are not managed in such clinics.[7,8] However, despite the use of specialised multidisciplinary clinics for the management of TED, many patients in the UK are managed outside of such specialised clinics. Reasons for this are likely to be multifactorial, including lack of resources and funding, and lack of awareness about these latest guidelines.

It is hoped that the new TEAMeD guidelines and the initiation of more multidisciplinary clinics, will facilitate early diagnosis and better treatment of patients with this debilitating and disfiguring disease.

PARIZAD AVARI, CLAIRE FEENEY, VASSILIKI BRAVIS, STEPHEN ROBINSON, KARIM MEERAN & VICKIE LEE
Imperial College Healthcare NHS Trust

Figure 1. Survey of endocrinologists and endocrine surgeons in London* (n=86). ■, Yes; ■, no; ■, do not know. © P Avari *et al.*



*The survey was conducted at an endocrinology conference in London; however, it is possible that not all doctors are London-based.

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IODINE STATUS: DETERMINATION AND OPTIMISATION IN THE UK AND BEYOND

WRITTEN BY JOHN LAZARUS

In 2015, a 3-year Horizon 20/20 grant (EUthyroid) was obtained from the EU for €3 million to document aspects relating to iodine status in around 28 European countries.

The work funded by this grant has now finished, and results of many investigations have included finding significant variation in iodine assays, widespread variation in monitoring practice across Europe and a very low knowledge base concerning iodine in the population. Other work packages concluded that determination of serum thyroglobulin is a good measure of iodine status and that iodine deficiency in pregnancy does impact negatively on child neurodevelopment.

Although some European countries have legislation to encourage the use of iodised salt at the household level and have thereby achieved adequate iodine nutrition, many countries with large populations still have suboptimal iodine status.

THE KRAKOW DECLARATION

The end of the EU grant was marked by presentation of a declaration to serve as a landmark for the development of adequate iodine nutrition in Europe. This took place at a meeting in Krakow, Poland in April 2018, and has resulted in the Krakow Declaration on Iodine (**www.iodinedeclaration.eu**).

This document indicates the 'Tasks and Responsibilities for Prevention Programs Targeting Iodine Deficiency Disorders'. Iodine deficiency disorders (IDD) represent a global health threat to individuals and societies. The Krakow Declaration notes that adverse effects of iodine deficiency are diverse and impose a significant burden on public healthcare systems.

Although this fact is well established, IDD prevention programmes receive surprisingly little attention from policymakers, opinion leaders and the public. European epidemiologists, endocrinologists and nutritionists investigating IDD are increasingly concerned about the deteriorating commitment of policymakers to addressing public health strategies against IDD in European populations. Hence, the signatories of the Krakow Declaration on Iodine ask for support from all stakeholders across Europe and beyond, to pool resources and expertise to ensure that future generations can realise their full potential without any restrictions resulting from exposure to iodine deficiency.

THE SITUATION IN THE UK

So what is the iodine situation in UK? In 2010, some of us in the British Thyroid Association had noted that several small surveys of iodine status in pregnant women in the UK showed significant iodine deficiency in more than 50% of individuals in the first trimester.

Mark Vanderpump and colleagues then performed a survey of urinary iodine in nearly 800 teenage girls, and showed low iodine status right across the UK.[1] These alarming data led to the establishment of the UK Iodine (UKI) Group (**www.ukiodine.org**) in 2012. This is a multidisciplinary group which aims to advocate for recognition of optimal iodine nutrition in the UK, particularly in at-risk groups such as pregnant women.

> ***'The UK is one of only 25 countries that does not routinely consume iodised salt. This must change.'***

Over the past 6 years we have submitted comments to the Standing Advisory Committee on Nutrition (SACN), published letters in the press and been interviewed on radio concerning the suboptimal iodine status of the UK. The most recent data from the NDNS (National Diet and Nutrition Survey) showed a median urinary iodine concentration (UIC) in 16- to 49-year-old women of 102µg/l (i.e. close to the World Health Organization (WHO) limit of 100µg/l). While these values do just meet the WHO criterion for adequate intake, in this important group NDNS admits that the criterion for iodine sufficiency during pregnancy and lactation (median UIC of 150–249µg/l) is not met. These data are similar to those from other countries in Europe who have adequate iodine levels in the non-pregnant population, but levels which are very inadequate when it comes to sustaining pregnancy.

MOVING FORWARD

We must continue advocacy at all levels to inform the general population and government health officials about iodine deficiency in the UK and the future effect on child development. Colleagues at the University of Surrey have already published evidence that iodine deficiency in the first trimester of pregnancy has resulted in suboptimal school performance in 9-year-old children.[2]

In the absence of any significant consumption of iodised salt in the UK, we should encourage routine iodine supplementation before and during gestation. We must inform officials and the population that iodised salt is only very marginally more expensive than ordinary salt. Also, we agree strongly with cardiovascular colleagues on the necessity of reducing daily salt consumption, but the introduction of iodised salt will not affect this intention.

The Iodine Global Network (IGN) has made great progress in the world over the past 30 years in that around 100 countries now consume iodised salt. The UK is one of only 25 countries that does not routinely consume iodised salt. This must change.

JOHN LAZARUS
Regional Co-ordinator, West and Central Europe IGN

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HILARY M DRANE (*née* GRUNDY)

The endocrine community was saddened to hear of the recent passing of researcher Hilary Drane. In the world of steroid hormone research, the identification, isolation and characterisation of a new hormone constitute a pivotal moment in biology, and often pathology, which is consequently a time of great activity and excitement. In 1953, while working with Sylvia Simpson (later Tait) and James Tait at the Courtauld Institute of Biochemistry at the Middlesex Hospital, London, Hilary Drane played a central role in the discovery of aldosterone, the primary mineralocorticoid in mammals.

Hilary received her degree (BSc in Household and Social Sciences) from King's College London in 1947 and, due to her interest in hormone assays, found work at the Middlesex Hospital with Sylvia Simpson and physicist James Tait, who were interested in adrenal hormones.

At this time, there was considerable activity in the research world to identify new hormones. Edward C Kendall and Philip S Hench (Mayo Clinic, Rochester, MN, USA), Tadeus Reichstein (University of Basel, Switzerland) and many other groups working independently had isolated and characterised more than 30 steroids from the bovine adrenal gland in the years leading up to the Tait laboratory's discovery. The importance of these discoveries is evident in that Kendall, Hench and Reichstein were awarded the Nobel Prize in Physiology or Medicine in 1950 for 'their discoveries relating to the hormones of the adrenal cortex, their structure and biological effects'. However, at that point, whether there remained other adrenal hormones to be found was an open question.

The group in which Hilary Drane worked at the Middlesex Hospital was striving to identify and characterise new adrenal hormones, in particular the 'amorphous fraction', which they named due do its inability to be crystallised. This fraction could revive adrenalectomised dogs with noteworthy potency.

Hilary Drane's work in the lab was to develop methods of estimating the mineralocorticoid (sodium-retaining activity) of adrenal fractions, using the then new technique of paper chromatography. This involved using primitive equipment such as borrowed drainpipes, and subsequently graduating to second-hand fish tanks to run the chromatograms. These new methods allowed for greater separation of the fractions and thus the mineralocorticoid activity was identified as being different from the known fractions linked to cortisol or other adrenal steroids.

The hormone responsible was found to be aldosterone (originally named electrocortin), the primary mineralocorticoid hormone in mammals and some species of fish. From an evolutionary perspective, it was first seen in lungfish, a species in which the conservation of sodium is critical for terrestrial activity.

Hilary commenced her doctoral studies at the University of Oxford in 1952 and following her marriage and move to Canada in 1954, worked in the Nutrition and Endocrinology Departments of the University of Toronto (1955-1957). She returned to the UK and worked with Sir Richard Doll on 'the secretion of blood group substances and various diseases'.

Following the birth of her two children, she continued her research at the Central Veterinary Laboratory (CVL) for 18 years during which time she investigated the activity of other steroid hormones, oestrogens and phyto-oestrogens using radioimmunoassay and other state-of-the-art techniques. One memorable event during her time at CVL was participating in a lively EU debate on the use of growth hormones in meat. She was particularly unhappy with the thought that a post-Brexit UK might allow something against which she had so strongly (and successfully) argued.

In 1983, she ceased her active research and moved to Paris; however, it wasn't long before she was invited to edit the English translation of *Hormones: from molecules to disease* by Etienne-Emile Baulieu.

The significance of the discovery of aldosterone in the Tait laboratory has its own history. Contemporary research into mechanisms of cardiovascular disease and the benefits of 'aldosterone blockers' for heart failure stem from early studies by Hans Selye, who used the terms 'glucocorticoid' and 'mineralocorticoid' to describe the actions of adrenal fractions.

Selye and colleagues demonstrated inflammatory (granuloma formation) and fibrotic actions of deoxycorticosterone in dogs. While this was originally thought to be a glucocorticoid effect, the work was performed before the discoveries of the Grundy (Drane), Simpson (Tait) and Tait team. Deoxycorticosterone is both a precursor for aldosterone and a potent mineralocorticoid in its own right.

In 1992, Brilla and Weber (Columbia, MO, USA) reignited this area of research to show that aldosterone in the presence of a medium–high salt intake could produce tissue fibrosis in the heart. And so began over two decades of research into the pathogenic actions of aldosterone and its receptor (cloned in 1987 by Arizza *et al.*, La Jolla, CA, USA) in the heart.

Early work showed that the tissue fibrosis was independent of the classic sodium-retaining actions of aldosterone/mineralocorticoid receptor (MR) described so many years previously in the kidney, and was due to local non-epithelial tissue actions of the MR in the heart. The clinical and experimental studies that followed resulted in the recommendation of the aldosterone blocker spironolactone for the treatment of heart failure, and promoted the development and marketing of a new more selective MR antagonist (eplerenone).

The initial recognition of aldosterone's clinical significance was based on adrenal insufficiency and sodium retention for survival. Given the rare nature of the condition, this took some time. For many years it was used as a potassium-sparing diuretic in the treatment of hypertension. Today it is thought that ~10% of essential hypertension is attributable to excess aldosterone production. Moreover, aldosterone blockers are now being tested for many forms of heart disease. Almost 65 years after its discovery, aldosterone remains a rich and dynamic research field.

It is clear that Hilary was a driven and talented researcher, whose hard work has contributed to better understanding of adrenal hormones and helped to improve patient care, even today. She maintained her interest in aldosterone research throughout her long life and was delighted to be able to participate in the 50th anniversary celebrations.

In retirement, she and her husband split their time between the UK and New Zealand and in each home they created beautiful gardens which they enjoyed sharing with others. Hilary delighted in meeting people, loved the natural world and had an ongoing habit of seeking answers to questions. She was attending lectures, taking language lessons and reading avidly until she passed away.

MORAG YOUNG
Head of Cardiovascular Endocrinology,
Hudson Institute of Medical Research

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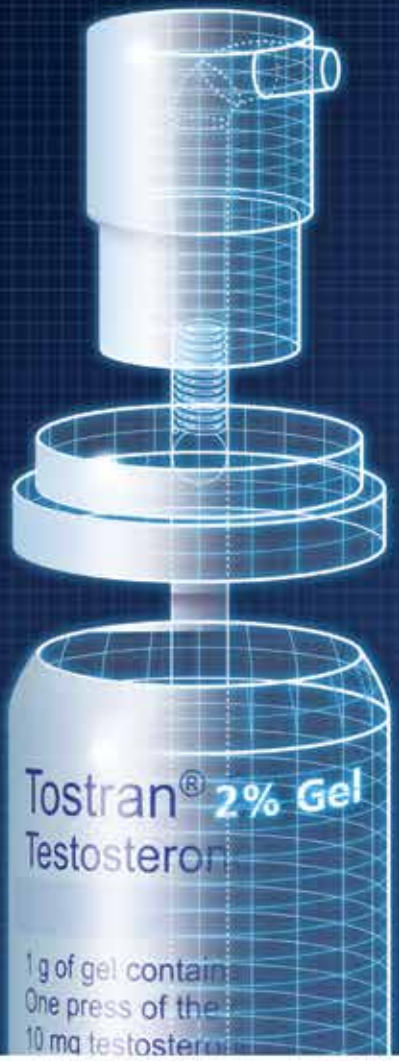

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References: 1. Tostran® Summary of Product Characteristics. 2. eMIMS January 2018. 3. Morgentaler A, et al. Steady-state pharmacokinetics. SMSNA Annual meeting 2011.

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