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THE ENDOCRINOLOGIST

THE MAGAZINE OF THE SOCIETY FOR ENDOCRINOLOGY

A challenging ENVIRONMENT

Special features
PAGES 6–15

A word from THE EDITOR...

A warm welcome to the summer edition of *The Endocrinologist*! This issue delves into how our changing lifestyle and environment is affecting our health and wellbeing. In his conversation with Louise Hunter, Roelof Hut follows up his talk at SfE BES 2022 by discussing the impact of the mismatch that climate change is bringing between seasons and photoperiods (page 10). A number of articles discuss endocrine disrupting chemicals (EDCs) and how animal models and human studies have enhanced our understanding on their mechanisms of action and resulting pathophysiological responses. Reading these articles and the opinion piece by Stuart Milligan (page 14), it is evident that while we have begun to understand and identify the mechanism of how EDCs and our environment are impacting our overall health and that of generations to come, the interventions to tackle this are less tangible and fraught with complexities. The concept of 'One Health' remains an important challenge, and something that I urge early career researchers to consider when thinking about their next steps.

Later in this issue you'll see that your Society needs you! There are several governance vacancies (page 19). Being a member of a committee is an opportunity to contribute to the voice of UK endocrinology, be it through public engagement initiatives, position statements, or lobbying government. Having sat on several committees over the years, I can vouch for it being a very rewarding experience – it's also a great way to network and get to know fellow endocrinologists from around the UK.

John Newell-Price, who has long been an active member of the Society, was recently elected as the first ever non-US-based President of the Endocrine Society across the pond. We got the scoop on his plans in the interview on page 16.

Wishing you all a happy, restful and (not too!) warm summer vacation.

KIM JONAS

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The Society's new strategy

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 AUTUMN 2023 issue: **7 July 2023**.

Front cover image ©Shutterstock

CALL FOR CLINICAL RESEARCH GRANT APPLICATIONS

The Clinical Endocrinology Journal Foundation (formerly the Clinical Endocrinology Trust) is offering research awards in the field of clinical endocrinology up to a maximum of £25,000. Preferred applications would be multicentred studies with a defined clinical outcome, involving quality improvement or audit. Other applications will also be considered, as long as they are clinically relevant. Application guidance and forms are available from **www.endocrinology.org/grants**. Apply by **15 July**.

OUR AWARD-WINNING PODCAST: BACK FOR SERIES 3

Look out for the new series of Hormones: The Inside Story. Launching in August, it features topics such as 'Can my pet pick up my stress?' 'Are my genes to blame for my diabetes?' and 'The science behind sexual desire'. The series is available from Apple, Spotify, or wherever you like to listen.

FOLLOW AND SHARE: YOU AND YOUR HORMONES ON TWITTER

We have launched a You and Your Hormones Twitter account to help achieve our mission of providing students, teachers and the public with accurate information and resources about endocrinology. Could you could help us to promote reliable endocrine-related resources online by sharing and following our new account at **www.twitter.com/Your_Hormones**?

SHARE YOUR EXPERTISE IN THE CLINICAL RESOURCE HUB

Has your clinic introduced something that has improved your practice or service delivery? If the answer is yes, you could improve clinical service delivery and unify patient care by sharing it with the wider endocrine community!

We are currently looking for resources relating to clinical pathway guides, virtual care, Patient Initiated Follow Up (PIFU) and patient safety.

Log in at **endocrinology.org/members** to explore and share.

ADVERTISE YOUR VACANCIES TO OUR COMMUNITY

Attract the best talent by sharing your job, studentship and grant opportunities with our membership. Check current vacancies at **www.endocrinology.org/careers/jobs**.

CLINICAL TRANSFORMATION BITESIZE WEBINARS

Go online and register for our upcoming Bitesize webinars: 'Digital health and pathways' (5 July) and 'Nurse-led services for clinicians/all healthcare professionals' (6 September). If you have topic suggestions for these short, informal webinars, please send them to us at **careers@endocrinology.org**.

SOCIETY CALENDAR

26 June 2023
SfE BES ABSTRACT DEADLINE

12 September 2023
ENDOCRINE GENETIC TESTING
Society Endorsed Event
Manchester, UK

13–15 November 2023
SfE BES 2023
Glasgow, UK

GRANT AND PRIZE DEADLINES

3 July 2023
MEDAL NOMINATIONS

9 August 2023
TRAVEL GRANT

20 September 2023
PUBLIC ENGAGEMENT GRANT

25 October 2023
PRACTICAL SKILLS GRANT

8 November 2023
EARLY CAREER GRANT

8 November 2023
EQUIPMENT GRANT

8 November 2023
ENDOCRINE NURSE GRANT

22 November 2023
MEETING SUPPORT GRANT

HOT TOPICS

SOCIETY FOR ENDOCRINOLOGY OFFICIAL JOURNALS

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

JOURNAL OF ENDOCRINOLOGY

Androgen therapy in male rats with chronic kidney disease

Individuals living with chronic kidney disease (CKD) endure profound bone loss and arterial calcification. The contribution of hypogonadism to these ailments is unknown, as is the utility of androgen therapy to this patient cohort.

To give insight into this issue, David *et al.* induced CKD in male rats with or without dihydrotestosterone treatment, and compared them with control cohorts.

Consistent with induction of CKD, mice exhibited 10-fold increased serum creatinine and 15-fold increased parathyroid hormone levels when compared with control groups. The study found that androgen therapy had no impact on measures of trabecular bone volume or on arterial calcification.

Read the full article in *Journal of Endocrinology* **257** e220319

JOURNAL OF MOLECULAR ENDOCRINOLOGY

Hormonal regulation of the breast cancer microenvironment

This review article by Sarah Boyle is part of a collection of articles highlighting the breadth and depth of research being undertaken in basic endocrinology by early- and mid-career researchers.

It nicely gathers current knowledge regarding the association of hormone receptor profiles with composition of the microenvironment; how hormones directly influence stromal cells, immune cells and cells associated with the vasculature; and the paracrine mechanisms that lead to the formation of a tumour-promoting extracellular matrix.

The article provides a valuable and timely review, which shows the increasing importance of hormone receptors in cancer cell proliferation and malignant properties of cancers.

Read the full article in *Journal of Molecular Endocrinology* **70** e220174

ENDOCRINE-RELATED CANCER

Experimental models for phaeochromocytoma and paraganglioma

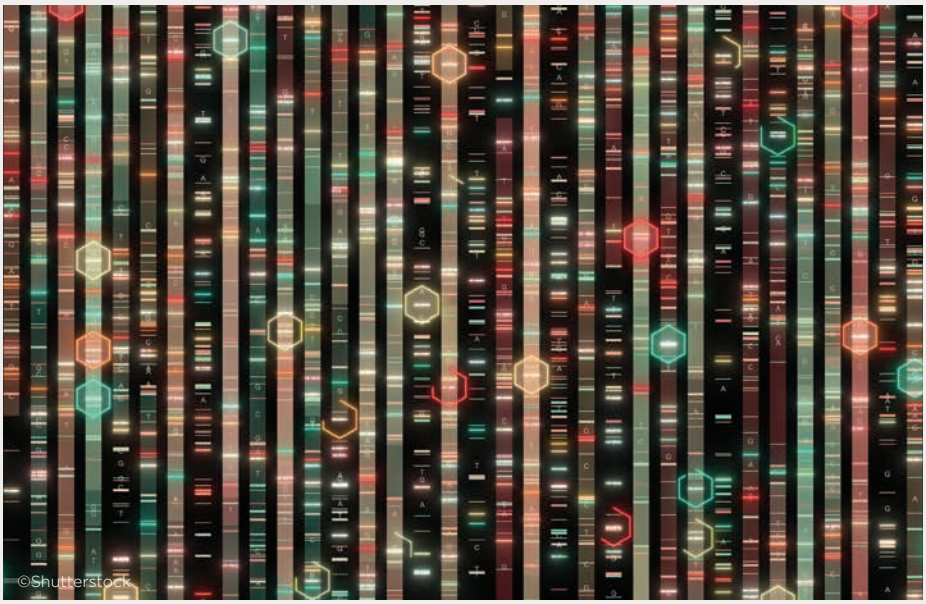
In this article, Tischler and Favier explore some of the most fundamental aspects of cancer biology, in the form of the experimental model. The focus here is on phaeochromocytoma and paraganglioma, topics where we do not have the necessary basic understanding of pathobiology in order to progress with suitable preclinical testing.

Due to the seemingly rare nature of both conditions, we lack appropriate models to test potential drug targets. This paper discusses the challenges and most recent advances in the production of test models, with a particular focus on *in vitro* studies and the necessary considerations as we move forward.

Read the full article in *Endocrine-Related Cancer* **30** e220405

ENDOCRINE HIGHLIGHTS

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



A draft human pangenome reference

We live in an era where the generation of big datasets is commonplace. However, the reference datasets that are used to align and assign analyses lack genetic diversity and, therefore, carry limitations and caveats when interpreting results.

Liao *et al.* have published the interim results of the Human Pangenome Reference Consortium, which aimed to produce the first human pangenome reference sets for common big data analysis. Taking the near-complete diploid genomic information from 47 diverse individuals, the research team has carried out multiple RNA- and DNA-based sequencing modalities, including 10x genomics, microarray, high-fidelity and structural variant genotyping, to generate the human pangenome.

Complete findings and datasets will be published in a follow-up to this study. However, these interim data provide a valuable insight into how they differ and add diversity compared with current reference datasets. Moreover, the results of this study will provide important genetic diversity in reference ranges for big datasets across multiple sequencing platforms.

Read the full article in *Nature* **617** 312–324

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

ENDOCRINOLOGY, DIABETES & METABOLISM CASE REPORTS

Graves' orbitopathy in a patient with an eye prosthesis

Ali and colleagues report the case of a 54-year-old female who presented with thyrotoxicosis and signs of Graves' orbitopathy affecting her right eye (clinical activity score 4/10). She had a prosthetic left eye, as a consequence of previous trauma. Shortly after presentation, she noticed altered position of her prosthesis, with the eye tilting upwards. Magnetic resonance imaging (MRI) demonstrated swelling of inferior and medial recti muscles bilaterally.

This case is, therefore, an important reminder that Graves' orbitopathy is a condition that affects the tissues of the orbit, rather than the eyeball itself. It shows the value of MRI scanning in the assessment of Graves' orbitopathy.

The patient received treatment with rituximab, after refusing glucocorticoid therapy because of concerns about side effects. She also required oculoplastic intervention (botulinum toxin to upper eyelid, plus blepharotomy surgeries) to limit the effects of corneal exposure in her right eye. A euthyroid state was achieved and maintained with a block-and-replace treatment regimen.

Read the full article in *Endocrinology, Diabetes & Metabolism Case Reports* doi:10.1530/EDM-22-0341

ENDOCRINE CONNECTIONS

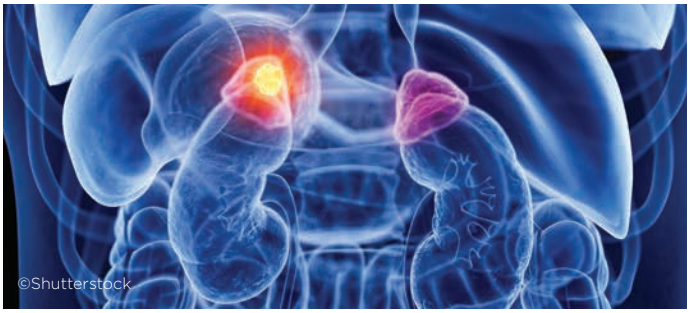
Endocrine autoimmunity in relatives of patients with Addison's disease

People with Addison's disease display a complex array of autoimmune conditions, potentially genetically transmitted. Finchna *et al.* measured circulating antibodies in relatives of patients with Addison's disease and examined their correlation with existing genetic risk factors.

Using this cohort of 112 female and 75 male relatives, the group examined antibody measures. They found thyroid autoantibodies to thyroid peroxidase and thyroglobulin were detectable in 25.1 and 17.1% of the relatives respectively.

The study found that first-degree relatives of patients with Addison's disease, carriers of the *PTPN22* rs2476601 T allele, are at particular risk of developing autoantibodies to endocrine antigens.

Read the full article in *Endocrine Connections* **12** e230008



Monthly vitamin D supplementation and fractures

The role of vitamin D in fracture risk remains controversial. A recent meta-analysis demonstrated no reduction in fracture risk in those taking regular vitamin D supplementation, whilst a meta-analysis of randomised controlled trials suggested that annual vitamin D supplementation was associated with an increased hip fracture risk.

To evaluate the role of vitamin D supplementation in fracture risk, Waterhouse and colleagues undertook a population-based, double-blind, randomised, placebo-controlled trial of oral vitamin D3 supplementation (60,000IU per month) in adults aged 60–84 years living in Australia. In total, 21,315 participants were randomised to vitamin D or placebo, and participants were followed for up to five years. The main outcome assessed was total fractures.

In this analysis, 20,326 participants were included (vitamin D, n=10,154; placebo, n=10,172). Over a median follow-up period of 5.1 years, 5.6% of participants in the vitamin D group and 5.9% of participants in the placebo group had one or more fractures. Monthly vitamin D supplementation did not have an effect on overall fracture risk (HR 0.94; 95% CI 0.84–1.06). However, the HR for total fractures reduced with increasing follow-up time.

This study demonstrates that monthly supplementation with vitamin D was not associated with increased fracture risk. Whilst there was a suggestion that longer term supplementation may reduce fracture incidence, further research is required.

Read the full article in *Lancet Diabetes & Endocrinology* **11** 324–332

ENVIRONMENTAL EDCs AND DECLINING MALE REPRODUCTIVE HEALTH

WRITTEN BY MADISON QUINTANAR, LUCY SHRIBMAN & MICHELLE BELLINGHAM

Exposure to endocrine-disrupting chemicals (EDCs) has been of growing concern to human and animal health over recent years.[1] EDCs comprise a group of chemicals that can alter the release or action of endogenous hormones, and thus have the potential to alter normal physiological functions if they enter the body. Many EDCs are found in everyday items, such as packaging and food containers, personal care products, children's toys, medical devices and pesticides, which end up in the environment (e.g. in surface or urban water and sewage) and are detectable in body tissues.

Human and animal exposure is ubiquitous. There is now a wealth of evidence to show that exposure to EDCs, particularly during gestational and pre-pubertal life, is implicated in testicular dysgenesis syndrome (TDS). This encompasses several male reproductive abnormalities of increasing prevalence, such as cryptorchidism, hypospadias, impaired semen quality and testicular germ cell cancer.[2] Studying the effects of EDCs in humans is complex and has largely been limited to epidemiological studies. However, animal research has given a greater insight into our understanding of the role of environmental EDCs in declining male reproductive health.

ANIMAL STUDIES

Early evidence suggesting that exposure to EDCs may significantly affect the morphology of the male reproductive system in various species came from accidental exposures in wildlife, e.g. work by Edwards *et al.*[3] In addition, several laboratory studies in rodents (some described below) have provided further substantial evidence that exposure to environmental EDCs can be detrimental to male reproductive health.

For example, rats exposed to benzo-a-pyrene (a chemical produced from incomplete combustion) exhibit reduced testis weight, lowered plasma and intratesticular testosterone concentrations, increased germ cell apoptosis, and decreased spermatozoa production.[4,5] Similarly, prenatal exposure to bisphenol A, a chemical found in plastics, resulted in decreased sperm counts and motility in adult mice[6] and disrupted meiotic progression during spermatogenesis in rats.[7]

Other chemicals, such as the pesticide methoxychlor, have been shown to cause inhibition of testicular steroidogenesis in adult rats,[8] which showed a reduction in proteins important for testosterone biosynthesis and production (steroidogenic acute regulatory protein, and 3β- and 17β-hydroxysteroid

dehydrogenase). However, these effects were reversed after 72 hours.[8] Another study in mice looked at gestational exposure to both di(2-ethylhexyl)phthalate (DEHP; a plasticiser) and polychlorinated biphenyls (formerly used in industrial manufacturing), which caused decreases in testicular weight, seminiferous tubule diameter, spermiogenesis, Leydig cell quantity, intratesticular testosterone, epididymal sperm count and sperm viability.[9] Furthermore, *in utero* and lactational exposure to DEHP alone increased epididymal weight.[10]

Exposure to butylparaben, a chemical used in cosmetics, caused progressive spermatogenic cell detachment in rats that were orally exposed, and induced apoptotic cell death in the testes,[11] as well as reductions in epididymal weight, sperm count and testosterone concentrations.[12]

While there is a lot of evidence linking effects of environmental exposure to EDCs and testicular dysgenesis in F1 generations, more recent evidence in mice has shown testicular changes in up to the third generation after maternal exposure. It is postulated that intergenerational effects of EDCs can occur via epigenetic DNA modifications.[13] Though more research is required, this evidence could provide a deeper understanding of the longer term effects of EDC exposure in both human and animal populations.

'Some studies have utilised a 'real-life' model of EDC exposure, using sheep exposed to pasture treated with biosolids.'

REAL-LIFE MIXTURE EXPOSURES

Much of the research on EDCs and male reproductive function has utilised rodent models, due to their quick generation time, and has exposed them to high doses of single chemicals or limited mixtures of chemicals. However, such models do not replicate human chemical interactions, which involve chronic exposure to low level chemical mixtures in an outbred population.

To address the need for experimental models that are more relevant to human exposure, some studies have utilised a 'real-life' model of EDC exposure, using sheep exposed to pasture treated with biosolids.[14] Biosolids are produced from anthropogenic wastewater, and thus contain a complex mixture of EDCs (including many of the chemicals mentioned above) to which humans are exposed.

Studies have shown that maternal exposure to pasture treated with biosolids alters adult testis structure, including an increased number of Sertoli cell-only tubules.[14] As well as the testes of exposed sheep having a similar phenotype to testes in humans with TDS, genetic analysis of the testes of animals exposed to biosolids also displayed high similarity with the genes altered in those of human patients with TDS,[15] providing yet more evidence that low-level exposure to EDC mixtures is implicated in TDS.

CONCLUSION

Animal models have been crucial in understanding the effects of EDCs in male reproductive dysfunction. However, studies using animal models of 'real-life' chemical exposure are urgently required, to provide a better understanding of the mechanisms through which everyday exposure to chemicals can have multi-generational effects on the reproductive health of animals and humans, and how these effects may be mitigated.

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REFERENCES

1. Skakkebæk NE 2002 *Hormone Research* **57** Suppl 2 43.
2. Bay K *et al.* 2006 *Best Practice & Research Clinical Endocrinology & Metabolism* **20** 77–90.
3. Edwards TM *et al.* 2006 *International Journal of Andrology* **29** 109–121.
4. Archibong A *et al.* 2008 *International Journal of Environmental Research & Public Health* **5** 32–40.
5. Chung J-Y *et al.* 2011 *Environmental Health Perspectives* **119** 1569–1574.
6. Rahman MS *et al.* 2017 *Environmental Health Perspectives* **125** 238–245.
7. Liu C *et al.* 2013 *Cell Death & Disease* **4** e676.
8. Vaithinathan S *et al.* 2008 *Archives of Toxicology* **82** 833–839.
9. Fiandanese N *et al.* 2016 *Reproductive Toxicology* **65** 123–132.
10. Albert O *et al.* 2018 *Toxicological Sciences* **164** 129–141.
11. Alam MS *et al.* 2014 *Acta Histochemica* **116** 474–480.
12. Oishi S 2001 *Toxicology & Industrial Health* **17** 31–39.
13. Pocar P *et al.* 2012 *Toxicological Sciences* **126** 213–226.
14. Bellingham M *et al.* 2012 *International Journal of Andrology* **35** 317–329.
15. Elcombe CS *et al.* 2022 *Environmental Toxicology & Pharmacology* **9** 103913.

ENVIRONMENTAL EDCs AND HUMAN HEALTH

WRITTEN BY ANDREA C GORE

Endocrine-disrupting chemicals (EDCs) are man-made compounds that can interfere with any aspect of hormone signalling.[1] Humans regularly come into contact with EDCs in daily life, through their presence in household products, plastics, personal care products and pesticides, and through our diet.

Examples of EDCs include bisphenol A (BPA) used in plastics, phthalates in cosmetics and intravenous tubing, industrial and commercial chemicals that contaminate food, and perfluoryl alkyl substances (PFAS) in consumer products. PFAS are particularly noteworthy because they are considered 'forever chemicals', due to their high persistence and ability to accumulate in the body.

Because EDCs can interfere with hormone actions through a variety of mechanisms, including hormone release, transport, signalling, metabolism and degradation,[2] these chemicals have the potential to contribute to, or even cause, diseases and dysfunctions of the endocrine system and its targets, including the brain.

'Pregnant rats exposed to the fungicide vinclozolin had male offspring that developed latent reproductive disease.'

EDCs ARE LINKED TO ADVERSE HEALTH OUTCOMES

Although there is overwhelming evidence and acceptance that environmental factors, such as EDCs, lead to increased disease burden,[3] it is difficult to prove a cause-and-effect link between exposure to a specific chemical and a negative health outcome. Despite this, several lines of evidence give strong confidence that EDC exposures predispose to endocrine and neurological diseases.

1. The prevalence of obesity, diabetes, thyroid disease and neurobehavioral problems, among others, has increased in parallel with the increased manufacture of organic chemicals.
2. Incidents involving known human exposures to specific chemicals, as happened with contaminated cooking oil in Japan and Taiwan, have revealed neurobehavioural and other problems in the children of exposed mothers.
3. Epidemiological studies have consistently linked higher body burdens of EDCs, typically measured in serum, urine, amniotic fluid or umbilical cord blood, to various endocrine and behavioural disorders.
4. Animal models of exposure to a chemical or mixture, and subsequent manifestation of an endocrine problem, can reveal not only causality, but also potential underlying mechanisms. This last body of work, performed mainly in rats and mice, is highly translational to humans, because the biological processes by which hormones act are conserved across all mammals, and indeed all vertebrates.

THE SPECIAL VULNERABILITY OF THE FETUS AND INFANT

The field of environmental health has long recognised the particular sensitivity of developing organisms to environmental contaminants and stressors. This discipline, referred to as the 'developmental origins of health and disease',[4] is foundational to endocrine and neurological health. During these life stages, often referred to as critical periods, the organism is rapidly developing and hormone actions are tightly regulated. Indeed, deviations from appropriate hormone levels can permanently affect a developing organism in a manner that may set a trajectory for a lifetime of function or dysfunction.[5,6]

EDCs CAN EXERT THEIR ACTIONS ACROSS GENERATIONS

Clearly, EDCs have direct effects on an organism. However, this may not end with the individual. In 2005, it was reported that pregnant rats exposed to the fungicide vinclozolin had male offspring that developed latent reproductive disease. Furthermore, their offspring (the grandchildren) and the subsequent generation (great-grandchildren) also had disease phenotypes.[7] Numerous studies since then have demonstrated multigenerational obesity, behavioural and reproductive problems, and other issues.[8,9]

This research has been referred to as transgenerational epigenetics, because the mechanism of heritability is non-genomic (i.e. not due to DNA mutation) but, rather, due to a heritable epigenetic mark such as DNA methylation, histone modifications or non-coding RNAs.[5]

WHAT CAN WE DO TO MINIMISE EXPOSURE TO EDCs?

It may seem hopeless to avoid EDC exposures due to their ubiquity, but it is possible to reduce contact. In the case of personal care products, consumers can consider looking for cleaners and cosmetics that have fewer added chemicals and scents. When using sunscreens to filter out UV rays, choose products with ingredients such as zinc oxide and titanium dioxide, rather than chemical sunscreens.

Most human exposure is through the diet, and there are several behavioural changes that can help. When eating fresh produce, wash thoroughly (tap water is generally fine) to remove pesticide residues. It is always recommended to eat fresh rather than processed food. Processing can add chemicals, even inadvertently, when food is prepared. Moreover, food packaging is a major source of chemicals due to leaching, particularly when heated. Never microwave food in plastic – rather, transfer to a ceramic, glass or similar container.

We should take particular care to minimise purchasing food in non-reusable containers such as plastic beverage bottles. These contribute to the world's burden of plastics,[10] and most are either not recycled at all or are only partly recycled. Using a refillable, non-plastic container avoids contributing to that cycle. Furthermore, filtered tap water is readily available in most places and is an excellent way to improve environmental health.

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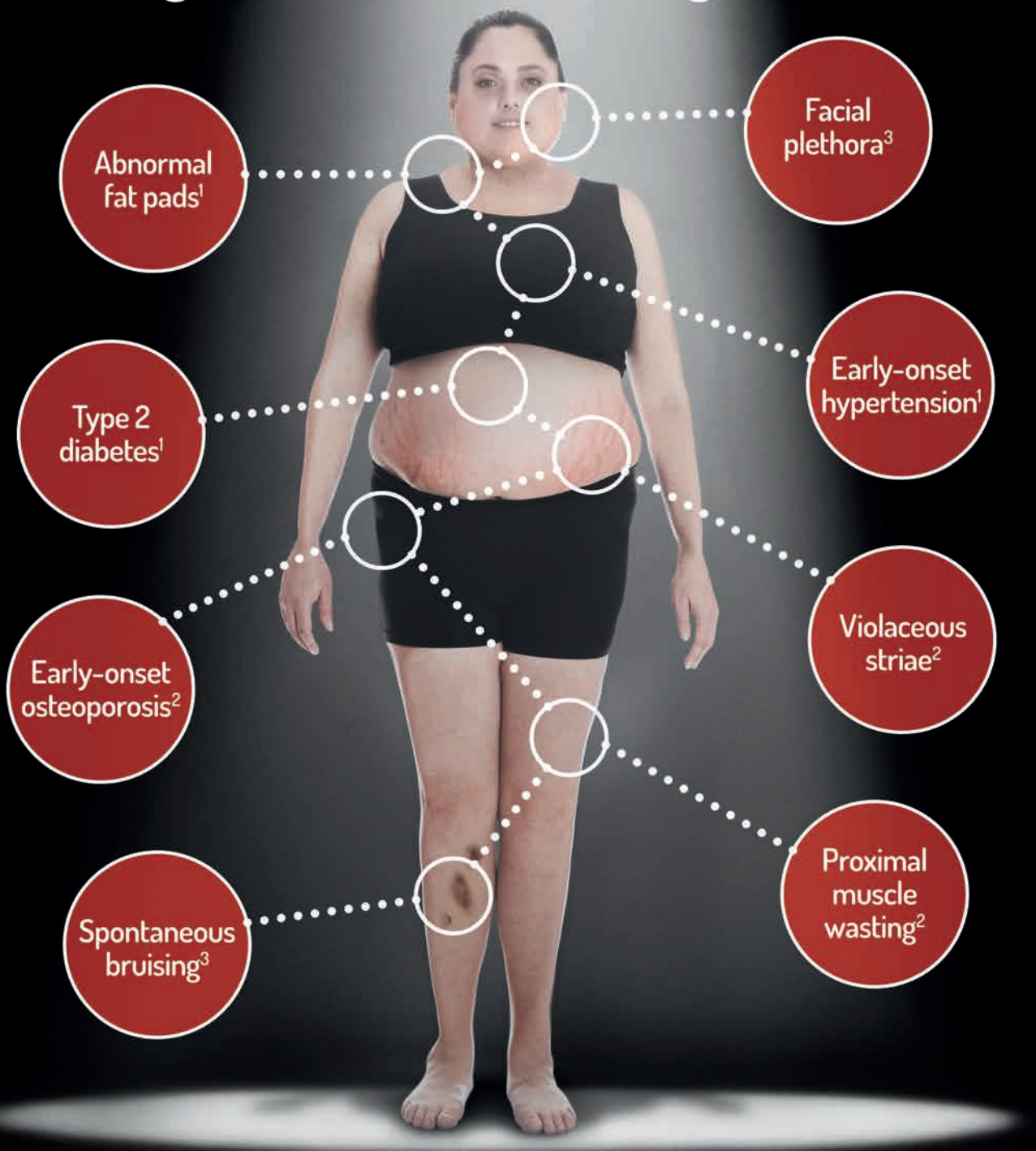
REFERENCES

1. Zoeller RT *et al.* 2012 *Endocrinology* **153** 4097–4110.
2. La Merrill MA *et al.* 2020 *Nature Reviews Endocrinology* **16** 45–57.
3. Gore AC *et al.* 2015 *Endocrine Reviews* **36** E1–E150.
4. Barker DJ *et al.* 2022 *International Journal of Epidemiology* **31** 1235–1239.
5. Streifer M & Gore AC 2021 *Advances in Pharmacology* **92** 73–99.
6. Kay JE *et al.* 2022 *Current Environmental Health Reports* **9** 535–562.
7. Anway MD *et al.* 2005 *Science* **308** 1466–1469.
8. Robaire B *et al.* 2021 *Environmental Research* **204** 112063.
9. Walker DM & Gore AC 2011 *Nature Reviews Endocrinology* **7** 197–207.
10. Landrigan PJ *et al.* 2023 *Annals of Global Health* **89** 23.

Although the condition might be rare...



...the features are common

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

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

HRA Pharma
Rare Diseases

Connect the dots

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

UK/NPR/0007 Date of preparation: April 2022

AN INTERVIEW WITH... ROELOF HUT

Winter moth (*Operophtera brumata*). ©Shutterstock

Roelof Hut is Professor of Chronobiology at the University of Groningen, The Netherlands. He was one of the speakers at the 'Cutting edge: endocrinology in a warming dirty world' symposium at the Society for Endocrinology BES conference 2022, where he described the impact of global warming on animal thermoregulation and reproductive cycles. Louise Hunter, from *The Endocrinologist*'s Editorial Board, sat down with Professor Hut to learn more about his work.

Louise: What have the challenges been in studying global warming's impact on animal physiology?

Roelof: To date, studying global warming has mostly been the domain of ecologists and conservationists. There hasn't been sufficient interest from the physiology community, in my view. To assess the impact of climate change on animal health and behaviour, we need long term time series data: not only ecological data, but also molecular and physiological data (e.g. DNA sampling). If molecular biologists and endocrinologists are involved in studies from the start, those data can be collected. We can also combine data from these long term collections with laboratory studies, to see if results in the lab corroborate or explain what we see in the field.

L: Working with ecologists, you've been able to obtain fascinating insights into the impacts of climate change, particularly on animal reproductive cycles. Can you give some examples?

R: Sure. With climate change, there is a mismatch between seasonal patterns in photoperiod (day length) and temperature. Between species, reproductive cycles are differentially responsive to changes in photoperiod and temperature. With global warming, we see that moth eggs hatch earlier in the year.[1] This places selection pressure on predators of moth caterpillars to also lay their eggs earlier in the year. We have shown that in the great tit (*Parus major*), gonadal development, but not egg laying, is sensitive to photoperiod.[2] For egg laying to occur subsequently, another cue (e.g. temperature) is needed. If the great tit cannot adapt to synchronise its reproductive cycles with that of moth caterpillar availability – with increasing sensitivity to temperature, for example – its populations will dwindle.

To give you an example of our work in mammals: voles are a great species to study, as we have a very good understanding of their population cycles from historical trapping records. In the common vole (*Microtus arvalis*), our census data tell us that reproduction occurs earlier in cold springs (and vice versa). In the lab, we've shown that photoperiod and temperature interact to regulate reproductive organ development, with temperature being the dominant cue in the spring (we see larger reproductive organs under cold, rather than warm, conditions).[3] Now that climate change is causing springs to become warmer, you can imagine how later reproduction, and therefore a shortened breeding season, would affect vole numbers. It's possible that this may be one of the factors contributing to the collapse in vole populations that has been seen in Europe. And we don't yet know how this is affecting the populations of higher predator species.

L: How might your findings be used to protect species from the effects of global warming?

R: We have studied the winter moth (*Operophtera brumata*) in the field and in the lab. As I've stated, we know that global warming is causing moth eggs to hatch earlier. In the laboratory, we've looked at gene expression in winter moth embryos, to find out which temperature-responsive genes have an impact on embryo development.[1] Natural variation in these genes might put some winter moth populations at particular risk from climate change (e.g. those showing homozygosity at a particular allele). If we can identify these populations, we can take steps to protect them, by introducing more genetic variation, for example.

L: Do you think your findings have relevance to human biology?

R: Human beings are unusual in that we don't show seasonality in our reproductive cycles. So we can't necessarily extrapolate our findings to humans. But what I can say is that we have seen that nature has some capacity to adapt to global warming, given that genetic diversity is sufficient. Human have inhabited coastal zones in high population numbers, but they also rely on food production with very limited genetic diversity; with that we have placed ourselves in the danger zone!

REFERENCES

1. Van Dis NE *et al.* 2022 *Molecular Ecology* **31** 5795–5812.
2. Salis L *et al.* 2019 *Journal of Avian Biology* doi:10.1111/jav.02197.
3. Van Rosmalen L *et al.* 2022 *Molecular Ecology* **31** 3360–3373.

IMPROVED DIET AND EXERCISE IN PREGNANCY PROTECTS BABY'S HEART DEVELOPMENT

WRITTEN BY PAUL D TAYLOR, SAMUEL J BURDEN, KATHRYN DALRYMPLE AND PABLO LAMATA

Maternal obesity is known to increase the risk of congenital abnormalities and alter growth of the offspring.[1] However, little is known about the impact of maternal obesity on baby's cardiac development in the womb. Controversy remains over the relative roles of adverse nutritional exposures during pregnancy, inherited genes from mum, and a shared postnatal environment of similar diet and lifestyle habits, in explaining relationships between maternal obesity and risk of later heart complications in the child.[2]

However, our recent analysis of cardiac imaging techniques suggests that maternal obesity causes remodelling of baby's heart and decreases heart chamber size,[3] implicating a direct effect of maternal obesity on fetal cardiovascular development during pregnancy. An observation consistent with our extensive preclinical studies in rodent models of obesity in pregnancy.[4] This overview will discuss recent findings supporting the *in utero* developmental programming of the fetal heart in pregnancies complicated by obesity.

Well-conducted randomised control trials in the antenatal period provide the opportunity to discriminate between pregnancy and postnatal influences on heart health in children born to women with obesity. The UK Pregnancy Better Eating and Activity Trial (UPBEAT)[5] was a study of 1,555 pregnant women with obesity (body mass index (BMI)>30kg/m^2; mean BMI 36.3 kg/m^2, SD 4.8) who were randomised in early pregnancy to either a 'lifestyle' intervention (involving professional dietary advice and planned physical activity during pregnancy) or standard antenatal care. Remarkably, in neonates born to women with obesity, resting heart rate (when asleep) was approximately 10bpm higher than in infants born to mothers of a healthy BMI <25kg/m^2).[3] Heart rate variability (HRV) of the normal beat-to-beat interval, a measure of central nervous system function, was significantly lower in infants born to obese versus healthy weight mothers, suggesting increased sympathetic activity (fight or flight response) as a potential underlying cause.[3] At six months, resting heart rate was markedly lower in infants of mothers randomised to the intervention, after controlling for other maternal influences such as parity, ethnicity, smoking status, maternal age, years spent in full time education, and infant birthweight.[6] This provided the first indication that the UPBEAT lifestyle intervention in obese pregnancy may be protective of longer-term heart health in infants born to obese pregnant women.

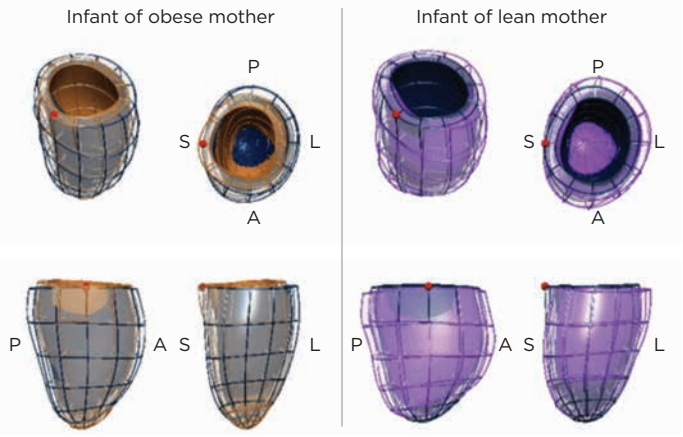


Figure. The remodelling pattern in the left ventricle (LV) of the newborn associated to maternal obesity. The figure illustrates two panels, the two extremes of the anatomical change (orange and velvet) overlaid to the average anatomy (dark blue), with four complementary views in each panel (red sphere indicates the location of the RV; A, anterior; P, posterior; S, septal; L, lateral). These patterns were found as the mode 4 of the statistical shape model built from 3D meshes personalised to the segmentations of the short axis stack (SAX) at end diastole. The pattern displays an elongated LV and reduced sphericity (specially in the antero-posterior direction) in infants born to mothers with BMI ≥ 30kg/m^2.

Evidence for persistent effects of maternal obesity on infant cardiac structure and function is provided by a recent echocardiography imaging study of the hearts of three-year-olds from UPBEAT.[7] Compared to children of women with a normal weight, children born to women with obesity in the standard care arm demonstrated thickening of the walls of the heart, specifically the left ventricular septal wall, after controlling for potential confounders. Evidence of specific remodelling around the left ventricle of the heart included higher left ventricular mass indexed to the child's size and an increase in the ratio of left ventricular mass to ventricular end-diastolic volume, a marker of cardiac remodelling that is well established in hypertension and obesity. There was also evidence of contractile dysfunction with lower ejection fraction and indications of impaired left ventricular relaxation. By contrast, those children whose mothers were in the intervention arm of the study did not show evidence of cardiac remodelling; rather there was a significant reduction in heart wall thickness and heart mass compared to children of women in the standard care arm.

Children in the UPBEAT standard care arm, at three years of age, continued to show elevated resting heart rate compared to children of mothers with a normal BMI, even after adjustment for confounders. HRV analysis revealed a decrease in variability (more variability is typically healthier), and an increased 'fight or flight' response relative to the group with normal weight. The UPBEAT intervention tended to improve all parameters of autonomic nervous system function but were not statistically significant, suggesting that a larger sample size may be needed to see the effect of the intervention on the autonomic nervous system.[7]

Most recently, to further investigate the impact of maternal obesity on fetal heart development, we employed novel heart atlasing techniques[8] and 3D computer modelling to evaluate 'cardiac shape' by magnetic resonance imaging (MRI).[9] Newborn babies underwent imaging in the first 48 hours of life using a 'feed and wrap' technique to encourage babies to sleep during the 30-minute scan. Infants born to mothers with obesity had a markedly different heart shape at end-diastole with significantly reduced 'sphericity' (left ventricular volume/length) compared to infants born to lean women (see Figure). Reduced sphericity of the heart, or cardiac remodelling, is commonly seen in various adult cardiovascular diseases, including hypertension, and can result in reduced contractility of heart and reduced cardiac output. It is important to note that this may not be pathophysiological at a young age and so further longitudinal studies will be needed to determine risk. However, a decreased sphericity might predispose the infant left ventricle to increased wall stress, which could

activate pathways linked with left ventricular hypertrophy (thickening of the myocardium), as evident in our three-year-old data. If sustained, this could lead to the deterioration of cardiac function.

In conclusion, maternal obesity may adversely impact the fetal autonomic nervous system and heart development that is apparent up to three years of age. The extent to which increased fetal/neonatal heart rate, secondary to maternal obesity, impacts on neonatal cardiac development and function remains to be established. We can hypothesise that these sub-clinical changes in a child's heart structure and function may amplify over time, as evidenced by overt clinical disease in young people born to women with obesity,[2] and the increased cardiovascular mortality and morbidity observed in adults born to obese women in the Scottish cohort study.[10] The UPBEAT complex antenatal lifestyle intervention in obese pregnancy appears to protect against elevated infant heart rate, limits changes in cardiac structure and function in childhood, and infers the *in utero* origins of cardiac remodelling in obese pregnancy.

REFERENCES

1. Mitanchez D & Chavatte-Palmer P 2018 *Acta Paediatrica* **107** 1156–1165.
2. Razaz N *et al.* 2020 *The Lancet Diabetes & Endocrinology* **8** 572–581.
3. Groves AM *et al.* 2021 *Archives of Diseases in Childhood. Fetal and Neonatal Edition* **107** 481–487.
4. Taylor PD *et al.* 2014 *Acta Physiologica* **210** 508–523.
5. Briley AL *et al.* 2014 *BioMed Central Pregnancy and Childbirth* **14** 74.
6. Dalrymple KV *et al.* 2020 *Pediatric Obesity* **16** e12725.
7. Taylor PD *et al.* 2022 *International Journal of Obesity* **46** 2145–2155.
8. Marciniak M *et al.* 2022 *European Heart Journal – Cardiovascular Imaging* **23** 1645–1653.
9. Cox DJ *et al.* 2019 *Pediatric Research* **85** 807–815.
10. Reynolds RM *et al.* 2013 *The British Medical Journal* **347** f4539.

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DO BUILT ENVIRONMENTS SHAPE OUR HEALTH?

WRITTEN BY LOUISE FOLEY, CORNELIA GUELL, JENNA PANTER & DAVID OGILVIE

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Physical inactivity is a major contributor to morbidity and mortality around the globe, not only through an increased risk of diabetes, but also through heart disease, stroke, cancer, dementia, depression and arthritis. Inactivity is estimated to account for 9% of premature deaths worldwide.[1]

This knowledge, however, does not seem to have been translated into effective action. More than a third of adults in the UK report not doing the minimum amount of physical activity recommended for health by the Chief Medical Officers, despite a range of campaigns aimed at educating or cajoling the public into getting active. Evidence suggests these individually targeted approaches often produce modest and short-lived improvements at best – an underwhelming result given the magnitude of the challenge.

Most of the world's population now live in cities, with the global urban population expected to grow by nearly 2% per year until 2020. There is good evidence that the urban form influences physical activity or inactivity: in particular, whether people use active or motorised forms of transport. This suggests that changing the built environment could produce broader, more sustained effects on physical activity across the population than individually targeted approaches. Research suggests that changes such as introducing traffic calming or road user charging, or building dedicated walking and cycling routes, can increase levels of walking and

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cycling for transport, and thus physical activity. However, strong evidence to guide practice has been slow to emerge.[2]

SEEKING REAL WORLD ANSWERS

The lack of evidence reflects the difficulty of conducting research in this emerging field at the intersection of transport and health, which draws scientists out of the sterile confines of the laboratory into the messy world of real lives and political agendas. Robust science to understand the effect of changes in the built environment on changes in behaviour and health depends on using creative methodological approaches to extend the repertoire beyond the stalwart of clinical research, the randomised controlled trial (RCT).

'…changes such as introducing traffic calming or road user charging, or building dedicated walking and cycling routes, can increase levels of walking and cycling for transport, and thus physical activity.'

RCTs entail randomised controlled comparisons over time, and are generally agreed to be the best way to identify whether a treatment causes an effect. However, real world 'treatments' which have the potential to affect health, but which are not amenable to randomisation, happen all the time. Examples include banning smoking in public places, alcohol taxation or congestion charging. The effects of these 'treatments' can and should be investigated, not least because the underpinning policy should be guided by evidence. Recent Medical Research Council (MRC) guidance calls for the use of natural experimental studies, typically involving non-randomised controlled comparisons over time, to generate stronger evidence of the effects of environmental and policy changes.[3]

RESEARCH IN PRACTICE

As part of the Centre for Diet and Activity Research at the MRC Epidemiology Unit in Cambridge, our Physical Activity and Public Health research programme has used the natural experimental approach to evaluate the effects of new transport infrastructure on active travel and physical activity. This has included the assessment of a new 'guided busway' in Cambridge, comprising a new bus network, park and ride sites and a traffic-free path for pedestrians and cyclists, as well as new dedicated cycling and walking routes in other UK cities, and a new urban motorway built through a residential area of Glasgow.

The first two studies have shown that building new walking or cycling infrastructure facilitates these behaviours in those living nearby.[4,5] In the busway study, the effects of the new provision were particularly pronounced amongst those who were previously the least active – the group with the most potential health gain from taking up more activity. Findings from the motorway study, which investigates effects on travel, physical activity and well-being, are expected to be released later in 2016.

ADDRESSING LIMITATIONS

A key limitation of natural experimental studies is that the lack of randomisation increases the possibility that comparison groups differ in ways that affect their response to treatment, which might bias estimates of the treatment effect. Therefore, all three studies were carefully designed to ensure that comparison groups were as similar as possible apart from their exposure to the intervention, to minimise this inherent risk of bias.

This entailed comparing people who lived nearer to or farther from the new infrastructure, and accounting for differences in individual, geographical or household characteristics. Additionally, in the motorway study, three geographical areas were carefully delineated around the new motorway, an existing motorway built decades earlier, and an area with no motorway, to provide additional comparisons.

Over time, these studies – conducted in a range of contexts, including people from various socio-economic backgrounds, and examining different types of transport infrastructure – will allow us to draw more generalisable conclusions about the likely health effects of changing particular aspects of the urban environment. This body of work is already informing transport and urban planning policy, ultimately aiming to help transform our cities into places that support physical activity and health for all.

2023: AN UPDATE FROM THE URBAN MOTORWAY STUDY

A new 5-mile section of the M74 motorway was opened in Glasgow in 2011. We conducted a natural experimental study to find out more about road traffic accidents, activity patterns and well-being in the local area, and to explore if and how these changed as a result of the motorway. We used a combination of repeat surveys with local residents conducted in 2005 and 2013, qualitative research with residents and key informants, and complementary analyses of police road traffic accident data and government travel surveys.

On balance, the new motorway appeared to have promoted car use, and we found no evidence that it had reduced road traffic casualties. Although it did help to connect some local residents with amenities and people in other places, those living nearer to the motorway tended to experience poorer mental well-being over time than those living further away.

Although the effects of the new motorway might have been different if it had been built somewhere else, our findings highlight how some of the benefits claimed for this type of investment may either not be achieved or be achieved for some at the expense of others. This should be taken into account in future transport planning.

LOUISE FOLEY, CORNELIA GUELL, JENNA PANTER & DAVID OGILVIE
Centre for Diet and Activity Research, MRC Epidemiology Unit, Cambridge

The Centre for Diet and Activity Research, which is a partnership between the University of Cambridge, the University of East Anglia and the MRC, is one of five Centres of Excellence in Public Health Research funded through the UK Clinical Research Collaboration (UKCRC). The Physical Activity and Public Health research programme is a core programme at the MRC Epidemiology Unit.

REFERENCES

1. Lee IM *et al.* 2012 *Lancet* **380** 219–229.
2. NICE 2008 *Physical Activity and the Environment: Guidance on the Promotion and Creation of Physical Environments that Support Increased Levels of Physical Activity*. London: NICE.
3. Craig P *et al.* 2012 *Journal of Epidemiology & Community Health* **66** 1182–1186.
4. Panter J *et al.* 2016 *American Journal of Preventive Medicine* **50** e45–e53.
5. Goodman A *et al.* 2014 *American Journal of Public Health* **104** e38–e46.

BIOLOGICAL DYSFUNCTION IN A FOG OF SYNTHETIC CHEMICALS

WRITTEN BY STUART MILLIGAN

'Endocrine-disrupting chemicals (EDCs) represent not just a threat to public health or indeed to global health, but to planetary health. Pervasive in our environment – in foods, packaging materials, cosmetics, drinking water, and consumer products – EDCs have been linked to a myriad of non-communicable diseases such as obesity, type 2 diabetes, thyroid disorders, neurodevelopmental disease, hormone-dependent cancers, and reproductive disorders.'

These are the opening words of the executive summary of a series on EDCs in *The Lancet: Diabetes & Endocrinology*.[1] How have we got into such a dire position? In retrospect, it is easy to see the answer.

Biological systems have evolved over at least the last 3 billion years. The survival of even the simplest life forms depended on their ability to regulate their internal environments and to respond to changes in the external world. As multicellular organisms evolved, the development of vascular systems allowed endocrine signals to co-ordinate functions within each organism. The Cambrian explosion of life forms (~540 million years ago) was accompanied by the rapid evolution of nuclear receptor signalling, controlling the critical processes of development, metabolism, homeostasis and reproduction. Many of the ligands for nuclear receptors were derived from natural metabolites (fatty acids, terpenoids, porphyrins and amino acids) and some became endocrine signals (e.g. steroid and thyroid hormones).

A CENTURY OF CHEMICAL DEVELOPMENT

There is a striking contrast between the long timescale over which biological signalling systems have evolved and their very recent exposure to man-made chemicals. Scientific advances and technical innovations in the last 100 years or so have allowed the development of thousands (~50,000++) of extraordinarily useful, but entirely novel, organic chemicals for industrial and agricultural uses.

These chemicals and their breakdown products are ultimately released into the environment. Some are very stable and environmentally persistent, while others are much more transient but produced in very large amounts. Some deliberately target biological systems (e.g. pharmaceuticals, pesticides, fungicides, herbicides, anti-microbials), while the structure and hydrophobic/amphiphilic properties of many others (e.g. plasticisers, pigments, flame retardants, surfactants, heat stabilisers, anti-oxidants, UV and light stabilisers, impact modifiers, foaming agents, fillers, lubricants, non-stick compounds etc.) enable them to interact with various degrees of affinity and specificity to a wide range of biological molecules, including a range of components of signalling systems (e.g. nuclear receptors, enzymes, binding proteins etc.).

'There is a striking contrast between the long timescale over which biological signalling systems have evolved and their very recent exposure to man-made chemicals.'

Many of the compounds are very stable and lipophilic (properties upon which their usefulness is often based) and they bioaccumulate and biomagnify up food chains.

IMPACT ON BIOLOGICAL SYSTEMS

Within the body, the chemicals are like a sticky and occasionally toxic mist, at times obscuring and compromising the finely tuned operation of cellular systems. Endocrine and other signalling systems are particularly vulnerable. Their exquisite sensitivity, dynamic nature and inbuilt amplification cascades mean that even small initial perturbations by environmental chemicals can produce large effects.

Immediate responses may be inhibitory, stimulatory, antagonistic or additive, or any combination of these. The non-specific nature of the perturbations means that, whatever the response, it is likely to be detrimental or – at the very least – non-adaptive. Of particular concern is that exposures in early life can produce small perturbations of developmental pathways that result in large, irreversible effects in later life. Epigenetic changes can be responsible for effects in germ cells that pass through subsequent generations. Depending on the specific chemical(s) and the amounts, duration and timing of exposures, the overall impacts of environmental chemical exposures on individual fitness and survival may range from negligible to lethal, but are usually completely unknown.

'Within the body, the chemicals are like a sticky and occasionally toxic mist, at times obscuring and compromising the finely tuned operation of cellular systems.'

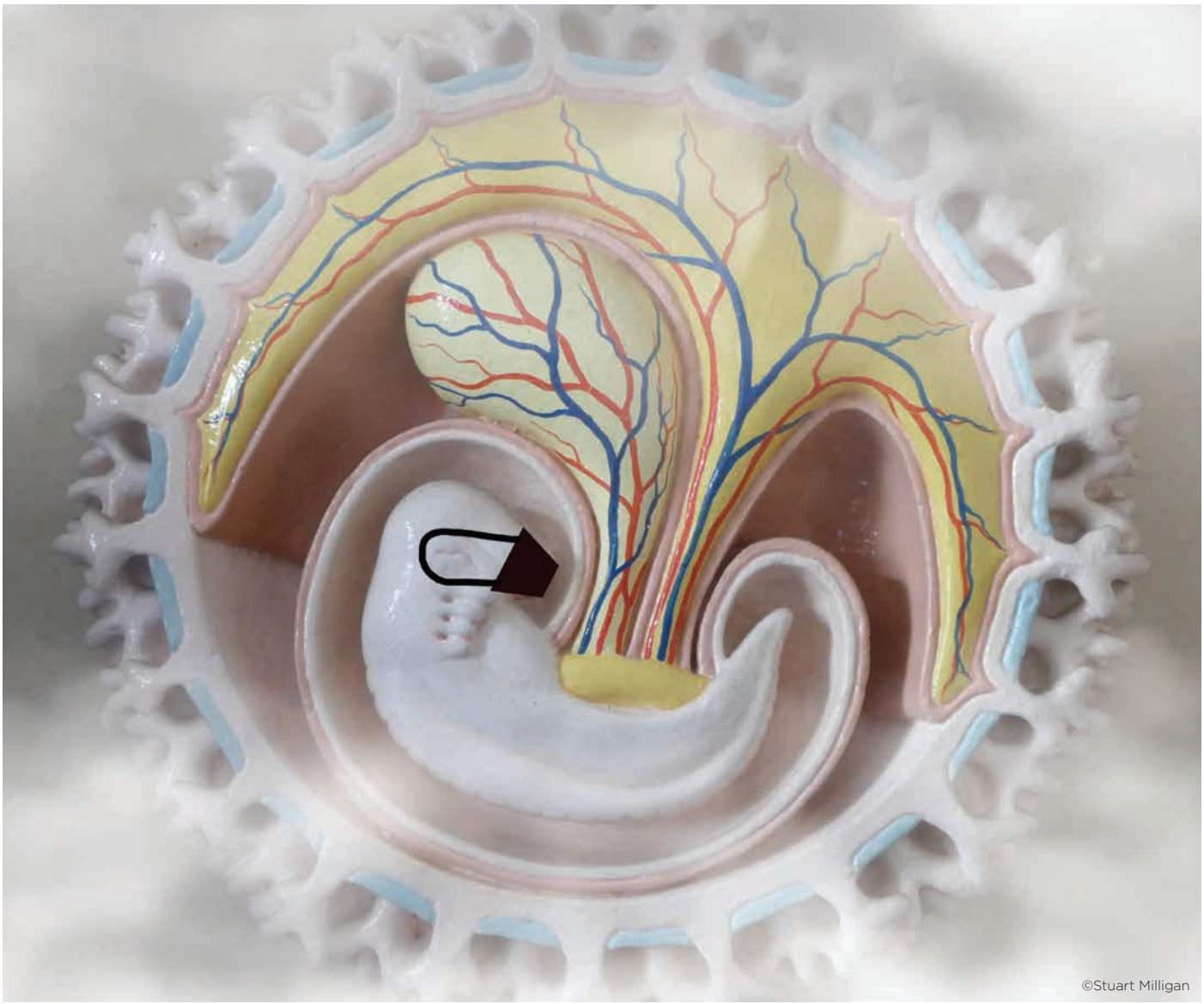
INITIAL EVIDENT EFFECTS

The issue of environmental chemicals came to prominence due to a variety of obvious reproductive disturbances in species as diverse as oysters, fish and alligators. The release of 'oestrogenic' and other compounds from plastics highlighted potential routes of general exposure. Reproductive effects in humans (especially testicular dysgenesis syndrome: low sperm counts, hypospadias, cryptorchidism, testicular cancer) provided a useful focus for both scientists and the press.

As studies expanded, it became clear that the chemical disruption was much wider. In humans, a wide range of adult health issues (ranging, for example, from obesity and metabolic disorders through cancers, neurodevelopmental and reproductive disorders) have been linked with early life exposure to a range of exogenous chemicals (e.g. bisphenol A, phthalates, polybrominated fire retardants, perfluoroalkyl substances, organophosphate pesticides).

THE COMPLEXITY OF MIXED EXPOSURE

Experimental studies of individual chemicals have helped to identify the chemicals of particular concern to humans and to set some regulatory limits. But real-life exposures are to variable mixtures of chemicals simultaneously, in varying amounts and combinations, for variable durations and at different times in the life cycle.



The importance of assessing real-life risks is illustrated by the report by Caporale *et al.*,[2] based on a prospective population-based study linking adverse health outcomes with prenatal EDC exposure. Human-relevant concentrations of a mixture of bisphenol A, phthalates and per- and polyfluoroalkyl substances were then shown to disrupt a variety of biological pathways in human fetal primary neural stem cells and cortical brain organoids *in vitro*, as well as in two model organisms (*Xenopus* and zebrafish) *in vivo*.

LOOKING TO THE FUTURE

The uses of synthetic organic chemicals have undergone exponential increases accompanying the growth of the human population and its economic and technological development. The immense practical benefit of many of the chemicals inevitably means their production and use will continue. But EDCs are an integral part of the increasing pressures on all life forms on this planet.[3] Much greater thought needs to be given by industry, end-users and politicians to regulated disposal routes, to limit the entry of such chemicals into the general abiotic and biotic environments.

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REFERENCES

1. Endocrine-disrupting chemicals series 2020 *Lancet Diabetes & Endocrinology* www.thelancet.com/series/endocrine-disrupting-chemicals.
2. Caporale N *et al.* 2022 *Science* **375** eabe8244.
3. Wagner DL *et al.* 2021 *Proceedings of the National Academy of Sciences of the USA* **118** e2023989118.

AN INTERVIEW WITH... JOHN NEWELL-PRICE

THE ENDOCRINE SOCIETY'S NEW PRESIDENT-ELECT

John Newell-Price is Professor of Endocrinology at the University of Sheffield, and is an Honorary Consultant Endocrinologist and Head of Endocrinology at Sheffield Teaching Hospitals NHS Foundation Trust.

The Endocrine Society has named John as its 2024–2025 President – the first non-US-based President ever to be elected in the 106 years of the Society. He will take up his role as President-Elect at ENDO 2023. He tells us about his career, his aims as President, and his advice for aspiring endocrinologists.

What first attracted you to work in endocrinology?
Even as a medical student, I was fascinated by endocrinology, the interplay between hormones and the effect on human physiology – it all just made sense. Perhaps someone was also trying to tell me something, as the long case in my medical finals was a patient who had had Cushing's disease and Nelson's syndrome; in MRCP Part II it was a patient with a metastatic insulinoma; and my first case report as a Senior House Officer (SHO) was a patient with ectopic gastrin secretion from an ovarian carcinoma causing Zollinger–Ellison syndrome!

Please tell us about your career path to date
I spent my undergraduate years at Cambridge with clinical years at the London Hospital. After house jobs, I could not secure an SHO rotation and took a stand-alone six-month job at St Mark's Hospital. While there, I presented the case report above, that I'd seen at St Mark's, at the Barts Grand Round – and had what I can only describe as a thorough grilling from Mike Besser! The discussion was phenomenal and, afterwards, I deliberately targeted an SHO rotation that included Barts endocrinology for six months. I then spent an incredible seven heady years at Barts, working for and being trained by titans of clinical endocrinology to whom I remain deeply indebted: Mike Besser, John Wass, Ashley Grossman and John Monson. For three of those years, as an MRC Training Fellow for my PhD, I was in Adrian Clark's phenomenal molecular biology lab. It was very hard work, but I learnt so much, and the friends and colleagues I trained with then are now some of the leaders in UK endocrinology.

As well as the exceptional training, I presented data at numerous national and international meetings, taught many medical students and loved it all! In 1999, I had another two years left of a lecturer's contract when Tony Weetman and Richard Ross contacted me about whether I would be interested in moving to Sheffield. It was a risk, and as a family we had no ties to this part of the country, but we took a punt. I have now spent 23 fantastic years here in Sheffield working with Tony, Richard and others, and I am sure that you would not be interviewing me today had I not moved.

Over that time, with fabulous and talented colleagues, I have aimed to build the endocrine service and research in Sheffield into the truly exceptional centre that it is currently, and worked at national and international levels in various bodies, where I felt that could make a difference. The Society for Endocrinology has been a wonderful national 'home', where I feel that I have been able to make useful contributions, with the Endocrine Society being my 'international home'.

How did you first get involved with the Endocrine Society?
I attended my first ENDO meeting in Washington in 1995. I was completely blown away by the sheer range and scale of the meeting. There were many thousands of people, the clinical and science presentations and 'Meet the Professor' sessions were incredible and inspiring. The huge poster hall was a buzz of discussions – I had never experienced anything like it. I was presenting an oral communication on a study we had been doing on the use of desmopressin in the diagnosis of adrenocorticotrophin-dependent Cushing's syndrome. It was pretty nerve-racking, especially as, at that time, it was uncommon for a non-US person to present data, and I was just a junior fellow and representing Barts. However, I had lots of support and interest, and it just fuelled a desire to pursue an academic career in endocrinology. Later on, I was asked to be involved in the Endocrine Society's Clinical Practice Guidelines for Cushing's syndrome that came out in 2008 and 2015, and also to be on the Annual Meeting Steering Committee for three years, where I became lead for pituitary and adrenal themes. Lynette Neiman then asked me to be the overall Chair of the ENDO meeting in Chicago in 2018 when she was President, which was a huge piece of work, but an amazing and rewarding experience. I have had many other roles for the Endocrine Society, including on the Governance Task Force and the Clinical Practice Guidelines Committee. Most recently, I have been on the Board of Directors for the last three years. It has been and is a privilege to work with the many super-smart friends, colleagues and staff.

What are you most looking forward to achieving as President?
Doing as much as I can to deliver on the mission of the Endocrine Society. I aim to foster ever-closer working relationships with sister endocrine societies globally, champion those in the early stages of their careers – the Society has phenomenal programmes available to members, tackle pipeline issues for endocrinology, ensure basic scientists are valued within the Society, and ensure the patient voice is heard.

What are the biggest challenges facing endocrinology?
For clinical endocrinology, there is the global issue of recruitment into the specialty that transcends national boundaries. There are many different potential drivers, and these vary by country, but we need to better understand the common themes and work together to find solutions. For basic scientists and clinical researchers, funding remains a significant issue, and lobbying is needed at the highest levels to represent endocrine research priorities.

What do you most enjoy about your work?
Working in teams to solve problems, be they at a clinical or research level, or at a structural level, for example in the University and in healthcare delivery or medical and postgraduate education.

What are your words of wisdom for aspiring endocrinologists?
Be curious and have great attention to detail, listen and learn from your patients and put them at the centre of what you do, and work with patient support groups. Treat your training as an apprenticeship, and seek out the great units and people to work with, and be prepared to move cities and take risks. Look beyond local and national boundaries and join and contribute to societies such as the Endocrine Society, go to the annual ENDO meetings, and enjoy learning from and interacting with the global endocrine community.

Society for Endocrinology

SfE BES GLASGOW 2023

Join us in GLASGOW

for the UK's leading endocrine conference

13–15 November 2023

After last year's success, we can't wait to reconnect at the UK home of endocrinology, where you will be able to learn, network and discuss your work.

The Programme Committee has once again developed an exciting and inspiring itinerary, featuring the latest world-class science, best clinical practice and innovations from our field.

To view the full programme and find out how you can register today, visit: **www.endocrinology.org/sfebes-2023**.

Why not submit your abstract to SfE BES 2023?

Sharing your research at the conference is a fantastic opportunity to get useful feedback and ideas to progress your work, as well as boosting your professional profile with networking opportunities.

The submission deadline is **Monday 26 June 2023 (11.59pm BST)**.

GET THE LATEST INFORMATION...

#SFEBES2023

Make a difference:
JOIN THE SOCIETY'S GOVERNANCE TEAM

Are you passionate about championing endocrinology? Do you want to help shape the future of your Society? Then why not apply for one of our 2023 governance vacancies?

We need many voices to be represented in the Society's leadership, so we can adapt to support endocrinology into the future. We're on the lookout for members from all career levels, backgrounds, locations and specialties, who can bring fresh perspectives to our Council of Management, and Committees to maximise the impact of our Society.

WHY JOIN THE SOCIETY'S GOVERNANCE?

By taking on one of these roles, you will make a difference. You will help to support the next generation of endocrinologists, improve patient care and support people in making better decisions about their health. In doing so, you will expand your professional network and have the opportunity to use your skills in new ways.

COUNCIL VACANCIES

- 3 Elected Council Members
- General Secretary Elect
- Programme Secretary Elect

COMMITTEE VACANCIES

A variety of vacancies are available on the following Committees:

- Clinical Committee
- Corporate Liaison Committee
- Early Career Committee
- Nurse Committee
- Programme Committee
- Public Engagement Committee
- Science Committee

There are also opportunities to become an Endocrine Network Convenor, and to sit on the Leadership and Development Awards Selection Panel.

TESTIMONIALS

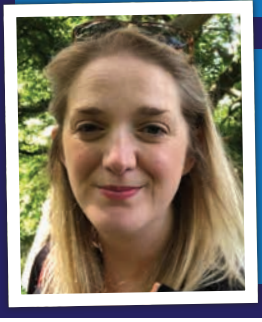
Don't take our word for it, hear how joining the governance team made a difference to some of our members...

"I have learnt much from others, both junior and senior, and have enjoyed the exchange of ideas. I have been able to shape events and strategies using my expertise. I have fine-tuned my non-clinical skills and have brought many ideas back to my local hospital trust, directly benefiting my patients and colleagues.'

STEPHANIE BALDEWEG Clinical Committee

"Working on Society activities will repay you in many more ways than you can possibly imagine, so get involved. Citizenship roles in the Society feel really rewarding, and will help you past bumps in your career where maybe your day-to-day work is not quite what you desire!'

RUTH ANDREW General Secretary



"One of the major benefits has been the networking opportunities. This has been particularly valuable at this early stage of my independent career, establishing collaborations and having people to support and review grant applications.'

KIM JONAS Programme Committee

LEARN MORE AND APPLY

Find out more about our current vacancies and how to apply at **www.endocrinology.org/about-us/governance/apply-for-a-role-within-your-society**.

A strategy to ensure that ENDOCRINOLOGY AND YOUR SOCIETY THRIVE

Like any organisation, it's really valuable for the Society to reflect occasionally on its priorities for the next few years. Our Society exists to bring together and support the UK endocrinology community and to ensure that our discipline remains vibrant.

We need a strategy to inform us how best to achieve that.

WHY IS STRATEGY IMPORTANT?

Having clear strategic goals helps us to make our vision a reality. Taking into account the current environment outside the Society and the present challenges experienced by our community is really important.

A good strategy does not have to be complicated. It should be a straightforward and effective framework that allows an organisation to decide which activities to concentrate on in a given timeframe.

Our strategy should be a helpful tool that is regularly reviewed and ensures that every element of the Society is working towards the same aims, so that our resources can be deployed most effectively.

WHY NOW?

It is a really good time for the Society for Endocrinology to be setting a new strategy for two principal reasons:

1. We are emerging from a global pandemic, which has changed the way organisations and individuals work, meaning our members are facing different challenges with different expectations from the Society.
2. There are challenges facing the Society's trading subsidiary, Bioscientifica, which mean the Society's main revenue stream will be reduced over the next few years.

Financial stability, operational efficiency and robust governance...

… underpin the success of the Society, whatever its strategic priorities. With these in mind we know we must:

- diversify and develop our revenue streams
- improve our membership system and processes
- continue to implement recommendations from our governance review 2020/21.

WHO SETS THE STRATEGY?

The Trustee–Directors of the Society, who sit on Council, are collectively responsible for setting and monitoring Society strategy, with support and advice from the office team, led by the Chief Executive.

An in-person strategy day for Council took place in Birmingham on 1 February 2023. The Society used two independent facilitators to advise on and run the event. The day included the Trustee–Directors and the Chairs of all of our committees, who are non-voting, ex-officio members of Council.

Following the strategy day, Council has further debated and refined the strategic goals and objectives to produce a draft strategy for member consultation. You can read this opposite.

THANK YOU FOR YOUR VIEWS!

We have asked for constructive feedback on this strategy from all our members across the breadth of our specialty. If you haven't yet been able to respond, please email your comments and suggestions as soon as you can, and no later than **29 June**, to **members@endocrinology.org**.

MÁRTA KORBONITS, President
IAN RUSSELL, Chief Executive

Our draft strategy 2024–2027

Our vision: A world where the importance of endocrinology is recognised, and the understanding of hormones and their actions is improved and applied, so that people live longer, healthier and happier lives.

Our mission: To promote and advance the understanding of endocrinology, bringing together the UK endocrine community to share ideas and advance our discipline.

GOAL 1: FOSTER A COLLABORATIVE, INCLUSIVE AND FRIENDLY ENDOCRINOLOGY COMMUNITY

…providing a welcoming home for the endocrine community to increase skills, develop ideas and share best practice, as individuals advance through their scientific and clinical careers.

WE WILL DO THIS BY:

- providing opportunities for knowledge sharing, learning and development to all members throughout their careers
- ensuring that the UK contributes to, and benefits from, the international endocrine community
- ensuring that equality, diversity and inclusion principles and practices run through all of the Society's activities.

GOAL 2: FACILITATE THE ADVANCEMENT OF ENDOCRINE SCIENCE

…bringing researchers together, supporting their development, and providing platforms for knowledge dissemination and discussion, to generate new knowledge that translates to better patient care.

WE WILL DO THIS BY:

- supporting high quality 'bench to bedside' and 'bedside to bench' research, by fostering networking, collaboration and training
- enabling dissemination of knowledge across endocrine science and medicine
- encouraging scientists and healthcare professionals to carry out research.

GOAL 3: IMPROVE AND SUPPORT THE EQUITABLE DELIVERY OF EXCELLENT ENDOCRINE PATIENT CARE

…supporting the training of healthcare professionals and sharing best clinical practice.

WE WILL DO THIS BY:

- facilitating the generation, sharing and adoption of excellent clinical practice among the endocrine community
- supporting high quality training in endocrinology that meets evolving clinical needs of our members
- promoting patient involvement in their own care and understanding of treatments, through working with patient support groups
- raising the profile of endocrinology and diabetes as an attractive career choice for clinicians, nurses and associated professionals.

GOAL 4: BE AN ACCURATE, TRUSTWORTHY VOICE ON HORMONES

…by delivering expert scientific and clinical information and by equipping our members with the skills to tackle misinformation and promote good science.

WE WILL DO THIS BY:

- delivering expert, evidence-based information on endocrine-related public policy issues to policymakers
- delivering expert, trustworthy information on endocrine subjects to non-experts to tackle misinformation
- providing information and resources to support teachers of endocrinology at schools, colleges and higher education institutions.

Helping to adapt ENDOCRINE SERVICES POST-PANDEMIC

During the COVID pandemic, the pressures on endocrine healthcare services in the UK were highlighted in the national Getting It Right First Time (GIRFT) report on endocrinology and the Society's Defining the Future of Endocrinology document. Key challenges included long waiting times for clinic appointments, increasing referrals, a concern about clinical risk, and a static or declining workforce.

Last autumn, the Implementation Working Group within the Society for Endocrinology's Clinical Committee circulated a questionnaire to all members of the Society, to explore implementation of the recommendations from these reports.

The intention was to understand the pressures that our members were facing on their services, and their priorities. The 320 responses showed wide variation in practice and innovation to adapt to pressures in endocrine services, both before and after the COVID pandemic.

The Recovery and Transformation agenda in England was being rolled out to cope with the clinical backlog following the pandemic, with similar initiatives in the other nations. However, many responses showed that members remained concerned about their services, and wanted advice on how to make further clinically appropriate changes.

THE OUTCOMES

The Implementation Working Group is now a significant part of the Clinical Committee's agenda, with clinical services discussed at every meeting. We are working with NHS England and GIRFT to ensure that these bodies are fully informed of best practice by the Clinical Committee and the Clinical Reference Group, ensuring that innovation is not stifled.

The Society has expanded and launched the Clinical Resource Hub, with additional materials to support business planning, exemplars of new ways of working and useful documentation around referral assessment and patient-initiated follow-up (PIFU).

Following the first successful webinar in September last year, we now have a full programme of 'bitesize' webinars running throughout 2023 and discussing clinic transformation themes. These include insights from clinical colleagues who have made positive changes to their services.

We also discovered that many services had endocrine specialist nurses to help with the workload, far more than were members of the Society. A questionnaire is now being developed to address the specific needs of this group.

SUGGESTIONS

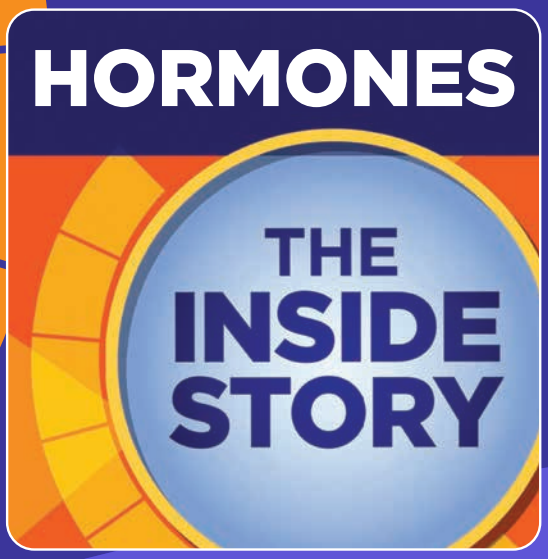
If you have more examples of service change, or requirements for documentation and/or guidance which are not available currently on the Clinical Resource Hub, please contact **clinical@endocrinology.org**.

DOUGLAS ROBERTSON
Associate Medical Director, Mid Cheshire Hospitals NHS Foundation Trust
Chair, Defining the Future of Endocrinology Implementation Working Group
Member, Society for Endocrinology Clinical Committee

RETURNING THIS SUMMER

Series 3 of our award-winning podcast!

Society for Endocrinology



In the latest series, leading experts discuss the secrets of sexual desire, whether your pet can pick up your stress, and if you can blame your diabetes on your genes, or your health problems on your thyroid.

> Interesting and **really useful information**. So worth listening to!

> Fantastic, **really insightful** and interesting science podcast.

> Well researched and well presented podcast that makes the subject of hormones **accessible to a wide audience**. A great balance between interviews with experts and additional comments by the presenter. The sound editing and nice touches of humour are great additions. **Highly recommended!**

> **Really love this podcast** – interesting stories and guests, sounds great and nice to hear the science of hormones covered in a sensible but fun way. Thank you!

> I'm really enjoying this podcast – **perfectly pitched**. I'm learning a lot and finding the episodes really absorbing.

All reviews 5 star from Apple Podcasts

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Gain experience in **SCIENCE COMMUNICATION**

Become a Social Media Content Creator for **You and Your Hormones**

Would you like to boost your science communications skills and help the Society to creatively engage with new audiences on social media? Then consider applying to join the You and Your Hormones team as a Social Media Content Creator.

We have recently launched a Twitter account for You and Your Hormones (**@Your_Hormones**). You and Your Hormones is our public-facing website, which provides reliable online information and learning resources for students, teachers and the general public on hormones and hormone-related conditions. The Twitter account aims to widen the website's reach, and to connect the general public with accurate, interesting and reliable information on hormones.

That's where you come in.

We are looking for passionate members who are interested in using social media for science communication to apply to our newly launched public engagement opportunity: Social Media Content Creator.

WHY SHOULD YOU APPLY?

- You'll gain experience in science communication on social media.
- You can improve your writing skills for non-specialist audiences.
- You'll help us combat misinformation online by promoting accurate and reliable science.
- You'll have the opportunity to work with fellow members from across our endocrine community.

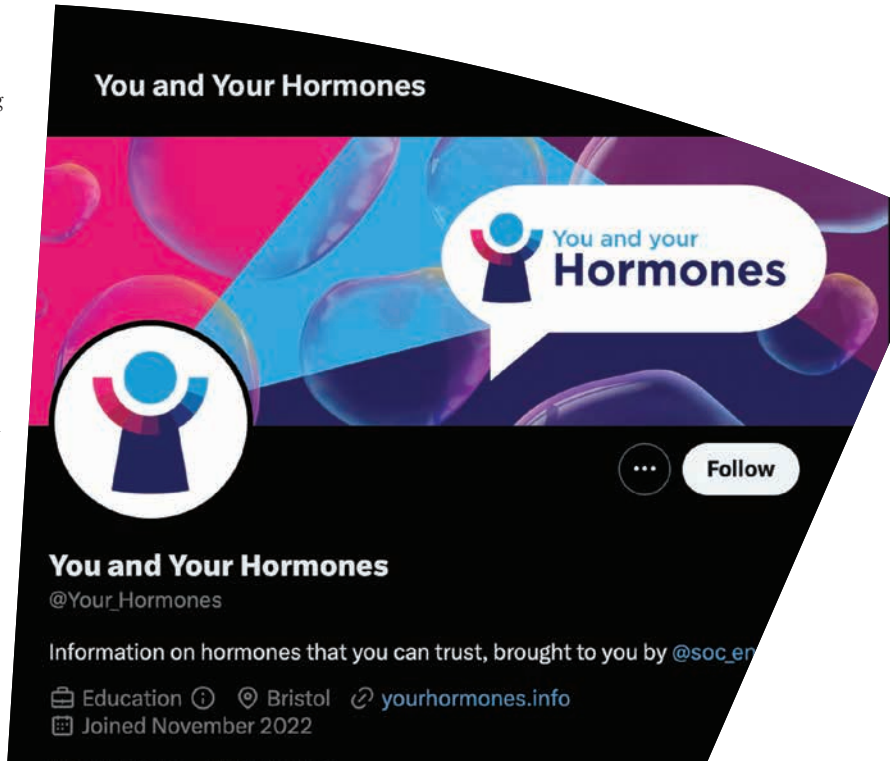
WHAT DOES IT INVOLVE?

- Creating content for Twitter takeovers at least once a month.
- Engaging with a wide range of social media users.
- Generating creative ways to communicate endocrinology to Twitter users.
- Ensuring information is accurate, reliable and easy to understand.
- Working alongside supportive communications and marketing team members.

Opposite, you can hear from two of our members who have both been involved in 'Twitter takeovers' on **@Your_Hormones**…

HOW TO APPLY

Apply online at **endocrinology.org/YYHContentCreator**. Please note, only members will be considered for this role.



My Twitter takeover experience
...AND WHY YOU SHOULD TRY IT TOO

ABBIE BYFORD

I am a final year PhD student at the University of Leeds researching the impact of maternal diabetes on the placenta. I am a member of the Society for Endocrinology's Public Engagement Committee, and enjoy taking part in public outreach, using art to teach people about my pregnancy research.

Tell us about your career so far

I have been a student at Leeds for nine years, first studying for my undergraduate degree and masters in neuroscience, and now my PhD on maternal diabetes in pregnancy. During my PhD, I joined the Society for Endocrinology and, last year, I joined the Public Engagement Committee.

Why did you specialise in endocrinology?

When I saw the advertisement for my current PhD project investigating maternal diabetes and its impact on the placenta, I was intrigued. Although my undergraduate degree was in neuroscience, I was really interested in researching pregnancy and learning about a new topic. This introduced me to the fields of reproductive endocrinology and diabetes, as well as to the Society.

What experience have you had in public outreach?

I received funding from the Society for Endocrinology and the Pathological Society to develop my own placenta-themed lino printing activity (PlacentArt), which I have carried out at local and national outreach events, including the University of Leeds Be Curious Festival, Otley Science Festival and the Nottingham Festival of Science and Curiosity (see *The Endocrinologist* issue 146, page 28). As a member of the Society's Public Engagement Committee, I am also on the You and Your Hormones Editorial Board.

How was your @Your_Hormones Twitter takeover?

I enjoyed thinking about which aspects of my research would be interesting to members of the public, and then creating a quiz from those aspects to engage them. As Twitter has a character limit, it was also important to think of short, snappy Tweets that would simplify complex topics. It was also a great opportunity to direct people to the You and Your Hormones website.

Why apply for the Social Media Content Editor role?

As social media is so widely used today, it is the perfect platform to engage members of the public with endocrinology. It's a great opportunity for Society members to gain public engagement experience and communicate their areas of research, or current hot topics, to the public. I would really recommend being involved.

Are you interested in doing more public outreach?

I really enjoy taking part in public outreach, and this experience has encouraged me to be more involved in engagement through online platforms.

MANON OWEN

I am a PhD student who is passionate about science communication, and the challenge of breaking down complex scientific concepts into language that everyone can understand. When I'm not in the lab, you will either see me in the pub with friends or on long walks across the mountains of Snowdonia!

Tell us about your career so far

I am currently a third year British Heart Foundation PhD student at the University of Leeds, studying the effects of diabetes on fetal growth and cardiometabolic outcomes during pregnancy. Prior to starting my PhD, I studied biomedical science at the University of Birmingham. I undertook an elective industrial placement year at the Cancer Research UK Centre for Drug Development, where I worked on phase I/II oncology clinical trials as a student Quality Assurance and Medical Writing Assistant.

Why did you specialise in endocrinology?

I find it fascinating how much subconscious influence our hormones have each day, affecting our activities, behaviour and mood more than we think. They have a huge impact on our short and long term health. Pregnancy is a period where there is a significant shift in hormones to cause changes to the body to support a developing fetus. I therefore wanted to further explore how a slight hormonal imbalance in pregnancy can have a domino effect, not only on the person who is pregnant, but also on the long term health of the child.

What experience have you had in public outreach?

I have previously been involved in various scientific outreach opportunities, reaching diverse audiences. These range from developing and hosting scientific activities for families in scientific and cultural festivals, to being interviewed on BBC Radio Cymru and being a producer for Pint of Science online live show. During my placement year with Cancer Research UK, I also developed layperson summaries of clinical trial results by working with patient involvement groups.

How was your @Your_ Hormones Twitter takeover?

It was great to have the opportunity to take over the **@Your_Hormones** Twitter account, as I could come up with my own ideas and be as creative as possible when explaining difficult concepts. I created question polls throughout the day and had live interaction with the public. It was also really cool to see how many profiles my Tweets had reached, and therefore the impact of my takeover.

Why apply for the Social Media Content Editor role?

You are given the opportunity to come up with your own ideas for the **@Your_Hormones** social media content. With such a large following, you have a great platform to make an impact in your own unique way.

Are you interested in doing more public outreach?

Absolutely! Since my first takeover I have been thinking about more ideas that I would like to implement, to increase social media engagement and public interest.

THROUGH ADVERSITY EMERGES OPPORTUNITY

WRITTEN BY PAUL M STEWART

It has been a privileged and exciting journey, as I look back on my 40 years in the NHS as a clinical academic, spanning research, patient care and academic leadership. Throughout my career, there has always been a professional conflict between wanting to achieve one's best for patients or personal/team research aspirations, set against fiscal restraint. One senses that, for many, this has now reached a crisis point. Why is this so and what might the future have in store?

THE CURRENT SITUATION

Over the last 40 years, we have collectively added approximately seven years to life expectancy, but this has come at a price. Set against a flat/low growth economy, we spend approximately 10% of our gross domestic product (GDP) on healthcare, but the demand cost is escalating at a rate of 5–8% each year.

Yes, we have made major inroads into reversing premature death from cardiovascular disease and cancer, but at the expense of an aged population with co-morbidities and non-communicable disease. The demographic change to the population we must now serve has contributed to significant workforce pressures across all healthcare workers, with priority moving to 'care' versus 'cure' exacerbated by a non-aligned and rudimentary social care system.

To our cost we have prioritised secondary and tertiary care services at the expense of public and population health, creating a 'National Disease Service' rather than a holistic NHS that can address the main health challenges of the day through prevention, screening and early diagnosis.

Since Aneurin Bevan's inception of the NHS in 1948,[1] the core principle has remained the same: 'available to the whole population freely'. It is part of our constitution and British culture. I remain a passionate advocate for our outstanding NHS but, if we want to continue to deliver the 'highest service to all based on need', then we must think of new funding models that are fair and equitable, but which offer greater personal buy-in and responsibility for our health. I am often bemused by how healthcare works better for our pet dog than it does for my treasured family members.

There are big decisions for society to address, but I have real scepticism that this will ever happen, so long as this is left to the whim of politicians and to manipulation as a government election tool. Surely our personal health is too important for this?

In research and innovation (R&I) and, specifically, biomedical and health research, we have punched well above our weight globally. For 1% of the world's population and 4% of global spend on research and development, we produce 16% of the world's highest cited outputs. Our impact, as evidenced through successive research excellence framework cycles, has been world-leading.[2,3]

We have always benefited immensely from an alignment of the Medical Research Council (UK Research and Innovation), medical charities (notably the Wellcome Trust, Cancer Research UK and British Heart Foundation) and National Institute for Health Research (NIHR). We must hope this continues, following recent changes at the Wellcome Trust. However, the ramifications of Brexit and our ongoing participation in Horizon Europe remain a real threat to future research funding. In recovering from the

COVID-19 pandemic, I feel particularly concerned for our early career researchers and the plight of aspiring clinical academics, faced with current university funding models that have unwisely relied too heavily on international students from China and the Far East.

HOPE FOR THE FUTURE

But I remain confident that we can and will evolve. Prevailing winds include recent NHS legislation and the introduction of integrated care systems for more effective co-ordination of healthcare delivery.[4] There is, at last, an acceptance that R&I needs to be a critical part of NHS activity, because it improves quality and outcomes for patients, and both major political parties seem to have accepted the importance of R&I, pledging target figures of 3% of GDP for research.

> *'The current opportunities are real and within reach, so much so that I wish I was starting out again on my own career, rather than sitting here sharing my opinions…'*

There seems to be a more conciliatory tone to association with Horizon Europe with detailed discussion around so-called plan B alternatives should this not come to fruition.[5] Future research careers continue to be a major focus of work across the Academy of Medical Sciences. Working with its stakeholders, numerous initiatives are either in place or under development

that will make a difference, particularly for clinical and non-clinical researchers post-PhD.[6]

As endocrinologists, we need to be agents who will bring about change. We are in the midst of the so-called 'fourth industrial revolution'.[7] The exciting infusion of computation, digital, artificial intelligence/machine learning and engineering technologies into biology and medicine offers immense potential to change how we deliver future healthcare in a more sustainable way. In continuing to pioneer new therapies for our endocrine patients, endocrinologists must become key investigators in large interdisciplinary research teams comprising bioscientists, engineers, mathematicians/digital and data analysts, behavioural psychologists, medical technologists and patients themselves, to address the major challenges of the day, be they obesity, frailty, health inequality or climate change.

The health technology sector and its convergence with digital, artificial intelligence, diagnostics and genomics constitutes one of the most rapidly growing industries globally. Embracing and partnering with the life sciences industry,[8] we can be the change agent that underpins 'better health, better wealth', becoming the solution to NHS and research sustainability, rather than being viewed as another government hand-out, as and when affordable.

It has always been a challenging working environment: particularly so across the critically important NHS–university ecosystem. But the personal and professional rewards as you all 'make a difference' are immense. The current opportunities are real and within reach, so much so that I wish I was starting out again on my own career, rather than sitting here sharing my opinions…

Grasp the opportunities and enjoy the experience!

PAUL M STEWART
Professor of Medicine (Emeritus), University of Leeds;
Clinical Vice President, Academy of Medical Sciences

The views discussed herein are personal and not necessarily those of any organisation to which I am affiliated.

REFERENCES

1. UK Parliament 1946 *National Health Service Act* www.parliament.uk/about/living-heritage/transformingsociety/livinglearning/coll-9-health1/health-01.
2. UK Department for Business, Energy & Industrial Strategy 2016 *International Comparative Performance of the UK Research Base* https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/660855/uk-research-base-international-comparison-2016.pdf.
3. Research Excellence Framework 2022 *Overview Report by Main Panel A and Sub-panels 1 to 6* www.ref.ac.uk/media/1910/mp-a-overview-report-final-updated-september-2022.pdf.
4. The King's Fund 2022 *Integrated Care Systems Explained: Making Sense of Systems, Places and Neighbourhoods* www.kingsfund.org.uk/publications/integrated-care-systems-explained.
5. O'Grady C 2022 *Science* www.science.org/content/article/u-k-outlines-plan-b-research-funding-skirt-eu-impasse.
6. Academy of Medical Sciences 2023 *Programmes* https://acmedsci.ac.uk/grants-and-schemes/mentoring-and-other-schemes.
7. McKinsey & Company 2022 *What are Industry 4.0, the Fourth Industrial Revolution, and 4IR?* www.mckinsey.com/featured-insights/mckinsey-explainers/what-are-industry-4-0-the-fourth-industrial-revolution-and-4ir.
8. HM Government 2021 *Build Back Better: Our Plan for Growth – Life Sciences Vision* https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1013597/life-sciences-vision-2021.pdf.

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References:
1. Macimorelin 60mg Sachets Summary of Product Characteristics Consilient Health Ltd
2. Garcia JM *et al. J Clin Endocrinol Metab* 2018;103:3083–99

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UK-MAC-170 July 2022

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