

Endocrinology

DURING THE PAST DECADE there have been significant advances in the prevention, diagnosis and management of endocrine disease. Here I concentrate on two disorders with significant disease burden — diabetes and obesity.

Prevention. Preventing diabetes mellitus is a key goal in endocrinology. For type 1 diabetes, immunomodulation using nicotinamide and pre-emptive insulin therapy is being evaluated in high risk individuals (based on family history, autoimmune markers and metabolic profile).¹ For type 2 diabetes, the key strategy is the primary prevention of obesity.^{1,2}

Major trials in the 1990s have shown a continuous relationship between macro- and microvascular disease and hyperglycaemia, hypertension and dyslipidaemia. Current data indicate that remarkable improvements at the population level would be gained by achieving targets of glycohaemoglobin (HbA_{1c}) < 7%, blood pressure < 130/80 mmHg, and low-density lipoprotein cholesterol < 2.6 mmol/L, using available therapies (HMGCoA reductase inhibitors, ACE inhibitors, and angiotensin 2 receptor antagonists).¹ However, this knowledge is incompletely applied in practice and an important advance will be treating all patients with diabetes to established targets.

Diagnosis. Refinements in existing techniques, such as immunoassay and medical imaging, have allowed previously complex diagnostic algorithms (eg, assessment of thyroid status) to be performed cheaply and with a high degree of precision. Many monogenic endocrine disorders, including the multiple endocrine neoplasia syndromes, are now also identifiable by presymptomatic gene testing. With contemporary advances in molecular biology and bioinformatics, the search for susceptibility genes for diabetes, obesity and other polygenic diseases is also progressing rapidly.

Somatostatin-receptor (SR) imaging using radionuclide-labelled ligands allows localisation, staging and treatment planning in patients with SR-positive neuroendocrine tumours. An intraoperative γ -probe to localise labelled tissues (eg, with Tc-sestamibi) can also help localise occult tumour in patients with endocrine neoplasms.

Interventions. Effective interventions for established obesity include bariatric and gastric bypass surgery. Laparoscopic gastric banding has the advantage that it requires minimal access and is adjustable.² The pharmacological options for established obesity are currently limited. New drugs include the appetite suppressant sibutramine (a selective inhibitor of serotonin and noradrenaline reuptake) and orlistat (an intestinal lipase inhibitor). Individually, these agents achieve a 5%–15% weight reduction. Pharmacological agents that either suppress appetite or increase basal energy expenditure are likely to be developed over the next five years. Central factors (neuropeptide Y, melanocortins)



and adipocyte hormones (leptin) are potential pharmacological targets. Drugs which increase thermogenesis (β_3 -adrenergic-receptor agonists and mitochondrial uncoupling proteins) are also being evaluated.²

The thiazolidinediones are a new class of insulin-sensitising agents for treating type 2 diabetes. Non-sulfonyl-urea insulin secretagogues, such as the glinide class (eg, repaglinide), improve meal-related insulin release, but minimise the risk of hypoglycaemia. An increasing array of insulin analogues

(created by amino acid rearrangement in the insulin molecule) are available: rapid-acting agents (lispro and aspart insulin), and long-acting analogues (insulin glargine).

New ways of delivering insulin and monitoring glucose are also available or under trial. Inhaled (aerosolised) insulin is showing promise in clinical trials, although problems remain with delivery efficiency and thus cost. Mechanical pumps for continuous ambulatory subcutaneous insulin infusion are used increasingly,¹ offering improved glycaemic control for those willing to frequently monitor blood glucose level. Several technologies for continuous glucose sensing are also being developed, such as transcutaneous optical glucose sensing.

Pancreatic transplantation for treating type 1 diabetes has long been available in Australia. Limited donor availability and a better outcome have restricted this treatment to patients requiring renal transplantation. An alternative, islet-cell transplantation using modified low-dose immunosuppressive regimens, is showing early promise in clinical trials.¹

Developments in minimal-access endocrine surgery include laparoscopic adrenalectomy for benign adenoma (shorter hospital stay and lower morbidity), and minimal-access parathyroidectomy. The options for medical management of primary hyperparathyroidism are also expanding, with the identification of calcium-receptor agonists (calcimimetic drugs) which down-regulate parathyroid hormone secretion and normalise serum calcium level.

Conclusion. While diagnostic and therapeutic modalities currently under development offer much promise for managing patients with endocrine disorders, significant improvements in health could also be achieved by fully applying current knowledge, technology and existing pharmaceuticals.

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2. Mun EC, Blackburn GL, Matthews JB. Current status of medical and surgical therapy for obesity. *Gastroenterology* 2001; 120: 669-681. □