Community health councils

He was concerned that relations between these councils and the medical profession should not get off to a bad start. "We must be careful not to get into a position of mistrust and dispute with members of community councils," he said. "The councils ought to make it easier for there to be understanding between the community being served and those serving them. Sometimes there seems unnecessary antagonism on both sides, unfortunately."

For example, some community health councils had been interested in the frequency of induction in their local hospital. Obstetricians had resented this as an interference with their clinical freedom. "Something like induction is surely not a procedure an obstetrician would undertake without its acceptance by the patient. If the patient is doubtful she is entitled to an explanation. If within a community there is concern about

the treatment being given at the local hospital, then if the position is medically defensible the CHC can be given an explanation. They then ought to be able to help the community accept what is being done. If the practice is not openly medically defensible the doctor ought not to be doing it."

"We talk a great deal about clinical freedom," said Sir George. "Clinical freedom is not something handed out with a medical diploma. It is not a right of doctors—clinical freedom is a right of patients and is to be defended from intervention by authority as justifiable only when exercised in their interests. That implies that the patient should understand how the doctor has made his decision. Furthermore, as a profession we owe it to ourselves, and to our patient, that on-going studies by the profession itself of the outcome of treatment should be part of the health services of every district. Faith, or clinical impression, is no longer enough."

Today's Treatment

Endocrine and metabolic diseases

Pituitary diseases

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Several recent developments have influenced opinion and practice in managing disorders of the pituitary gland. Advances in protein chemistry have provided an almost complete range of natural or synthetic replacements for the hormones of the pituitary gland, available for use when needed. Some of the hypothalamic hormones have been identified, synthesised, and made available for clinical application. Methods of controlling excessive secretion of pituitary hormones have been improved. Hormone assays are now widely available and may be used to define precisely the nature and extent of disordered pituitary function, as well as to monitor the response to treatment. The laboratory service for these assays has recently been established in Britain on a regional and national basis in the National Health Service or university-supported establishments. A commercial hormone assay service is also available and can provide almost any test likely to be required.

The relevance of the close anatomical and functional relationship between the hypothalamus and the pituitary gland has received fresh emphasis with the introduction into clinical practice of hypothalamic hormones (see table). The first of these to come into use was thyrotrophin-releasing hormone followed by gonadotrophin-releasing hormone (GRH) and more recently growth hormone release inhibiting hormone (somatostatin). Several drugs also have analogous effects on this system

—for example, bromocriptine, clomiphene, levodopa, and the phenothiazines.

Effective management of pituitary diseases requires a grasp of all these considerations and of the opportunity that these developments provide for full correction of disordered function.

Pituitary disease may present in many ways. Endocrine effects from hypersecretion of a single hormone, usually growth hormone (GH) or adrenocorticotrophic hormone (ACTH), may predominate. Occasionally the output of more than one hormone may be increased. On the other hand, partial or complete failure to secrete one pituitary hormone or more may be found, or hypersecretion of one hormone—for example, GH—may be associated with failure to secrete some or all of the remainder. This potential variety of change helps to emphasise the value of hormone assays in management. In addition to disorders of function, structural changes in the gland, as a result of trauma, infection, infarction, and tumour, may in turn produce their own specific clinical features.

Pituitary tumours

Some of the visual symptoms associated with a pituitary tumour, most commonly a change in acuity, are readily recognised by patients: nevertheless, they may easily overlook a visual field defect large enough to be detected by confrontation. Features such as these are an urgent indication for neurosurgical advice and in most instances for decompression of the optic chiasma. The choice of procedure may lie between a craniotomy and a transfrontal approach to the sella turcica or an extracranial path by the trans-sphenoidal route may be chosen.

Many surgeons advise a course of radiotherapy after operation on chromophobe or eosinophil adenomas of the pituitary gland to deal with any tumour tissue that may remain. Others

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Pituitary hormones and hypothalamic hormones or factors that control production of the former. Secretion of pituitary hormones without a specific endocrine gland as target appears to be controlled by both releasing and release-inhibiting hormones formed in the hypothalamus. Hypothalamic factors are referred to as hormones when their chemical structure has been determined

Hypothalamic hormones and factors	Abbreviation	Pituitary hormone	Abbreviation	Target
Thyrotrophin releasing hormone	TRH	Thyroid stimulating hormone (thyrotrophin)	TSH	Thyroid gland
Corticotrophin releasing factor	CRF	Adrenocorticotrophic hormone	ACTH	Adrenal cortex
		Luteinising hormone	LH	Ovary
Gonadotrophin releasing hormone	GRH	Interstitial cell-stimulating hormone	ICSH	Testis
		Follicle-stimulating hormone	FSH	Ovary
Prolactin releasing factor	PRF	Prolactin		Testis
Prolactin inhibiting factor	PIF	Prolactin		Breast
Growth hormone releasing factor	GHRF	Growth hormone	GH	Breast
Growth hormone release inhibiting hormone (somatostatin)	GHRH	Growth hormone		Numerous
MSH release and inhibiting factors		Melanocyte stimulating hormone	M $\ddot{S}$ H	Melanocyte s

prefer to avoid an open operative procedure, particularly if the visual fields are intact, and instead attempt to destroy the tumour either by irradiation from external sources or by implanting sources of radiation such as yttrium-90 within the pituitary tumour. This may be done through a cannula inserted under radiographic control through the nose into the sella turcica. A similar route may be used to insert a probe carrying a cryosurgical device which allows the operator to destroy, by the application of cold, the tissue surrounding the tip of the probe. Thus a wide range of procedures is available for the treatment of pituitary tumours; the choice in each patient will depend on many factors, including the techniques available in any particular centre.

ABNORMALITIES OF HORMONE SECRETION

A pituitary tumour must be treated on its merits, both as a surgical problem of space-occupation with potential pressure effects and as a medical problem of hypersecretion or secretory failure, with the need to suppress or replace. Apart from pituitary disease, abnormalities of pituitary hormone secretion may arise from hypothalamic dysfunction.

PITUITARY HYPERSECRETION

Of the seven hormones produced by the anterior lobe of the normal pituitary gland, excessive secretion of three only—namely GH, ACTH, and prolactin—is likely to need intervention. Hypersecretion of GH is usually associated with acromegaly and an eosinophil adenoma of the pituitary gland. Persistent hypersecretion in these circumstances may be associated with diabetes mellitus and hypertension, in addition to the other features of acromegaly. There are good reasons, therefore, for suppressing GH secretion when assays show this to be persistent and excessive. Destruction of the tumour is usually attempted, but there is often some residual hypersecretion. Bromocriptine may be used to suppress secretion of GH in acromegaly, but the drug is still undergoing clinical trials.

Pituitary basophilism with a raised output of ACTH is responsible for many cases of Cushing's syndrome. When there is a tumour responsible for this in the pituitary gland, it is often so small as to be undetectable by the usual methods and bilateral adrenalectomy is still appropriate. In some patients treated in this way, the pituitary basophil adenoma may grow slowly over several years until it becomes clinically apparent, when it would merit treatment if it is producing local pressure effects. Sometimes persistent hypersecretion of ACTH and melanocyte stimulating hormone are associated, so that the patient becomes inordinately pigmented as in Addison's disease, in spite of adequate replacement treatment with corticosteroids (Nelson's syndrome).

Excessive secretion of prolactin is usually recognised because it is associated with galactorrhoea, though the hormone may be circulating in excess without this feature. There are many potential causes of galactorrhoea but a principal mechanism appears to be failure to maintain an appropriate level of pro-

duction of the hypothalamic prolactin release inhibiting factor. An important though rare cause is a craniopharyngioma, blocking the pathway between the hypothalamus and the pituitary gland, but destructive lesions of the hypothalamus, other endocrine disorders, and some drugs may be responsible. Bromocriptine is even more effective in suppressing secretion of prolactin than it is in suppressing GH in acromegaly. Hyperprolactinaemia may accompany secondary amenorrhoea and cause infertility that can be corrected by bromocriptine. Indeed, some patients under treatment with bromocriptine for acromegaly and for galactorrhoea have proved surprisingly fertile.

Hypopituitarism

The development and clinical application of a comprehensive range of assays for pituitary hormones make it more logical to describe pituitary failure in terms of the precise nature and extent of the hormone deficit rather than as a series of clinical syndromes, a concept more appropriate to a discussion on diagnosis than on treatment.

GROWTH HORMONE

Although failure of GH secretion is a feature of many patients with pituitary disease, the only clinical condition in which the use of this scarce and expensive hormone may be justified at present is in dwarfs who are shown by assays to be GH deficient. Species specificity and the need therefore to use material of human origin, coupled with the scarcity of therapeutic preparations, have restricted the use of this material. Where the conditions for use are fulfilled, however, and the child is aged under about 12, successful growth has been achieved. Supplies of growth hormone in Britain are distributed by the Medical Research Council for use in carefully selected cases.

THYROTROPHIN

Hypothyroidism is a common complication of pituitary insufficiency, but such patients should be treated with thyroxine, rather than attempting to use thyroid stimulating hormone as a substitute. When starting treatment it is important to ensure that adequate corticosteroid replacement treatment has been given before treatment with thyroxine starts; otherwise acute adrenal insufficiency or coma may be precipitated. Conventional doses up to 0.2 mg daily of thyroxine may be required in an adult.

CORTICOTROPHIN

Failure of ACTH secretion is the most important endocrine defect in hypopituitarism because it is potentially the most lethal. The need for replacement treatment is judged on the evidence of adrenocortical insufficiency, which may be shown

to be reversible by injecting ACTH. In view of the expense, the need to give ACTH or one of the synthetic analogues by injection, and the less predictable plasma levels of corticosteroids that may be achieved in this way, ACTH treatment is seldom used in treating hypopituitarism. Corticosteroids are usually used, and prednisolone or prednisone are to be preferred to cortisol or cortisone, since oedema is more likely to occur with the two latter steroids. Doses cannot be predicted precisely for every individual, but an average requirement would be 5 mg of prednisolone in the morning and 2.5 mg in the evening.

The usual precautions about increasing the dose of steroid two-, three-, or four-fold in the face of the stress of infection, injury, or operation—if necessary substituting a steroid given by injection—must be emphasised to the patient, who should be urged always to carry a card or to wear a bracelet indicating his requirements.

GONADOTROPHINS

Initiation of gonadal function in the adolescent of both sexes and its maintenance in the adult depends upon the stimulus provided to the ovary and testis by the pituitary gonadotrophins follicle-stimulating hormone (FSH) and luteinising hormone (LH) (interstitial cell-stimulating hormone). Production of these hormones by the pituitary gland depends in turn on the hypothalamic releasing hormone gonadotrophin releasing hormone (GRH) (luteinising hormone releasing hormone). The clinical features will vary according to the time of life at which hypothalamopituitary failure of gonadotrophin secretion develops. A late onset of puberty in either sex may cause much anxiety to patients and parents alike, and it may sometimes be reassuring to both to exclude pituitary disease by showing that pituitary function is normal. In most forms of pituitary disease with failure of hormone production, gonadotrophin secretion is usually the first to cease. Primary or secondary amenorrhoea may therefore be relatively early features of pituitary failure. In men, hypogonadism with failure to develop or maintain secondary sexual characteristics, impotence, or occasionally infertility may call for treatment.

In secondary gonadal insufficiency there is seldom any justification for attempting to treat deficiencies of this type with pituitary hormones, and almost all the advantages lie with replacement treatment using gonadal hormones. Numerous preparations of oestrogens and progestogens are available. A suitable combination is provided by many varieties of the contraceptive pill.

There are several methods available to replace androgen secretion in the male. Fluoxymesterone may be taken by mouth, and in doses of 5-20 mg daily it is usually satisfactory. The dose should never exceed 20 mg/day. Many long-acting preparations of testosterone which may be given conveniently at intervals of one to two weeks by intramuscular injection are also available. Fused pellets of testosterone, each with 200 mg of the androgen, may be implanted subcutaneously through a cannula under the skin of the anterior abdominal wall. Five pellets usually provide adequate androgen for six to nine months.

When infertility that has been shown to be due to pituitary or hypothalamic disorder and not to ovarian disease is the presenting complaint there are several methods of promoting ovulation. It is, of course, essential that the man should have been shown by seminal analysis to be potentially fertile before embarking on treatment to promote ovulation.

Treatment with clomiphene, given in courses of 50 mg twice daily for five days, may be followed by ovulation. GRH is under trial at present with similar objectives in mind. When the pituitary gland has been shown to be incapable of responding adequately to GRH or clomiphene, a suitable mixed preparation of FSH and LH (Pergonal), obtained from human menopausal urine, has been used successfully to treat failure of ovulation, and purer preparations of gonadotrophin, extracted from human pituitary glands have also been effective. These preparations of

gonadotrophins should only be used when facilities for monitoring the ovarian response by plasma assays of oestrogens and progesterone or by urinary oestrogen and pregnanediol assays are available.

Hormone treatment for male infertility requires full assessment of the patient with sperm counts before this is undertaken. The value of clomiphene and of gonadotrophins is being investigated.

PANHYPOPITUITARISM

This term is usually reserved for patients with complete failure of all the functions of the anterior lobe of the pituitary gland. They require replacement treatment with corticosteroids and thyroxine, and men may need androgen treatment. If they go unrecognised, stop their treatment, suffer an injury or a severe infection, or undergo an operation without their dose of corticosteroid being increased temporarily three- or four-fold they may lapse into coma, sometimes with hypothermia which may be rapidly fatal. In such a crisis they will require a full regimen of intravenous fluids and electrolyte replacement. Intravenous hydrocortisone should be given as an initial bolus of 100 mg, followed by infusion of 100 mg four-hourly, and antibiotics for any accompanying infection. Thyroxine replacement treatment is usually less urgent.

Diabetes insipidus

In addition to interference with the function of the posterior lobe of the pituitary gland and its connections with the hypothalamus, diabetes insipidus may also be associated with damage to the anterior lobe of the pituitary gland. It may develop after operations on or near the hypophysis, sometimes transiently and without evidence of damage to the function of the anterior lobe of the pituitary gland.

If the neurohypophysis is totally incapable of producing vasopressin the most satisfactory treatment, until recently, has been with pitressin tannate in oil, 5 units on alternate evenings by subcutaneous injection. Precautions were required to ensure that the hormone reached the syringe and the patient. If the response failed to persist for a full 48 hours, supplements of lypressin could be given by nasal spray every few hours until the next injection was due. Pitressin tannate in oil however has now been withdrawn from the market. A new synthetic analogue of vasopressin—namely, desmopressin—has recently been marketed. This drug is very effective, the response lasting 12-24 hours after each nasal instillation, but the treatment will cost about £1 daily compared with about 5p using pitressin tannate in oil.

Alternative methods of controlling diabetes insipidus successfully, provided the patient can secrete some vasopressin, include the administration of chlorpropamide, 100-250 mg daily; clofibrate, 1 g daily; or carbamazepine, 100-400 mg daily. Thiazide diuretics—for example, bendrofluazide 5 mg daily—may also be effective by itself or in combination with some of the oral preparations already mentioned. Potassium supplements should be given if oral diuretics are used.

Most functions of the pituitary gland can now be replaced when the need arises. The means are available and they should be used with monitoring services to ensure that the response is adequate but is not overdone.

At some schools there is a rule that children wear plimsolls only within the school building, probably to protect the floors. Is this undesirable for health?

Apart from those with sweaty feet, for whom open sandals are more comfortable, good fitting plimsolls are admirable for children.