Surgical Treatment of Endocrine Disorders

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FOREWORD

Modern endocrinology originated from simple clinical observation—the syndrome of Graves' disease associated with goitre, the syndrome of acromegaly associated with pituitary tumours. Later came the concept of the pituitary gland as the conductor of the endocrine orchestra, a concept now known to have only a limited relevance. We now recognize a complete endocrine system, with glands different in mode of action but co-ordinated by a multitude of stimulatory and inhibitory mechanisms and together subserving all the metabolic activities of the body.

In contrast with our growing appreciation of the integrated nature of the endocrine system our organization for treating endocrine disorders has been characterized by increasing specialization and exclusiveness so that diseases of different endocrine glands are treated variously by neurosurgeons, gastroenterologists, urologists, paediatricians, gynaecologists and generalists. This book cannot be expected to reverse the trend of specialism but it will at least ensure that each in his own narrow field may become fully informed about the whole area.

The title is *The Surgical Treatment of Endocrine Disorders* but this work is very much more than a textbook of operation techniques. We have progressed a long way since the days when surgeons were content to act the part of technicians and now it is a truism that the surgeon, like every other member of the therapeutic team, must be fully conversant with each problem as a whole. This is especially true in relation to the endocrine system, for all aspects of the care of patients with hormonal disease, the diagnosis and prognosis, the choice of treatment and the after-care, depend to an exceptional degree upon full knowledge of the disease process and the relevant laboratory findings.

This book is a product of the collaboration of nearly a dozen authors, under the general editorship of Dr. William Hamilton, who in his capacity as a paediatric physician also acts as co-author of the chapter on the male

reproductive system and the chapter on the breast. It is a tribute to his influence and the willing co-operation of his colleagues that the book presents such a uniform standard of excellence.

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PREFACE

The modern endocrinologist is primarily a physician. However without the assistance of colleagues in the fields of biochemistry and surgery his ability to diagnose and treat would undoubtedly be impaired.

It is now the practice in the larger centres for colleagues with cognate interests to form themselves into teams, through which the maximum expertise is channelled to the patient. The 'endocrinology team' is no exception for the diagnosis and treatment of endocrine disease is not the prerogative of a single individual. In the team the surgeon is not 'the last resort' nor 'the snatcher of brands from the burning'; he is frequently the doctor without whose treatment the patient will perish. The areas wherein this is true are the subject of the book.

It should not be considered strange that a surgical treatise is edited by a physician. The physician (endocrinologist) is concerned with the whole endocrine system; the surgeon is an expert in the management of endocrine disease in a restricted field relating to one gland. In addition, individual surgeons report their work and research in journals devoted to their own specialty and it is therefore difficult to keep abreast of the surgical developments in all fields. This book aims at bringing together in one volume up-to-date information on all surgical aspects of endocrine disease. 'Endocrine surgery' is truly advancing fast on many fronts at the same time.

Finally because surgical standards are constantly rising, it is becoming increasingly difficult for the physician to gain entrance to the surgeon's sanctum sanctorum. The need for a shower, sterile garments, masks, headgear and the like, before approaching, not the patient on the table but the array of sophisticated instruments surrounding the patient, all make it extremely difficult for the interested physician 'to pop in and have a look'.

The object of the book is to provide a ready reference for those interested in the surgical problems presented by endocrine disease and for whom the operating theatre is less accessible.

It is not a surgical textbook. There is in it sufficient practical surgery for the surgeon and sufficient diagnostic instruction for the physician. Each

contributor is an expert in his field. Each has written lucidly bearing in mind that he has written for surgeons, physicians and students at both undergraduate and postgraduate level.

William Hamilton

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1 The Pituitary and Hypothalamus

ROBERT TYM

INTRODUCTION

In the past 20 years many new techniques have been developed for operating upon and irradiating the pituitary region, though none has brightened the prospects quite so dramatically as the introduction of the operating microscope. This has enabled the trans-sphenoidal microneurosurgical technique to be perfected. Over the same two decades new methods have been developed in both endocrinology and radiology to delineate more clearly functional and anatomical abnormalities in the hypothalamic, sellar and parasellar regions. Thus it can now be said of the neurosurgery and radiotherapy of the pituitary region that it has become less a problem of dramatically saving life or sight and more a problem of trying to re-establish and maintain a normal endocrine milieu.

There are three broad pathologies which require neurosurgical intervention. These are:

(1) Pituitary adenomata where it is necessary to combat the local effects, or general effects or both.

(2) Sellar or parasellar lesions not primarily of pituitary origin but affecting or endangering pituitary or hypothalamic function.

(3) Generalized carcinomatosis of the breast or prostate and certain types of diabetic retinopathy likely to be improved by removal of the pituitary.

Full consideration of all aspects, diagnostic and surgical of these conditions would be virtually inexhaustible if it were comprehensive. Craniopharyngiomata, parasellar aneurysms, the empty sella syndrome and suprasellar meningiomata will be considered later, but little or nothing will be said of glial tumours and hamartomata of the optic chiasm and hypothalamus, intrasellar chordomata, pituit-

ary and parapituitary metastatic lesions, pituitary and parapituitary abscesses and granulomata and sphenoidal sinus mucoceles. These last mentioned conditions are clearly rare but because they enter into the differential diagnosis of lesions in the pituitary region, they are enumerated here.

PITUITARY ADENOMATA

Pituitary adenomata are classified according to (1) the type of adenoma and (2) the size of the adenoma.

The type of adenoma

(a) The clinically non-secreting adenoma.

(b) The adenoma secreting excess corticotrophin resulting in Cushing's disease.

(c) The adenoma secreting excess growth hormone resulting in acromegaly or gigantism.

(d) The pituitary hypertrophies—principally that associated with juvenile myxoedema.

(e) Generalized lipodystrophy—where the clinical syndrome, though associated with an increase in ACTH secreting cells in the pituitary gland is not improved by the removal of the gland.

In the past a simple classification of adenomata based on the staining characteristics of haematoxylin and eosin on the intracellular granules of the predominant adenoma cell was accepted. There are at least three factors which now make such a criterion for classification obsolete. First, many 'chromophobe' adenomata are undoubtedly associated with either acromegaly or Cushing's disease. Secondly, more recently developed histological staining techniques indicate that there is cellular specificity for each of the seven anterior pituitary hormones—one cell type, one hormone. Third, by the more recently developed hormone assay techniques an excess of a hormone other than corticotrophin or growth hormone has been demonstrated in the serum of patients with pituitary adenomata in whom there is no clinical evidence of hormone excess.

It is not appropriate, either, to classify an adenoma as 'endocrine inactive' even though it could be shown that no hormone was being secreted in excess. As adenomata increase in size they nearly always interfere mechanically with the functioning of the rest of the normal gland and later with the pituitary stalk and hypothalamus. Thus there is created a secondary disturbance of the endocrine system. It

may well be eventually, when hormone assay is more routine and when histochemical and other methods of examining adenomatous tissue are agreed reliable, that all the pituitary adenomata will be reclassified according to the specific pituitary cell predominating and the amount, if any, of the specific hormone being secreted.

In this context it may be justifiable to predict that the next secreting pituitary adenoma to gain 'independent recognition' will be a prolactin-secreting adenoma. Prolactin secretion is under a dual hypothalamic control—first through a releasing hormone and second through a release-inhibiting hormone. Thus circulating prolactin levels may be high either because of a prolactin-secreting adenoma or alternatively because another type of adenoma may be of such size as to interfere mechanically with the hypothalamus or pituitary stalk so vitiating the effects of the inhibiting hormone. The non-adenomatous portion of the pituitary is then free to secrete prolactin in excess. There is further clinical difficulty in the apparent inconstancy of the relationship between high circulating levels of prolactin and galactorrhoea. Whether a prolactin-secreting adenoma is a 'primary' adenoma of the pituitary or 'secondary' to a primary hypothalamic disorder which results in an excessive secretion of the releasing hormone or a decrease in an inhibiting hormone is uncertain. These possibilities will be mentioned subsequently in relation to radiotherapy.

The commonest pituitary hypertrophy is that associated with pregnancy. The gland may exceed 1 ml in volume. In juvenile myxoedema there is an occasional non-adenomatous growth of the pituitary up to 3 ml, well beyond the limit of normal pituitary size. This increase, which does not appear to be progressive beyond about 3 ml, is not considered to be adenomatous but is presumed to be a response to a long-standing over-production of TRH which produces an increase in the number of TSH-secreting cells in the pituitary.

Slightly enlarged sellae, especially in association with primary or secondary amenorrhoea, suggest pituitary hypertrophy secondary to an excess production of gonadotrophin-releasing hormones. Such suggestions certainly complicate the management of these patients who are also suspected of having a small pituitary adenoma which is interfering with the normal functioning of the pituitary gland.

The size of the adenoma

INTRASELLAR ADENOMA (STAGE I)

The adenoma varies in size from 1 to 30 ml. Adenomata usually

start in the antero-inferior portion of the anterior lobe and as they expand in a spherical fashion, they enlarge the sella and push the non-adenomatous portion of the gland posteriorly and superiorly. Whether an adenoma remains below the diaphragma sellae as it grows probably depends upon the size of the opening in the diaphragma through which the pituitary stalk enters the sella.

ADENOMA EXTENDING THROUGH THE DIAPHRAGMA UPWARDS TO REACH THE HYPOTHALAMUS AND THE OPTIC CHIASM (STAGE II)

Various forms of the classical syndrome of panhypopituitarism and bitemporal hemianopia are produced.

ADENOMA EXTENDING WIDELY BEYOND THE SELLA (STAGE III)

The presentation is as an intracranial space occupying lesion large enough to interfere with general as well as local brain and cranial nerve function (to produce various forms of paralysis) and with the intracranial hydrodynamics (to produce raised intracranial pressure and papilloedema).

Growth characteristics of the adenomata

The 'doubling time' of a pituitary adenoma, i.e. the time taken to double its volume at a constant growth rate, is in the region of 6 to 9 months. Intra-adenoma cyst formation or haemorrhage greatly increases the rate of increase in volume. There is a more rapid increase in volume during pregnancy either due to faster cell growth or to oedema. If ovulation is artificially induced as in a case of amenorrhoea secondary to a pituitary adenoma that has either been missed completely or misjudged in size, then pregnancy may precipitate a rapid deterioration in vision as a result of chiasmal compression at mid or late term. Emergency operation is then indicated. Central necrosis of an adenoma may slow its rate of increase in volume or decrease its size. The adenoma may even be destroyed altogether.

Eventually an enlarging adenoma is likely to become asymmetrical. With an intrasellar adenoma a matching asymmetry of the sellar floor develops which gives a characteristic appearance of a 'double

floor' when seen in the lateral X-ray. The floor may eventually become eroded and if the adenoma grows down through the dural lining of the sella it will invade the sphenoidal air sinus and from there the posterior nasopharynx. Spontaneous cerebrospinal fluid (CSF) rhinorrhoea then occurs. Lateral growth from inside the sella leads to invasion of the cavernous sinus with sixth and other cranial nerve involvement.

At a late stage some of the corticotrophin-secreting adenomata causing Cushing's disease change their growth characteristics and become malignant. They invade and destroy the brain, cranial nerves and bone and lead to fairly rapid death. Such malignant change occurs in up to 10 per cent of inadequately treated cases.

'Pituitary apoplexy'—acute intra-adenoma haemorrhage

Spontaneous haemorrhage or acute haemorrhagic necrosis occurs within both apparently normal pituitary glands and pituitary adenomata. The normal gland, the optic nerves and chiasm, and the hypothalamus and stalk, continue to function almost normally despite a considerable amount of slow distortion from a slowly growing mass emerging from the sella. They do not however continue to function when distorted by a rapidly expanding mass such as may follow intra-adenoma haemorrhage. Local neurological defects and general endocrine deficiencies may then develop very rapidly, with catastrophic effects such as a decrease in the level of consciousness and disordered thermoregulation and salt and water metabolism. These effects arise from sudden hypothalamic compression. In addition there is blindness from sudden chiasmal or optic nerve compression; bilateral sixth nerve paralysis and eyelid oedema from sudden compression of the cavernous sinuses; and profound panhypopituitarism from sudden loss of all secretory power of the normal gland. Blood may also leak from the haematoma, through the capsule, into the CSF to produce some or all of the devastating clinical features of an acute subarachnoid haemorrhage more usually seen following the rupture of an intracranial aneurysm. Not all cases are catastrophic, though many need urgent surgery or trans-sphenoidal stereotactic aspiration of the clot. In some, pituitary apoplexy heralds a hitherto unsuspected adenoma. Other fortunate survivors are reported to have had spontaneous cure following the apoplexy. Both the adenoma and the acromegaly disappear when the haemorrhage or necrosis destroys all the functioning adenoma cells.

NON-PITUITARY SELLAR AND PARASELLAR CONDITIONS

Craniopharyngioma

A craniopharyngioma may be of any size, up to 300 ml, and when at its largest it may occupy one-half the volume of a cerebral hemisphere. A craniopharyngioma originates in or above the sella or inside or outside the third ventricle. The rate of growth is unknown. Probably each tumour grows at an inconstant rate rendered more erratic by cyst formation. The clinical complications to which they give rise depend mainly upon three factors: the site of origin, the age at which expansion starts, and the rate and direction of expansion. In general the rate at which clinical disturbance of function develops is a good indication of the rate at which further trouble can be expected.

Craniopharyngioma cysts are primary or secondary. Primary cysts are lined with craniopharyngioma (epithelial) cells and contain an often viscid fluid rich in cholesterol. The cholesterol may escape into the CSF and give rise to a series of self-limiting episodes of chemical meningitis. Secondary cysts appear to be loculations of CSF produced by arachnoidal adhesions in the vicinity of the tumour. Many craniopharyngiomata calcify, the density of calcification giving an indication of tumour age. Flaky calcification suggests a younger, more rapidly growing tumour. The calcification does not necessarily delineate its overall size and shape and the calcified portion is not necessarily the portion that is currently increasing in size. Calcification in the parasellar region does not establish the diagnosis of craniopharyngioma for almost any adenoma, tumour or aneurysm in the region may calcify. Craniopharyngiomata however do so most often.

The various sites of origin and directions of growth enable the craniopharyngiomata to produce all the same combinations of clinical signs and symptoms as the non-secreting pituitary adenomata. Some appear to stop growing and remain of constant size for long periods. Non-progressive visual loss then becomes associated with marked optic atrophy and the effects of prolonged hypopituitarism over the patient's growth period results in pituitary dwarfism. It is then very tempting to let sleeping dogs lie but unfortunately craniopharyngiomata cannot be relied upon to sleep for ever.

Growth upwards in the midline indents the hypothalamus and third ventricle from below and in addition to all other effects it may obstruct the foramina of Munro to produce internal hydrocephalus from dilatation of the lateral ventricles. Papilloedema may then be

superimposed upon optic atrophy. Growth of the tumour upwards and laterally into one or other cerebral hemisphere usually leaves the patient with an intact endocrine system but suffering from the effects of cerebral hemisphere damage, i.e. hemiparesis, dementia, various forms of agnosia and difficulties with spacial orientation.

Accompanying any compression of the optic chiasm there is a concomitant compression of the supra-optic region of the anterior wall of the third ventricle, the site of the supra-optic nucleus where damage is likely to interfere with the production of antidiuretic hormone (ADH). If compression is prolonged then spontaneous or steroid therapy-provoked diabetes insipidus will ensue from a decline in ADH production.

Suprasellar meningioma

It is an axiom that a suprasellar meningioma does not cause endocrine disturbances—by which is meant that it does so rarely. The site of origin of a meningioma is the dura between the anterior rim of the sella and the entrances of the optic nerves into their canals. As they expand, usually in the shape of a cauliflower, they envelop, stretch or compress one or both optic nerves. Despite the name, such tumours only rarely extend above the sella. Involvement of the chiasm depends upon how near (pre-fixed) or how far (post-fixed) the chiasm is from the entrances to the optic canals. A large tumour of 15 ml may cause a lot of damage to vision but leave the chiasm, the rest of the hypothalamus, the stalk and the pituitary gland undisturbed. They are often difficult to diagnose because the visual loss is initially subtle. A *frontal meningioma* arising in the anterior fossa of the skull, or from the sphenoidal ridge may reach a considerable size (100 ml) before diagnosis and before it interferes with intracranial hydrodynamics to produce raised intracranial pressure. Detection may be delayed if there is neither blindness (or only unilateral blindness) nor epilepsy. Eventually, by sheer size the brain is so distorted that the hypothalamus is shifted backwards and the pituitary stalk becomes sharply kinked over the dorsum sellae (the posterior rim of the sella). This shift, however, is so gradual that there is no disturbance of endocrine function. If the backwards shift of the hypothalamus is more rapid, caused for example by an *extradural haematoma*, then transient diabetes insipidus from a neuropraxia of the secretory neurones of the stalk may follow, presuming the patient survives. The venous portal system is less vulnerable to distortions so that there is no failure of the anterior pituitary.