the detrusor muscle may compensate for appreciable obstruction at the bladder neck; conversely, large residual amounts of urographic media may be found in the absence of true obstruction.⁹ Bladder calculi will be seen on the plain film and diverticula and tumours at cystoscopy—so that the only justification for routine urography becomes detection of incidental lesions. For no other condition is an investigation recommended simply because it might result in the chance finding of disease distant from the focus of clinical attention.

The investigation is positively indicated if a patient has haematuria, unexplained uraemia (up to 15 mmol/l), urinary tract sepsis, or a history of renal disease or stones. Nevertheless, not surprisingly doctors are sometimes reluctant to condemn a patient to a long waiting list without some objective radiographic reassurance that a serious alternative explanation for the symptoms—such as a bladder tumour or early high pressure chronic retention—has not been overlooked.

Formal urodynamic evaluation is unnecessary in patients with uncomplicated prostatic hypertrophy. If a neurologically normal man over 60 with an enlarged prostate complains of hesitancy, frequency, and nocturia and has a poor independent urinary flow rate then he needs a transurethral resection. When irritative symptoms (frequency, urgency, urge incontinence) predominate, however, urodynamic assessment may be vital to avoid removing the prostate from a man with non-obstructive detrusor instability. Flow rate and pressure flow studies will usually suffice, and complex videocystometry should be reserved for equivocal cases.⁹

In most specialist urological units routine cross matching of blood for patients undergoing transurethral prostatectomy is no longer considered necessary. Grouping and saving the serum will suffice if an arrangement is made with the laboratory whereby blood can be made available at short notice. Blood should be cross matched for high risk groups—the very frail, patients with anaemia or blood dyscrasias, or those with prostates estimated to weigh over 50 g.

Clinical evaluation, examination for fitness for anaesthesia, basic blood tests, grouping and saving of serum, a plain abdominal radiograph, and bacteriological examination of the urine are all that should be required preoperatively in most patients admitted with acute urinary retention. What these patients need is a prompt return to life without a catheter. If malignancy is suspected, serum acid and alkaline phosphatase concentrations should be measured. Transrectal ultrasonography may be required, but bone scanning can wait until histological examination has confirmed malignancy. The same applies to patients with chronic retention, but renal function studies and urography or ultrasound should be conducted if upper tract dilatation is suspected and urodynamic studies if low pressure chronic retention is suspected. The man presenting with chronic symptoms of outlet obstruction requires the same assessment as the patient with acute retention. Urography, urodynamics, transrectal or abdominal ultrasonography, and computed tomography should be reserved for specific indications rather than used routinely as part of an irrationally overcomprehensive investigation programme.

P H O'REILLY

Consultant Urological Surgeon,
Stepping Hill Hospital,
Stockport SK2 7JE

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The search for a hormonal switch for obesity

Very rarely is obesity caused by a primary endocrine disturbance such as hypothyroidism or hypercortisolism, and most patients do not have any obvious cause, hormonal or otherwise.¹ Feeding behaviour in man is controlled by a multiplicity of signals, but the search has continued for a peptide that might finally control appetite. We do not seem to be near to finding such a peptide.

The regulation of feeding behaviour is highly complex since the conscious appreciation of hunger and satiety is dependent on so many factors including genetic predisposition,² all the senses, mood, cultural habits, socioeconomic status, intercurrent illness, and, last but not least, food availability.³ The functional distinction between a ventromedial hypothalamic satiety centre and a ventrolateral hypothalamic feeding centre has served as a valuable experimental model⁴ and may be relevant in certain types of genetically obese mice as well as in the rare cases of hypothalamic obesity in man.⁵ Other brain areas, however, are also important in feeding behaviour, especially the paraventricular nucleus of the hypothalamus, the globus pallidus, and the amygdala.³ These hypothalamic centres may sort and integrate afferent information from both the periphery and other brain regions. The centres produce an efferent autonomic response as well as a conscious appreciation of the need to eat.

Many hypotheses have tried to provide an all embracing explanation for appetite regulation and its disorders, but we are not as simple as the mollusc pleurobranchia, which eats everything in sight until its appetite is switched off by its egg laying hormone.⁶ In man we must consider the afferent input from taste, smell, and sometimes even auditory and visual stimuli. Additionally there are important autonomic afferent signals from stomach, gut, and perhaps liver that may interact with messages (dependent on specific hypothalamic receptors) from certain nutrients and metabolites such as glucose, glycerol, amino acids, and possibly free fatty acids.^{3,7-9}

Against this complex background are feedback signals mediated by classical hormones both old and new, and since many of the peptide hormones are synthesised in both the brain and the periphery (especially the gut and pancreas) there is much speculation on the specific production and target sites in relation to appetite control. Important among these are thyroid hormones¹⁰ and glucocorticoids,¹¹ which stimulate appetite, and cholecystokinin, bombesin, somatostatin, and pancreatic glucagon, all of which can produce some degree of satiety.¹² Although in man

1 Bauer DL, Garrison RW, McRoberts JW. The health and cost implications of routine excretory urography before transurethral prostatectomy. *J Urol* 1980;123:386-9.

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exogenous insulin stimulates appetite,¹³ giving insulin intracerebroventricularly to rats suppresses it¹⁴; and rats treated with antiinsulin antibodies show an increase in food intake.¹⁵ Knoll has claimed the existence in human serum of a potent anorexigenic glycoprotein—with a molecular weight of 40 000–60 000 and comprising 87% carbohydrate and 12–8% amino acids—that he has named “satielin.”¹⁶ Full characterisation and further confirmatory studies are now required. Most recently a polypeptide produced by macrophages has been isolated that can induce a severe cachectic and shock like state when given to experimental animals; it also has widespread effects on the immune system.^{17–22} This molecule, named “cachectin,”²² is identical to tumour necrosis factor and may play a part in the cachexia and weight loss associated with malignancies.²²

Within the hypothalamus there appear to be important ventromedial serotonergic and ventrolateral dopaminergic inputs with possible inhibitory gabaergic interneurons.²³ But many neurotransmitters or neuropeptides have been reported to exert some effect on appetite when given either peripherally or intracerebroventricularly. Most are inhibitory including corticotrophin releasing factor, vasoactive intestinal peptide, thyrotrophin releasing hormone (and its metabolite cyclo-histidyl-proline-diketopiperazine), neurotensin, bombesin, calcitonin, calcitonin gene-related peptide, somatostatin, and cholecystokinin; but opioid peptides (particularly dynorphin, the endogenous ligand for K opioid receptors), enkephalins, and growth hormone releasing factor are stimulatory.^{3, 12–23}

Obese patients often have altered basal and stimulated hormone concentrations, including hyperinsulinaemia with peripheral insulin resistance, increased cortisol turnover with reduced adrenocorticotrophic hormone responses, and impaired growth hormone and prolactin responses to most provocative stimuli.¹ Such secondary hormonal changes may each serve to exacerbate the primary disorder, and obese patients deal less efficiently with a calorie load than a lean individual.²⁷ Hyperinsulinaemia also occurs in certain rodent models of obesity through a cholinergic mechanism and may mediate the obesity in some but not all experimental animal models.²⁸ Because of the difficulty in assessing hypothalamic function in man some investigators have studied the regulation of anterior pituitary hormones. These patients show an appreciable impairment of growth hormone responses to all provocative stimuli,¹ including growth hormone releasing factor.^{29–30} The findings of reduced prolactin responses to insulin hypoglycaemia and thyrotrophin releasing hormone in obese patients are more conflicting. This lack of responsiveness may be caused by alterations to specific neurotransmitter pathways, hypothalamic peptide release, or pituitary function itself or by some other alteration in peripheral feedback signals. Such findings have led some to postulate a primary hypothalamic defect in obesity, but this seems unlikely since most changes occur as a consequence of obesity and return to normal after loss of body weight.^{1, 27} Recently a small subgroup has been identified in whom the impaired prolactin response to insulin hypoglycaemia is not apparently reversible by weight loss.^{31–32} Whether or not this reflects an endogenous hypothalamic defect in some patients remains to be established since no long term follow up data are yet available.

In conclusion, there have been no dramatic breakthroughs

in understanding and no revolutionary new concepts but rather a steady accumulation of data confirming the multiplicity of interacting factors that control feeding behaviour. If most human obesity is anything other than the consequence of a variably reduced individual ability to control a pleasant appetite and to balance intake and expenditure, then there are an enormous number of potential malfunctions that may each require highly specific treatment. Despite this the search continues for an overriding final mediating peptide that can switch off the feeding centre or switch on the satiety centre. The ability to control or administer such a peptide could provide a simple therapeutic approach.

C DIEGUEZ

Research associate

M F SCANLON

Reader in medicine

Neuroendocrine Unit,
Department of Medicine,
University of Wales College of Medicine,
Cardiff CF4 4XN

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