

# Selected abstracts from the RCPE Diabetes and Endocrinology Symposium 2009

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## **SHORT STATURE/DELAYED PUBERTY – WHOM, WHEN AND HOW TO TREAT?**

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Late puberty, particularly when accompanied by short stature, is the commonest reason for referral to a paediatric endocrinologist. Constitutional delay of growth and puberty is common in boys. Pathological causes include chronic systemic disease, a range of endocrine disorders and Turner's syndrome in girls.

Emotional and psychological consequences of pubertal delay are not dependent on underlying pathology. Treatment, when necessary, should aim to mimic closely normal pubertal progression so as to optimise growth, cosmetic appearances, bone mineralisation, testicular maturation in boys and psychological maturation (quality of life) – current regimens for either sex are not ideal.

Listen to and empathise with the patient – explanation and, where appropriate, reassurance is always important. Do not over-investigate – diagnosis is important, but you do not have to have underlying pathology to suffer emotionally with delayed puberty. Treat with androgen/oestrogen if necessary, with the intention of reproducing a physiological growth pattern and inducing and maintaining changes in secondary sexual development at a physiological age and tempo.

### *Further reading*

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- Zevenhuijzen H, Kelnar CJH, Crofton PM. Diagnostic utility of a low-dose gonadotropin-releasing hormone test in the context of puberty disorders. *Horm Res* 2004; 62:168–76.

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## **FUTURE TREATMENT OF TYPE 1 DIABETES (ISLETS/STEM CELLS/MONOCLONAL ANTIBODIES)**

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Patients with type 1 and 2 diabetes have insufficient insulin secretion to maintain blood glucose control. The

defective insulin secretion is due in large part to both a near complete (type 1 diabetes) or partial (type 2 diabetes) loss of beta cells. In type 1 diabetes the loss of beta cells is due to autoreactive T cells, while the mechanisms of increased apoptosis in type 2 diabetes is through endoplasmic reticulum stress. Hyperglycaemia can be reversed in both type 1 and 2 diabetes by restoring beta cell mass by pancreas transplantation. Shortage of organ donor pancreas and the need for immunosuppression limits this approach.

Islet transplantation showed promise, but insulin independence, if achieved, is short-lived. Beta cell regeneration from endogenous sources is an attractive option. Beta cell mass grows rapidly in childhood by beta cell replication and is then maintained in adulthood by formation of new beta cells from pancreatic progenitors, with a beta cell life span of approximately three to six months. In diabetes there is ongoing beta cell formation but at a rate that is insufficient to replace accelerated beta cell loss (shortened beta cell life span). One approach to restore beta cell mass would be to promote beta cell regeneration and suppress accelerated beta cell apoptosis.

An alternative approach being considered is to generate functional beta cells from human embryonic stem cells. There has been progress in this field recently, but the approach has important limitations to overcome, which include tumor formation and immune protection. Transdifferentiation of beta cells from bone marrow-derived stem cells and cord blood cells are also under active investigation.

### *Further reading*

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## **HIRSUTISM: A DERMATOLOGIST'S APPROACH**

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Endocrine factors regulate hair growth in two ways. Firstly, in most mammals melatonin and prolactin, acting directly and indirectly, modulate the intrinsic cyclical behaviour of the hair follicle to cause seasonal moulting.

Secondly, in humans and some other species, androgens cause changes in hair follicle size following sexual maturity. The nature and timing of these androgen-dependent changes vary according to body site – in most regions of the skin androgens stimulate hair growth, whereas on the scalp androgens may cause progressive miniaturisation of hair follicles in genetically predisposed individuals. Once established, these changes are only partly reversible, an important limitation of anti-androgen therapy.

Androgen-dependent changes in hair growth are more pronounced in men, but some degree of scalp hair loss and hirsutism are also common in women. Female hirsutism is often accompanied by other features of androgen excess. Female hair loss is less likely to be associated with hyperandrogenism, and there is some evidence for a multifactorial aetiology that includes non-androgenic pathways.

The diagnosis of hirsutism, a term conventionally applied to increased hair growth due to androgens, is usually easy, although the clinician needs to be aware that increased hair growth (hypertrichosis) does have other causes which, though rare, may superficially resemble hirsutism. Endocrinologists, dermatologists, beauty therapists and dieticians all have a part to play in the management of hirsutism. Non-systemic approaches include simple hair removal, electroepilation, laser hair removal and topical eflornithine, though not all are readily available on the NHS.

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## CHILDHOOD/ADOLESCENT DIABETES

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Clinicians working with young people with diabetes are frequently faced with challenges about how to discuss behaviour change to facilitate improved glycaemic control and sensitive issues around sex, drugs and alcohol. There is good evidence that psycho-educational interventions such as motivational interviewing improve both glycosylated haemoglobin (HbA<sub>1c</sub>) and quality of life measures, although a lack of skilled psychologists limits the availability of these interventions. Clinicians working in diabetes services report poor levels of training in communication skills.

The 'Talking Diabetes' training programme has been developed in Cardiff University, informed by data from a systematic literature review, telephone- and questionnaire-based surveys, focus group work, experimental consultations and serial meetings with a stakeholder advisory group. This web- and workshop-based

programme focuses on the importance of agenda-setting and the flexible use, where appropriate, of the three consultation styles ('directive', 'guiding' and 'following'). It is now being evaluated in a multi-centre, randomised trial in 26 centres around the UK by measuring the effects on HbA<sub>1c</sub>, quality of life and cost effectiveness in 697 young people with diabetes (the DEPICTED Trial). Results are expected early in 2010.

Given the limited availability of skilled clinical psychologists in the UK, greater attention now needs to be paid to improving the communication skills of clinical staff during routine clinic consultations, to help them deal with the majority of behaviour change/psychological issues that a patient may wish to discuss in order to improve their diabetes self-management.

### References

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## AUTONOMIC NEUROPATHY

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Diabetic autonomic neuropathy (DAN) is one of the most common and serious complications of diabetes. Despite this, it often goes unrecognised until it is well advanced, by which time it is associated with many disabling symptoms and premature death. Unlike other microvascular complications there are currently no simple tests that would allow for screening large numbers of people, leading to earlier detection and the deployment of interventions that would slow or possibly even reverse its progression. This has also limited the study of the natural history of the disorder and the impact of interventions in large-scale prospective trials. Novel techniques such as dynamic pupillography<sup>1</sup> and spectral analysis of heart rate variability<sup>2</sup> may allow for more widespread assessment and earlier detection of autonomic dysfunction, both in the research and clinical setting.

Diabetic autonomic neuropathy affects many organ systems, which may require specialised investigations. Clinical manifestations of DAN include resting tachycardia, orthostatic hypotension, constipation, gastroparesis, gustatory sweating, erectile dysfunction, sudomotor dysfunction, impaired neurovascular function, 'brittle diabetes' and hypoglycaemia unawareness. It has also been implicated as having an important role in sudden, unexpected death in people with diabetes.

Treatment options in DAN currently are based predominantly on symptom control. There is growing evidence that earlier identification of DAN could lead to the deployment of strategies, such as improving metabolic control and using therapies such as ACE inhibitors and beta blockers, to improve long-term outcomes. If diagnosis is delayed until the development of symptoms, the outcome is extremely poor, with five-year survival rates of only 50%.<sup>3</sup>

#### References

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- 2 Weston PJ, James MA, Panerai RB et al. Evidence of defective cardiovascular regulation in insulin-dependent diabetic patients without clinical autonomic dysfunction. *Diabetes Res Clin Pract* 1998; 42:141–8.
- 3 Vinik AI, Maser RE, Mitchell BD et al. Diabetic autonomic neuropathy. *Diabetes Care* 2003; 26:1553–79.

## DIABETIC FOOT

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Foot-related problems are the most common diabetes-related reason for admission to hospital. At any one time 2–5% of patients have a foot ulcer and around 1% have had an amputation. In some specialist centres the rate of

amputation is declining, and this is related to organisation of care and specialist multidisciplinary foot clinics. Foot screening and risk stratification has been demonstrated to identify the patients at greatest risk of foot ulceration, and such patients can be targeted with appropriate resources. There are educational initiatives that will result in the recognition of diabetes-related specialist skills in podiatry and orthotics.

Pregabalin, duloxetine, venlafaxine and oxycodone are all modern drugs with proven efficacy for treating diabetic neuropathy. Antibiotic sensitivities are changing and the risks of methicillin-resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile* have increased. In Scotland, flucloxacillin is now recommended as the first-line empirical antibiotic for diabetic foot infections, with doxycycline and co-trimoxazole or co-amoxiclav as first-line alternatives. Adding rifampicin is useful if there is associated osteomyelitis. Negative pressure wound therapy is an evidence-based wound treatment, especially for moist ulcers. Hydrotherapy as yet lacks evidence and is potentially expensive, although in the right setting it could be cost saving overall. Off-loading remains the cornerstone to the management of neuropathic foot ulceration and Charcot foot, while vascular interventions need exploring for any vascular problems.

Physicians looking after the diabetic foot have a variety of skills and interventions they need to develop.

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