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. 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.

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 overcomprensive investigation programme.

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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.6 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 pleurobranchus, which eats everything in sight until its appetite is switched off by its egg laying hormone.4 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.7,8

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 hormones9 and glucocorticoids,10 which stimulate appetite, and cholecystokinin, bombesin, somatostatin, and pancreatic glucagon, all of which can produce some degree of satiety.11 Although in man

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exogenous insulin stimulates appetite,\(^2\) giving insulin intra-

cerebroventricularly to rats suppresses it;\(^3\) and rats treated

together with antinsulin antibodies show an increase in food intake.\(^4\)

Knoll has claimed the existence in human serum of a potent

anorexigenic glycoprotein—with a molecular weight of

40000-60000 and comprising 87% carbohydrate and 12-8% amino acids—that he has named \"satiatins.\"\(^5\) Full character-

isation and further confirmatory studies are now required.

Most recently a polypeptide produced by macrophages has

been isolated that can induce a severe cachetic and shock like

state when given to experimental animals; it also has widespread effects on the immune system.\(^6\)\(^7\) This molecule,

named \"cachectin,\" is identical to tumour necrosis factor and may play a part in the cachexia and weight loss associated

with malignancies.\(^8\)

Within the hypothalamus there appear to be important

ventromedial serotoninergic and ventrolateral dopaminergic

inputs with possible inhibitory gabaergic interneurons.\(^9\)

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), neuro-

tensin, bombesin, calcitonin, calcitonin gene-related peptide,

somatostatin, and cholecystokinin; but opioid peptides

(particularly dynorphin, the endogenous ligand for K opioid

receptors), encephalins, and growth hormone releasing factor are

stimulatory.\(^9\)\(^10\)\(^11\)\(^12\)\(^13\)

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

proconvulsive stimuli.\(^9\) 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.\(^14\)

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.\(^14\) 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

proconvulsive stimuli,\(^9\) including growth hormone releasing

factor.\(^15\)\(^16\) The findings of reduced prolactin responses to

insulin hypoglycaemia and thyrotrophin releasing hormone in

obese patients are more conflicting. This lack of responsive-

ness 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.\(^17\) Recently a small

subgroup has been identified in whom the impaired prolactin

response to insulin hypoglycaemia is not apparently reversible

by weight loss.\(^11\)\(^12\) Whether or not this reflects an endogenous

hypothalamic defect in some patients remains to be estab-

lished 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 multi-

plicity 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.

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