Meeting abstracts from the 65th British Thyroid Association Annual Meeting

London, UK. 16 May 2017

Published: 19 September 2017

George Murray Lecture

L1 Papillary thyroid carcinoma (PTC) in 4,432 children and adults managed at the Mayo clinic during eight decades: lessons learned from the continuing analysis of temporal trends and long-term outcome
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Thyroid Research 2017, 10(Suppl 2):L1

In a time of over-diagnosis and over-treatment of the commonest endocrine malignancy (PTC), institutional databases, with large numbers of patients being carefully followed for long postoperative periods, become valuable resources to determine whether increasing sophistication in diagnosis and early treatment of both primary and recurrent disease are actually leading to improved rates of cause-specific mortality (CSM) and tumor recurrence (TR) in both MACIS low-risk (scores <6) and high-risk (scores of 6+) patients. Our 190 children, despite presenting with more extensive PTC than our 4,242 adults, recur at no greater frequency, die less often from PTC and usually coexist with distant spread. CSM in MACIS <6 children (n = 172) and adults (n = 3573) has not improved since 1976, despite more rapid detection and prompt treatment of recurrences. CSM in adults with MACIS high-risk PTC (n = 668) is improving, but one wonders whether head and neck surgeons, or perhaps radiation oncologists, are more responsible for this trend, rather than clinical endocrinologists. In this George Murray Lecture, the presenter will discuss the utility of prognostic factors, the impact of primary surgery on outcome, the ineffectiveness of radioiodine remnant ablation, and the introduction of ultrasound-guided percutaneous ethanol ablation (UPEA) to the management of primary and recurrent PTC.

S1 ‘GO into Orbit’ An update on GO pathogenesis
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Thyroid Research 2017, 10(Suppl 2):S1

I will provide a brief summary of the main inflammatory and immunological mediators in Graves’ orbitopathy (GO) and remind the audience of the link with Graves’ disease (GD). The likely thyroid/orbit shared antigen(s) will be discussed and the possible role of autoantibodies in mediating GO pathogenetic changes. The tissue remodelling processes leading to expansion of the orbital contents will be described, along with the current state of knowledge on their regulation and consequent identification of novel treatment targets. Finally I will comment on studies investigating the triggers of the autoimmune response, including my own experiences with induced in vivo models. I will explain how the gut microbiota might influence autoimmunity, how this might apply to GD and GO and give an overview of the INDIGO project.

S2 Thyroid circadian timing: role in physiology and thyroid malignancies
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Thyroid Research 2017, 10(Suppl 2):S2

Circadian clock represents anticipatory mechanism, highly conserved in the evolution, and impacting critically on most of aspects of the physiology. Although the circadian profiles of thyroid releasing hormone (TRH), thyroid stimulating hormone (TSH), thyroxine (T4) and triiodothyronine (T3) in the circulation have been well described, few studies have tackled the mechanisms underlying circadian regulation of the HPT axis function. Of note, an increasing body of evidence suggests a strong link between cellular circadian cycle, DNA damage, apoptosis control, and cancerogenesis. The talk will summarize current knowledge on the complex regulation of thyroid gland gene expression and influence by the circadian oscillator. Molecular makeup of the human thyroid oscillator, as well as potential link between thyroid malignant transformation and alterations in the clockwork, will be highlighted.

S3 New radiopharmaceuticals for PET imaging and radionuclide therapy in thyroid disease – from bench to clinic
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Thyroid Research 2017, 10(Suppl 2):S3

Over the last half-century, imaging thyroid disease with radionuclides has developed from “functional imaging” to “molecular imaging” where radioiodine was used to localise “thyroid function,” into “molecular imaging” following discovery and cloning of the sodium-iodide symporter (NIS) in the 1990s. Throughout this development it has maintained its role as a mainstay of diagnosis in thyroid disease, while iodine-131 therapy has maintained its position in radionuclide therapy. The advent of clinical PET in the last twenty years has highlighted the limitations of conventional gamma camera and SPECT imaging compared to the improved resolution, sensitivity and quantification offered by PET. Thus a search began for positron emitting alternatives to the conventional gamma emitters iodine-131, iodine-123 and technetium-99 m-pertechnetate. This was partially satisfied iodine-124, but its long half-life (4 days) and consequent high radiation dose, low positron abundance, and less than ideal PET imaging characteristics, spurred further searching for tracers labeled with the "ideal" positron emitter, fluorine-18. This presentation describes our work the development of PET tracers including resulting from this search, including F-18-tetrafluoroborate, F-18-fluorosulfonate and others, from conception and synthesis to clinical evaluation. In addition, the possibility of alternative radionuclides such as rhenium-188 for therapy of NIS-expressing thyroid tumours will be discussed.
S4 Thyroid disease in pregnancy. What use are obstetricians? Mike Marsh (michael.s.marsh@kcl.ac.uk) Department of Obstetrics and Gynaecology, King’s College Hospital, London, UK Thyroid Research 2017, 10(Suppl 2):S4

The talk will cover controversies concerning thyroid function tests in pregnancy, iodine supplementation in pregnancy, management of thyroid nodules and thyroid cancer in pregnancy, screening for thyroid disease during pregnancy, and the role of the obstetrician in management of women with thyroid disease in pregnancy.

S5 Thyroid disease in pregnancy: an endocrinologist’s perspective Kirsten Boelaert (KBOELAERT@bham.ac.uk) Institute of Metabolism and Systems Research, University of Birmingham and Queen Elizabeth Hospital, Birmingham, UK Thyroid Research 2017, 10(Suppl 2):S5

Pregnancy has a profound impact on the thyroid gland and is associated with important physiological changes to thyroid function. In addition, thyroid dysfunction and other thyroid diseases may be present before, during and after pregnancy and taken together these conditions represent a significant health burden affecting women of reproductive age. There is continued controversy regarding the definitions of normal thyroid function in pregnancy and whether mild thyroid dysfunction warrants follow-up and treatment. Evidence regarding optimal management of thyroid diseases in pregnancy is rapidly accumulating and the results of carefully conducted randomised controlled trials are changing recommendations regarding optimal practice. The American Thyroid Association (ATA) has brought out new guidelines regarding the management of thyroid disorders in the peri-partum period in March 2017 and UK guidelines are currently in development as part of a joint venture between the British Thyroid Association and the Royal College of Obstetricians and Gynaecologists (RCOG). In line with current practice in most fields of medicine a multi-disciplinary approach with close liaison between endocrinologists, obstetricians and health care professionals often results in optimal outcomes for mother and baby. This symposium aims to highlight the most recent evidence regarding management of thyroid disorders in pregnancy from an endocrine perspective.

O1 Frequent Occurrence of DUOX2 and DUOXA2 Mutations in Cases with Borderline Bloodspot Screening TSH who Develop ‘True’ Congenital Hypothyroidism C. Peters1, A. K. Nicholas2, G. Lyons2, S. Langham3, E. Serra4, E. Schoenmakers5, M. Muzza6, L. Fugazzola6, N. Schoenmakers1 1Department of Endocrinology, Great Ormond Street Hospital for Children, London; 2University of Cambridge Metabolic Research Laboratories, Wellcome Trust-Medical Research Council Institute of Metabolic Science, Addenbrooke’s Hospital, Cambridge; 3Department of Human Genetics, The Wellcome Trust Sanger Institute, Hinxton, Cambridge; 4Department of Pathophysiology and Transplantation, University of Milan & Division of Endocrinology and Metabolism, IRCCS Istituto Auxologico Italiano, Milan, Italy; 5Department of Paediatric Endocrinology & Diabetes, National Children’s Hospital, AMNCH, Dublin and University of Dublin, Trinity College, Dublin, Ireland; 6Department of Pharmacology and Therapeutics, McGill University, Montréal, Québec, Canada

Methods

Methods were characterized in vitro. Genotype-phenotype correlations were investigated in the wider kindred.

Results

The mutant IGF1 protein (c.2318 T > C, p.L773P) exhibited decreased plasma membrane expression in vitro due to impaired trafficking from the endoplasmic reticulum. Ten hemizygous males and 11 heterozygous females exhibited characteristic endocrine deficits. Intrafamilial penetrance is highly variable and a minority of heterozygous females are also affected. We identified and characterized a novel IGF1 mutation and investigated its associated phenotypes in a large Irish kindred.

References

[1] Peters C, Nicholas AK, Lyons G, Langham S, Serra EG, Schoenmakers E et al. 44th Annual Meeting of the British Society for Paediatric Endocrinology and Diabetes 2016 (OCS.7) Frequent occurrence of DUOX2 and DUOXA2 mutations in cases with borderline bloodspot screening TSH who develop ‘True’ congenital hypothyroidism. Endocrine Abstracts (2016) Vol 45

O2 A novel IGSF1 mutation in a large Irish kindred highlights the need for systematic familial endocrine screening in the IGSF1 deficiency syndrome Anne McGowan1*, Edna Roche1*, Olympia Koulouri1, Marc-Olivier Turgeon2, Adeline K Nicholas1, Emmeline Heffernan1, Ranna El-Khairi2, Greta Lyons1, Luca Persani3, Mehul T. Dattani1, Mark Gurnell1, Daniel J Bernard2, Nadia Schoenmakers1

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Methods

A novel, hemizygous IGSF1 mutation was identified by direct sequencing in two brothers with CeCH and its functional consequences were characterized in vitro. Genotype-phenotype correlations were investigated in the wider kindred.

Results

The mutant IGSF1 protein (c.2318 T > C, p.L773P) exhibited decreased plasma membrane expression in vitro due to impaired trafficking from the endoplasmic reticulum. Ten hemizygous males and 11 heterozygous females exhibited characteristic endocrine deficits. Ireland operates a TSH-based CH screening programme, which does not detect CeCH; therefore genetic ascertainment preceded biochemical diagnosis of moderate CH in four of seven boys, and their 75 year-old grandfather. Tissue manifestations of hypothyroidism were variable; normal free T3 (FT3) levels and low/low normal reverse T3 (rT3) measurements suggested that preferential deiodination of FT4 to FT3 may help maintain tissue euthyroidism in some individuals. However, jaundice, impaired growth, speech delay and obesity were associated with delayed diagnosis of endocrinopathy in four childhood cases.
Conclusions

As observed with other loss-of-function IGSF1 mutations, L773P results in variably penetrant IGSF1 deficiency syndrome. Our observations emphasise the need for multi-generation genetic ascertainment in affected families, especially where TSH-based CH screening programmes may fail to detect CeCH at birth.

O3

Alemtuzumab-induced thyroid autoimmunity: biological characterisation of autoantibodies to the thyrotropin receptor, and possible role as predictive marker of disease
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Thyroid Research 2017, 10(Suppl 2):O3

Background

Alemtuzumab (anti-CD52; ALTZ), an effective therapy for relapsing/remitting multiple sclerosis (MS), causes panlymphopenia with subsequent lymphocyte repopulation: 30-40% of patients develop second-order humoral autoimmunity, mainly thyroidal. Anti-thyrotropin-receptor (TSHR) autoantibodies (TRAb) can stimulate (TSAb), block (TBAb) or not affect (neutral) TSHR function, with TSAb causing hyperthyroid Graves’ disease (GD), and TBAb hypothyroidism. Low-affinity neutral TRAb could pre-exist in MS patients, then undergo somatic hypermutation to become high-affinity TSAb/TBAb post-ALTZ, causing thyroid dysfunction.

Methods

Sera from MS patients (Welsh Neuroscience Research Tissue Bank), 11 developing post-ALTZ thyroid autoimmunity (TA; 10 GD, 1 hypothyroidism) and 14 not developing it (NO-TA), evaluated at different time-points: 1) pre-ALTZ, 2) post-ALTZ before disease onset (TA) or latest time post-ALTZ (NO-TA), 3) post-ALTZ during/after thyroid dysfunction onset (TA only). Flow cytometry (FC) detected any TSHR-binding TRAb. Luciferase biassays (LB) detected both TRAb presence and bioactivity (neutral/TSAb/TBAb), also deduced from the corresponding thyroid function. TRAb positivity (TRAb+) was defined as FC or LB positivity.

Results

At time-point 1, 3/11 (27.3%) TA and 0/14 (0%) NO-TA patients were TRAb + (p = 0.07). At time-point 2, 5/11 (45.5%) TA and 4/14 (28.6%) NO-TA were TRAb + (p = 0.43). Among all TRAb + cases, TBAb were 2/7 (28.6%) in GD, 1/1 (100%) in hypothyroidism, and 3/4 (75%) in NO-TA.

Conclusions

A) Patients who developed TA tended to be TRAb + prior to ALTZ. Thus TRAb could provide a predictive marker of future TA. B) TRAb + patients were euthyroid at time-points 1-2, suggesting low-affinity antibodies unable to affect thyroid function. C) Post-ALTZ TBAb subtype is common.

O4

Clinical management experience: the One-Stop Thyroid Clinic, Singleton Hospital, Swansea
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Thyroid Research 2017, 10(Suppl 2):O4

Background

The weekly Thyroid Clinic is supported by Medical Physics, Cytopathologist and Respiratory Physiology technician colleagues. Approximately 350 new patients are assessed each year of which 140 receive outpatient radioiodine therapy. Referrals are reviewed by the Endocrinologist and patients informed by letter before attending clinic regarding the possibility of receiving radioiodine therapy. Patients undergoing fine needle aspiration cytology (FNAC) receive the report of the investigation during the same session. Those with large goitres suspected of having upper airways obstruction undergo respiratory function testing, including flow volume loop, at their initial clinic visit.

Methods

143 patients received outpatient radioiodine therapy for hyperthyroidism (1.4.2014-31.3.2015) of which 130 patients received treatment at their first clinic visit. Thirteen patients did not receive treatment for various reasons including failure to discontinue Carbimazole therapy, problems arranging appropriate family support or wish to further consider treatment options. Patients who underwent FNAC were sent a questionnaire to evaluate their experience.

Results

Following discussion in clinic, 130 patients received radioiodine therapy at their first visit Fifty-three of the 82 patients who underwent FNAC replied to the questionnaire and all were pleased to be investigated at their initial clinic visit. All but two were pleased to receive the result on the day.

Conclusion

A “one-stop thyroid service” reduces the need for unnecessary clinic visits, reduces travel time, time off work and inconvenience for patients and relatives, and reduces patients’ anxiety following cytological investigation.

O5

ETVS, an ETS family transcription factor, regulates telomerase expression in thyroid cancer
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Thyroid Research 2017, 10(Suppl 2):O5

Background

The TERT gene encodes the catalytic component of telomerase, and is silenced in healthy somatic cells. In thyroid cancer, desilencing of TERT can occur as a consequence of TERT promoter (TERTp) mutations (e.g. C228T) which create binding motifs for MAPK-activated ETS-factors. Clinically, co-occurrence of MAPK-activating mutations of BRAF or RAS with TERTp mutations strongly correlates with poorer patient outcomes. We also recently discovered that the protein encoded by the thyroid cancer susceptibility gene FOXE1, can indirectly associate with TERTp via the ETS-factor ELK1. The 29 ETS-factors are widely expressed and some exhibit functional redundancy. However, recent evidence indicates that in goblastomas it is GABP which is the dominant activator of mutant TERTp. Here, we sought to determine which ETS-factor(s) are relevant to TERTp activation in thyroid cancer.

Methods

ETS gene expression in thyroid tissue and cell-lines was quantified by real-time RT-PCR. The SW1736 thyroid cancer cell-line was manipulated with CRISPR/Cas9 to create TLuc1, which harbors a luciferase gene integrated downstream of the C228T-containing TERTp. TLuc1 was transfected with ETS-targeting siRNA, and forty-eight hours later reporter assays were performed. Co-immunoprecipitation experiments were performed using standard protocols.

Results

Gene expression profiling revealed that ELK1 and ETV5 were significantly increased in thyroid cancers compared with normal controls. An siRNA screen of ETS-factors found the greatest down-regulation (50%, p = 0.015) in luciferase activity following ETV5 ablation. Co-immunoprecipitation assays revealed that ETV5 and FOXE1 are also interacting partners.

Conclusion

We have identified ETV5 as the critical ETS factor activating mutant TERTp in thyroid cancer cells.
O6
Identification of novel sodium iodide symporter (NIS) interactors which modulate iodide uptake
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Thyroid Research 2017, 10(Suppl 2):O6

Background
By exploiting the canonical function of the sodium iodide symporter (NIS), ablative radioiodide therapy is an effective treatment for thyroid cancer and has been hypothesised as a viable treatment for breast cancer. However, up to a quarter of patients are unable to accumulate sufficient radioiodide for effective treatment due to decreased expression of NIS and/or reduced plasma membrane localisation. Currently, the regulation of NIS trafficking and its localisation at the plasma membrane is ill-defined.

Methods
To identify novel NIS-interactors, and unravel the mechanism of NIS trafficking, mass spectrometry analysis was performed on proteins co-immunoprecipitating with lentivirally expressed NIS in cell plasma membrane extracts. To determine the biological impact of these putative interactors on NIS, siRNA knockdown of the top shortlisted interactors was followed by radioiodide uptake assays. Further, to validate interactors that altered NIS function, co-immunoprecipitation and proximity ligation assays were completed.

Results
NIS activity was significantly altered by ADP-ribosylation factor 4 (ARF4) and valosin containing protein (VCP) in thyroid and breast cancer cell lines stably-expressing NIS. ARF4 downregulation significantly decreased radioiodide uptake by 75% and 44%, and VCP downregulation increased radioiodide uptake by 71% and 56%, in the thyroid and breast cell lines, respectively. In contrast, ARF4 overexpression significantly increased radioiodide uptake by 89% and 43%, and VCP overexpression decreased radioiodide uptake by 52% and 38%, in thyroid and breast cell lines, respectively. Through both co-immunoprecipitation and proximity ligation assays it was confirmed that NIS interacts with ARF4 and VCP. Analysis of TCGA data from N = 58 matched papillary thyroid cancers revealed ARF4 is significantly repressed and VCP highly upregulated in thyroid cancer, providing a new putative explanation for repressed NIS function.

Conclusion
These studies elucidating the regulation of NIS localisation have identified two novel potential therapeutic targets for enhancing radioiodide uptake in patients who are radioiodide-refractory.

O7
Resistance to thyroid hormone α (RTHα): therapeutic targeting of transcriptional repression in vivo
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Thyroid Research 2017, 10(Suppl 2):O7

Background
Thyroid hormones are essential for skeletal development and adult bone maintenance, and exert their actions in the skeleton via thyroid hormone receptor α (TRα). Patients with mutations of the TRα gene encoding TRα have growth retardation, skeletal dysplasia, constipation and variable cognitive abnormalities. These features are consistent with impaired thyroid hormone action in TRα target tissues, most notably the skeleton. Mutant TRα proteins have impaired T3 binding but increased affinity for interaction with the nuclear receptor co-repressor (NCoR). NCoR recruits histone deacetylases to DNA promoter regions, and its interaction with TRα results in repression of T3 target gene expression. The phenotype in patients with TRα mutations is therefore thought to result from enhanced repression of the basal activity of T3 target genes in TRα sensitive tissues such as the skeleton. We hypothesised, therefore that (i) inactivation of NCoR or (ii) treatment with a histone deacetylase inhibitor (suberoylanilide hydroxamic acid, SAHA) would ameliorate the phenotype in a TRα mutant mouse disease model.

Methods
To investigate this hypothesis, we analysed skeletal phenotypes of: (i) Thra1ΔID+/+ (wild-type), (ii) Ncor1ΔID+/+ (mutation in NCoR that prevents its interaction with TRα), (iii) Thra1ΔID+/Δ (a severe dominant-negative mutation of TRα that cannot bind T3), and (iv) Thra1ΔID+/Ncor1ΔID+/Δ (double mutant in which mutant NCoR does not interact with dominant-negative TRα). Adult mice were analysed following treatment with vehicle or SAHA (50 mg/kg body weight) from the age of 6 weeks for 2 months. The skeletal consequences of SAHA treatment were determined by x-ray microangiography, micro-CT scanning and biomechanical testing.

Results
Prevention of the interaction between dominant-negative mutation of TRα and NCoR ameliorated the skeletal dysplasia in Thra1ΔID+/+ mice, whereas treatment with the histone deacetylase inhibitor, SAHA, had no significant effect on linear growth, bone mineral content, cortical and trabecular bone structural parameters or bone strength.

Conclusion
These data suggest treatment with SAHA is unlikely to provide therapeutic benefit in individuals with severe TRα mutations. However, other compounds that target NCoR-TRα interaction or its downstream actions may have therapeutic potential especially in individuals with milder TRα mutations.

P1
Prostaglandin F2-alpha eye drops (Bimatoprost) in thyroid eye disease: a randomised controlled double blind crossover trial (BIMA study)
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Thyroid Research 2017, 10(Suppl 2):P1

Background
Reduced eyelid protrusion has been reported as a side-effect of prostaglandin analogue eye drops (Bimatoprost) in glaucoma treatment. The objective of this study is to determine if bimatoprost is effective at reducing proptosis in inactive thyroid eye disease (TED).
Methods
Following informed consent participants were randomised to receive bimatoprost or placebo for three months after which they underwent a two-month washout, before switching to the opposite treatment. The primary outcome was to compare the change in exophthalmometry readings over the two 3-month treatment periods. This was supported by photographic assessments. Allowing 15% dropout rate, 31 patients were randomised in order to identify a treatment effect of 1.6 mm (\(p = 0.05\), two-sided, power 0.88).

Results
There was female preponderance with 5:1 ratio and mean age of 55 (range 28-74). The median duration of TED was 7.6 (IQR 3.6-12.3) years. The majority were still suffering from diplopia (61.3%) with bilateral involvement (61.3%). Using multilevel modelling adjusted for baseline, phase and carryover, Bimatoprost resulted in -0.17 mm exophthalmometry change (95% CI -0.67 to +0.32) \(p = 0.490\). Subgroup analysis on monocular disease did not show any benefit.

Conclusions
Bimatoprost treatment over 3 months does not result in clinically meaningful improvement in proptosis. Over 60% of TED patients have diplopia, confirming the unmet clinical need in this patient group.

P2
An investigation into sodium-iodide symporter (NIS) dimerisation and its impact on radiodiode uptake in thyroid cancer
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Thyroid Research 2017, 10(Suppl 2):P2

Background
The thyroid's ability to accumulate iodide via the sodium-iodide symporter (NIS) is utilised to successfully treat most thyroid cancers with radiodiode. However, approximately 25% of thyroid cancers lose functional NIS expression and become unresponsive to radiodiode therapy, resulting in a poorer prognosis. Our knowledge of NIS regulation is limited, but as dimerisation of NIS has been proposed, we sought to investigate NIS dimerisation and function.

Methods
A homology model of NIS structure was built based on the bacterial transporter (glycine- and leucine-zipper motifs). FRET increased in the presence of both fluorophore-conjugated NIS constructs compared to single expression (1.52 ± 0.10 vs 1.08 ± 0.18, \(P < 0.0001\)), validating dimerisation. We mutated five residues identified from our homology model (D237A, Y242A, T243A, Q471A and P412A) and found a significant increase in FRET, indicating that dimerisation involves multiple or as yet undiscovered residues.

Conclusion
NIS dimerisation has been conclusively demonstrated using two discrete methodologies. Further work is ongoing to determine the critical residues, cellular localisation and regulation of NIS dimerisation and its impact on function.

P3
Seasonal variation and relationship between vitamin D and serum thyrotropin levels in euthyroid individuals
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Thyroid Research 2017, 10(Suppl 2):P3

Background
Seasonal variations in vitamin D concentrations is known to influence the hypothalamo-pituitary-thyroid axis but the clinical implications of this interaction are unknown. We investigated the seasonal variability and relationship between vitamin D3 [25(OH)D3] and serum thyrotropin (TSH) levels in euthyroid individuals.

Methods
Retrospective analysis of 401 patients referred to our hospital endocrine clinic with non-specific symptoms of tiredness who had simultaneous measurements of 25(OH)D3 and thyroid function. Patients were categorised according to the season of blood sampling and vitamin D3 status (optimal, sufficient, insufficient and deficient).

Results
As expected serum 25(OH)D3 levels were higher in the Spring-Summer season compared to Autumn-Winter [47.9 ± 22.2 vs. 42.8 ± 21.8 nmol/l; \(p = 0.021\)]. In contrast higher median TSH levels were found in the Autumn-Winter than in the Spring-Summer months [1.9 ± 0.73 vs. 1.8 ± 0.66 mu/l; 0.10]. An inverse relationship was present between 25(OH)D3 levels and serum TSH (\(r = -0.23; p < 0.00001\)) even after adjustment for age and sex. Regardless of season, higher TSH levels were found in patients with vitamin D insufficiency or deficiency in comparison to patients with optimal vitamin D levels.

Conclusion
Our study confirms that seasonal variability exists for 25(OH)D3 and TSH secretion in euthyroid subjects. An inverse relationship exists between vitamin D status and serum TSH levels. The clinical relevance of this interaction requires further study especially with regards to the potential benefits of vitamin D replacement in restoring TSH levels in patients with subclinical or borderline hypothyroid states.

P4
Auditing the effectiveness of a joint thyroid eye clinic
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Thyroid Research 2017, 10(Suppl 2):P4

Background
EUGOGO recommends that patients with thyroid eye disease (TED) be managed in joint endocrinology/ophthalmology clinics but there is limited evidence for their efficacy. In May 2010, a multidisciplinary clinic was established in Edinburgh (originally monthly; now running weekly).

Methods
Clinic data from 01/08/2012-01/08/2016 was audited and compared to pre-clinic data (2009). Associated resources included leaflets on selenium, smoking and immunosuppression.

Results
269 TED patients were seen over four years (median [range] age 51 [16-87] years, male-to-female ratio 1:3.8). Time from referral to first appointment improved as the clinic became better established. Overall, 24 (29%) urgent referrals were seen within 14 days and 53 (62%) routine referrals
were seen within 60 days. By the final year, 47% of urgent referrals and 71% of routine referrals were seen within 14 and 60 days respectively. Smoking status and selenium uptake were recorded for all patients. Of the 82 (30%) smokers, 18 (22%) successfully quit compared to a 6% quit rate in 2009. 71 (26%) patients had active disease (Clinical Activity Score (CAS)>3). Glucocorticoid treatment was considered in all cases with 46 (75%) receiving IV methylprednisolone (median CAS pre-treatment 4; post-treatment 2). 17 patients with active disease were not given steroids. 7 out of 8 patients who had short-course oral steroids reported a reduction in CAS so did not need IV treatment. 5 patients received rituximab.

Conclusions

Referral times, smoking cessation, selenium uptake and treatment of active disease have improved within the joint clinic, although there is still room for improvement.

P5
Recent liothyronine price increases have changed primary care prescription practice, with increased referrals to specialist care

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Thyroid Research 2017, 10(Suppl 2):P5

Background

The cost of liothyronine (T3) has significantly increased, possibly affecting prescription practices.

Methods

An online questionnaire was designed to assess current T3 use by UK endocrinologists and to determine whether the price increase resulted in a change in primary care prescription practices. Consultant grade members of the Society for Endocrinology Thyroid Network were invited to partake.

Results

Results were analysed from 50 consultant respondents; the majority (85%) were aware of the recent price increase in T3 and had received queries from GPs reluctant to prescribe T3 in the past month (82%); 73% had received patient queries. While most trusts (63%) had no restrictions in place for T3 prescription, almost half (44%) of CCGs provided guidance regarding restriction of T3 use to GPs. The majority (82%) found the BTA guidance on T3 use helpful, with most (61%) welcoming further advice. T3 was prescribed by the majority (73%) of respondents, but very infrequently (84%); <1 patient/month) and mostly due to patient request. Respondents indicated that very few (<5%) patients attending clinic were treated with T3 alone (98%). Only 9% used thyroid extract. Most respondents (57%) are equally likely to use T3 compared with 2 years ago.

Conclusions

T3 is used by the majority of UK consultant endocrinologists to treat hypothyroidism, but very infrequently. Price changes in T3 have raised GP concern regarding restriction of T3 use to GPs, and most respondents would welcome further advice on this issue.

P6
Can an electronic protocol improve thyroid hormone replacement in general practice?

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Thyroid Research 2017, 10(Suppl 2):P6

Background

Thyroid hormone replacement is frequently suboptimal but interventions that are proven to optimise therapy are lacking. We developed an electronic Protocol for Monitoring Patients on Thyroxine in General Practice (e-Prompt GP), an electronic alert system designed to prompt general practitioners to test and address out of range thyroid function tests in patients with hypothyroidism.

Methods

In this feasibility audit e-Prompt GP was installed in two general practices in Surrey, total population, 21,177, comprising 650 patients (3.1%) with hypothyroidism. Audits were undertaken at baseline and at 12 months (practice 1) and 3 months (practice 2) after installation. At each time point we determined the percentage of patients with hypothyroidism who had: (1) a thyroid function test in the preceding 12 months and (2) TSH concentration within the laboratory reference range of 0.35-5.0 mU/L.

Results

The proportion of patients who had had a thyroid test in 12 months increased from 89 to 93% in practice 1, and from 86 to 90% in practice 2. Likewise, the proportion of patients with reference range TSH improved from 66% to 74% in practice 1 and from 66 to 72% in practice 2.

Conclusion

An electronic protocol resulted in small improvements in the adequacy of thyroid hormone therapy in two general practices in this preliminary study. Controlled studies are needed to clarify the significance, applicability, and potential clinical relevance of this protocol in a wider variety of UK general practices.

P7
Use of alternative thyroid hormone replacement medication in a specialist clinic- an audit of compliance with national guidelines

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Thyroid Research 2017, 10(Suppl 2):P7

Background

Hypothyroidism describes the clinical syndrome in which there is a deficiency of circulating thyroid hormones. The prevalence of spontaneous hypothyroidism in the UK is 1-2%. Primary hypothyroidism is managed primarily with levothyroxine (L-T4), this is highly effective and safe however there is a subgroup of patients who are dissatisfied with this treatment and are interested in other ways to correct their thyroid function.

Method

This service evaluation reviewed the use of alternative thyroid hormone replacement in a specialist thyroid clinic to determine whether it is consistent with the National Guidelines. The results were obtained by assessing each patient’s clinic notes and identifying whether the use of alternative thyroid replacement therapy matched the guidelines set by the British Thyroid Association (BTA). Each case was scored as compliant, partially compliant or non-compliant.

Results

In total there were 58 patients (Female to male ratio, 57:1) in the cohort. The average age was 50.5 years. Of these patients 58% had been diagnosed with autoimmune hypothyroidism, 14% with subclinical hypothyroidism, 7% Post radiiodine hypothyroidism, 7% with post-thyroidectomy hypothyroidism and 14% of which diagnosis was uncertain. With those on treatment, thyroid stimulating hormone (TSH) was suppressed in 69%. A total of 44 (75%) of patients were on liothyronine (L-T3) or Natural Desiccated Extract (NDT) and 84% of them benefitted from this treatment. In the evaluation, 32 cases scored compliant, 21 partially compliant, 3 non-compliant and 2 cases were unavailable to be commented on.

Conclusion

Managing patients in a tertiary specialist thyroid hormone replacement clinic is effective in ensuring that National Guidelines are followed for these patients. Further studies are required to determine if this approach reduces their exposure to the risks of over-replacement.
Post thyroidectomy thyroid hormone replacement: a challenge

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Thyroid Research 2017, 10(Suppl 2):P8

Background
Graves’ disease and benign multinodular goitre are the common conditions requiring thyroidectomy in selected patient group as part of definitive management plan. Thyroid hormone replacement following total thyroidectomy is usually based upon the body weight (1.6 μg/Kg/day). A euthyroid state is maintained by monitoring serum TSH levels and adjusting the LT4 dose accordingly. Inadequate replacement with LT4 can be associated with persistent hypothyroid symptoms and if over-replaced, it can increase the risks of atrial fibrillation and osteoporosis.

Methods
We conducted a retrospective analysis of 138 patients who underwent total thyroidectomy, subdividing them into 2 groups, Graves’ disease (n =54) and benign multinodular goiter (n = 84). Adequacy of thyroid hormone replacement was identified by TSH level at 4-6 week post operatively and at a 12-month interval.

Results
The cohort included 111 women and 27 men with an average age of 50 years. Up to 50% of the cohort is sub-optimal in achieving biochemical euthyroid state. Older individuals were less likely to be over-replaced in both groups. In the multinodular cohort females were more likely to be over-replaced than males OR = 3.92 (95%CI 0.82, 18.6) p = 0.08. Young females (age <40 years) were substantially more likely to be over replaced OR = 9.17 (95%CI 2.51, 33.4) p = 0.001. In contrast, females with Graves’ disease cohort are likely to be under-replaced in comparison to males (TSH > 4.5) OR = 0.24 (95%CI 0.07 0.41) p =0.007. We were unable to explain this unusual pattern between the two groups.

Conclusion
The current guidance to replace levothyroxine in post-thyroidectomy patients has not achieved euthyroid state in all as expected. Every 2nd patient fails to achieve target TSH levels. Almost 30% of young females have a suppressed TSH which can substantially increase their risk of atrial fibrillation and osteoporosis. Several factors including patient compliance and insufficient monitoring in the community may be driving this outcome.

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