

Diabetes and Endocrinology: Learning from other Specialists Speakers' abstracts

A symposium held on 7 October 2010 at the Royal College of Physicians of Edinburgh

HOW I MANAGE DYSTHYROID EYE DISEASE

Mr Geoffrey E Rose, Consultant Ophthalmologist, Moorfields Eye Hospital, London

The clinical manifestations of thyroid eye disease (TED) are very diverse and are mainly due to inflammation early in the course of the disease, with leakage of fluid into tissues and a secondarily raised intraorbital pressure. Later in the disease, the inflammatory mediators lead to an activation of fibroblasts, with a loss of tissue compliance and function due to tissue fibrosis and an increase in the intercellular matrix within orbital tissues due to the deposition of glycosaminoglycans.

As TED tends to be self-limiting as thyrotoxicosis comes under control, the ophthalmic signs were traditionally treated by monitoring and no (or inadequate) immunosuppression was employed to stop the relentless process. This led to a marked prolongation of the ophthalmic disease and considerable disfigurement that often required extensive and multiples episodes of restorative surgery.

Although the 'wait-and-see' policy is still adopted by some ophthalmologists, contemporary management of TED relies on immunosuppression as early as possible in any patient with signs likely to lead to significant impairment of orbital functions – namely the presence of classical signs of inflammation, restriction of ocular ductions or the onset of proptosis or optic neuropathy. Most patients respond well to adequate doses of corticosteroids and low-dose retrobulbar radiotherapy is used in the majority of patients showing a response to steroids (with the exception of some diabetics). The aim is to have all patients off steroids within 3–4 months. Acute surgical intervention might be necessary in a very few patients with optic neuropathy persisting despite high-dose steroids or for severe corneal exposure problems.

Rehabilitative surgery is generally indicated when the ocular and endocrine disease has been controlled, and may include a combination of orbital decompression, strabismus surgery and lid surgery. The most significant change over the past decade has been in the use of aesthetic orbital decompression; this procedure having been previously regarded with horror because of massive incisions for poor results. The contemporary 'best result'

decompression is that performed through a minimal incision and, in almost all cases, will reduce exophthalmometry to within the normal range.

BEST PRACTICE AND FUTURE PROSPECTS IN THYROID CANCER

Dr Kate Newbold, Consultant Clinical Oncologist, Royal Marsden Hospital, London

The incidence of differentiated thyroid cancer is increasing but thankfully the disease-specific mortality is not following the same trend. This does mean, however, that there are more patients living with the diagnosis of thyroid cancer and for the majority this diagnosis will not impact on their life expectancy. In these patients the management of the disease must be balanced with treatment-induced morbidity and the stratification of the risk of recurrence becomes increasingly important. In a minority, thyroid cancer takes an aggressive course and conventional management includes surgical resection, thyroid stimulating hormone suppression and repeated administrations of radioiodine. Once refractory to radioiodine, there is no conventional treatment option, but with better understanding of the biology of thyroid cancer there has been an explosion of trials investigating novel agents such as tyrosine kinase inhibitors. These novel agents have shown promising activity in differentiated thyroid cancer but remain within the research arena at present.

Many aspects of the management of thyroid cancer are changing and these will be reviewed and discussed.

THE HAPPY THYROID CONSULTATION

Mrs Janis Hickey, Director, British Thyroid Foundation

With almost 20 years of listening to people with thyroid disorders, the British Thyroid Foundation (BTF) is well placed to provide feedback to medical and health professionals about patients' experiences of thyroid disorders and relationships with doctors. As well as providing information and support to thyroid patients, the BTF is an organisation that works closely with doctors and nurses, and communicating the patient perspective is one of the BTF's responsibilities.

The presentation explores common concerns, covering general thyroid as well as thyroid disease-specific areas that are of importance to the patient, and refers to BTF's campaigns that aim to improve the patient experience. Striking the balance between patients' concerns and medical evidence is not always easy and further thyroid research is perhaps needed before patients feel satisfied with the answers to their questions. Suggestions are made, however, that could leave more (if not all) patients feeling happier when they leave the consulting room.

GLYCATED HAEMOGLOBIN – NEW UNITS... AND A DIAGNOSTIC TOOL FOR DIABETES?

Professor Eric Kilpatrick, Consultant in Chemical Pathology, Hull Royal Infirmary/Hull York Medical School

The measurement and clinical use of glycated haemoglobin in the form of haemoglobin A_{1c} (HbA_{1c}) is changing rapidly. The past decade has seen the undoubted benefits of harmonising HbA_{1c} results to DCCT (NGSP) values so that results from different laboratories are more comparable with one another and with those in major clinical trials. Unfortunately, these results are not a true reflection of the actual amount of HbA_{1c} in the sample. Now that this amount can accurately be established there is a considerable educational challenge in adapting to the new IFCC or, more correctly, the SI unit for this test. Of reassurance is that this is the last change that should ever need to be made.

There is much interest in extending the use of HbA_{1c} to the diagnosis rather than just the monitoring of diabetes. Using this test for diagnosis has advantages compared with traditional glucose criteria, such as the lack of a need for the patient to be fasting. However, an HbA_{1c} diagnosis identifies a different group of patients to glucose, so some identified by this means may be normoglycaemic, while others excluded may be hyperglycaemic. Other, often silent, conditions affecting HbA_{1c} such as haemoglobinopathies and haemolytic diseases means that questioning a future diagnosis (or not) using this test may require a low threshold of clinical suspicion.

IS THE BRAIN A TARGET ORGAN IN DIABETES?

Professor Christopher Ryan, Professor of Psychiatry, Psychology, Health and Community Systems and Clinical and Translational Science, University of Pittsburgh, USA

Early neuropathology studies of brain autopsy material indicated that poorly controlled diabetes can induce a profound diabetic encephalopathy, but more recent reports have typically failed to find evidence of clinically significant functional or structural changes in the brain of people with diabetes. In this presentation I argue that distinct 'neurocognitive phenotypes' can be identified for

children and adults with type 1 or type 2 diabetes, that these reflect the operation of somewhat different pathophysiological processes and that these have different implications for the remediation and prevention of cognitive complications.

Studies of diabetic children demonstrate that the diagnosis of diabetes early in life is associated with a greatly increased risk of cognitive impairment, whereas diagnosis after a critical period has few significant cognitive sequelae. This pediatric research further suggests that the metabolic derangements occurring at around the time of diagnosis play a major role in inducing brain remodeling – likely via processes occurring at the blood–brain barrier. Studies of adults with type 1 diabetes have identified a second, and independent, pathological process – microvascular damage secondary to chronic hyperglycaemia. This mechanism is most strongly associated with mental slowing, which may be mainly a consequence of microstructural damage to white matter tracts and reductions in cerebral blood flow.

Studies of both adolescents and adults with type 2 diabetes reveal the presence of memory dysfunction as well as psychomotor slowing and, while these mild deficits are ubiquitous, they do not appear to worsen over time. Despite much discussion of diabetes as a risk factor for the development of clinically significant dementia, such effects are weak and not convincing.

A PRACTICAL GUIDE TO PITUITARY RADIOTHERAPY

Dr Sara Erridge, Consultant Clinical Oncologist and Honorary Senior Lecturer, Edinburgh Cancer Centre

Radiotherapy is a key component in the management of pituitary tumours, with local control rates exceeding 90% for macroadenoma and hormone normalisation in a significant proportion. However, this treatment is not without potential side effects so necessitates the identification of those most likely to benefit and a careful discussion of the risks. There are a number of methods of delivering this treatment, for example 3D conformal radiotherapy, intensity-modulated radiotherapy, single fraction and fractionated stereotactic radiotherapy. I will review the pros and cons of each.

ANDROGEN DEFICIENCY IN OLDER MEN... AND WOMEN

Professor Richard A Anderson, Professor of Clinical Reproductive Science, Queen's Medical Research Institute, University of Edinburgh

As men age, so their production of testosterone declines. This has long been recognised from cross-sectional studies, and has now been confirmed in

longitudinal analyses. This raises the key questions of whether testosterone replacement should be considered and, if so, when? This requires adequate assessment of the hypogonadal state, both symptomatically and biochemically. There has been a very substantial increase in testosterone administration to older men in recent years, but this has not been paralleled by increases in our understanding of the risks and benefits. Most well-designed studies have been of relatively short duration, and shown modest improvements in, for example, strength and body composition. Recent data based on large population studies have added to our understanding of which are the key symptoms, and how they relate to serum testosterone concentrations. These provide a basis for future well-designed studies of efficacy and safety.

Androgen treatment of women is yet more controversial. Advances in biochemical testing have in fact been regressive in our ability to determine serum testosterone concentrations in the female range. The predominant indication is low interest in sex, now termed hypoactive sexual desire disorder, and a female-specific testosterone patch is marketed for this in the context of surgically induced menopause. There have been well-designed placebo-controlled RCTs, which show modest increases in sexual desire and activity, but therapy is often discontinued by women themselves. As with men, long-term safety is not established.

SOLID PANCREAS AND ISLET CELL TRANSPLANTATION IN SCOTLAND

Mr John Casey, Consultant Transplant Surgeon, Royal Infirmary of Edinburgh

Transplantation of the whole pancreas (normally simultaneously with a kidney transplant) is an established treatment option for some type I diabetics, providing near-normal glucose control and protection from many of the secondary complications of diabetes. This is only an option for a small group of diabetic patients with advanced disease and even in the most experienced hands carries a high morbidity and mortality (40% and 3–5% respectively). Transplantation of islets alone offers an attractive alternative to whole pancreas transplantation and is associated with a lower incidence of serious complications.

There has been a worldwide resurgence over the past few years in the use of islet transplantation as a treatment for a sub-group of type I diabetic patients and clear benefits have been demonstrated in appropriate patients. These benefits have been reproduced in many centres worldwide and in the UK and include reduced insulin requirement (and, in many cases, insulin independence), greatly improved glycaemic control and,

most importantly, reversal of life-threatening hypoglycaemic unawareness.

The Scottish Pancreas Transplant programme has been based in Edinburgh for the past ten years and patient outcomes are on a par with the largest units worldwide. Funding has now also been released to provide an islet transplant and isolation facility based in Edinburgh for Scottish diabetic patients with hypoglycaemic unawareness. Over the past six months our islet lab has become established and we expect to perform Scotland's first islet transplant imminently.

POORLY CONTROLLED TYPE I DIABETES – STRUCTURED EDUCATION OR DIABETES TECHNOLOGY?

Professor Eric Renard, Professor of Endocrinology, Diabetes and Metabolic Diseases, University of Montpellier I, and Head of Clinical Research and Innovation Department, Centre Hospitalier Universitaire de Montpellier, France

The goal of the insulin therapy of type I diabetes is the maintenance of near-normal blood glucose levels, including an HbA_{1c} level close to 7%, with minimal occurrence of hypoglycaemia, and a combined optimal quality of life. The participation of the patient is crucial to reach control of type I diabetes. Beside techniques of insulin self-administration, the patient must be taught to perform self blood glucose monitoring and to adapt insulin doses accordingly. An optimally structured education should include the management of basal insulin needs, and both the prevention and the correction of glucose excursions at meal intakes and in case of interfering events. Moreover, the diabetes care team should be available when needed outside programmed visits.

Poor diabetes control is often the result of the failure in implementing delivered education in everyday life. Reformatted education that takes into account the obstacles to patient empowerment in diabetes care is always the first option to be considered. The recent development of telemedicine allows more frequent interactions with the healthcare team. Blood glucose variability in spite of a good implementation of diabetes education to multiple daily insulin injection (MDI) therapy, resulting either in HbA_{1c} level in excess or in frequent hypoglycaemia, is the main indication for pump therapy. Thanks to higher flexibility in tuning insulin delivery, pump therapy allows improvement in diabetes control. Continuous glucose monitoring (CGM) may be combined to pump therapy or associated with MDI. The benefits of pump and/or CGM options also depend from specific structured education.

BARIATRIC SURGERY IN TYPE 2 DIABETES

Mr Duff Bruce, Consultant in General Surgery, Aberdeen Royal Infirmary

Excess weight has serious implications for the patient and the health service. Foresight and the recent Office of Health Economics reports highlight both the economic costs of untreated severe and complex obesity and the benefits of treatment. Diabetes, cardiovascular disease, respiratory disease, fertility, pregnancy complications to mother and child and certain cancers are all markedly increased with increasing adiposity, but, more importantly, risks are reversed by weight loss. For example, weight loss following gastric bypass can result in the amelioration of type 2 diabetes in up to 80% of patients. Effective treatment is either cost-dominant (in the case of lesser degrees of overweight treated by Counterweight interventions) or recouped within one to three years when more severe and treated surgically.

Robust evidence supports surgery: a recent randomised controlled trial showed improved control of weight at two years in the surgical group. This was associated with 70% remission of type 2 diabetes (11% traditional group), reduced HbA_{1c} and fasting plasma glucose levels, reduced use of glycaemic control medications, fewer subjects with metabolic syndrome and greater improvement in insulin resistance, levels of triglycerides and high-density lipoprotein.

Diabetes guidelines, including those of the Scottish Intercollegiate Guidelines Network, endorse bariatric surgery for type 2 diabetes management (body mass index >35). In the UK only 2–4% of those clinically eligible have access to surgery. Debate at national levels strives to identify patient priority models and the development of multidisciplinary teams that can deliver this service. As a key patient group that can benefit, type 2 diabetes sufferers have an important stake in the outcomes of service-delivery discussions.