In short, the success of their lower-limb amputation as a treatment to provide a comfortable existence had depended on the accuracy of the initial assessment of their capabilities and the effectiveness with which the deficiencies in those capabilities had been supplemented. Admission to a rehabilitation unit geared to individual needs, at the time of issue of the preliminary walking pylon, enables such an assessment to be made and a realistic decision to be reached on the manner in which optimal mobility for each patient can be obtained.

The choice lies at present between wheel-chair life and the retention of the pylon (or a cosmetically acceptable development of the pylon) as the permanent prosthesis or the use of the pylon as a preliminary to the eventual use of a definitive limb. Not until this choice has been made by the combined decision of the medical and paramedical staff concerned in his care and its rationale has been demonstrated to the patient by his own performance can appropriate independence training and domestic reorganization be finalized. Such a decision, taken early in amputee life and subject to repeated review, would go a long way towards correcting the present concept of the geriatric amputee as an elderly patient to whom a prosthesis needs to be fitted and substituting that of an elderly patient whose potentially serious disability may be mitigated by a judicious combination of method training, prosthetic fitting, and the supply of suitable equipment.

Conclusions

From our experience during this survey and in the past three years we believe that the total problem of the geriatric amputee could be improved by: (1) better appreciation and application of preoperative and early postoperative physiotherapy to prepare the geriatric patient physically for amputation by strengthening muscles of which extra exertion will be required, in the stump, contralateral leg, and arms, and by prevention of flexion contractures; (2) more comprehensive psychological preparation for the mental trauma to which amputation gives rise; (3) better integration of prosthetic fitting and training with the total rehabilitation of the patient by his admission to an appropriate unit at the time of issue of the pylon for comprehensive assessment and walking and independence training; (4) better liaison between such a unit and the welfare services

responsible for patient care in the home, so that suitable social and domestic support will be forthcoming immediately he leaves hospital; and (5) greater readiness on the part of hospitals and limb centres to provide appropriate wheel-chairs and walking aids to geriatric amputees before discharge.

Amputation is frequently dismissed by surgeons as evidence of the failure of measures to maintain and improve the peripheral circulation, and this negative approach is often communicated to patients. The realization that amputation will herald the end of persistent pain or terminate a series of surgical procedures can only be impressed on a patient by careful and repeated explanation and will enable him to view the procedure in its true perspective. He will understand that as a part of a highly individualized rehabilitation programme amputation will help to ensure a limited but effective mobility, independence for all normal activities of daily living, and the ability to live at home in reasonable comfort, independence, and dignity.

This survey could not have been carried out without the unfailing and unstinted help of the staff of the Oxford Artificial Limb and Appliance Centre. Mr. G. R. Parry F.R.C.S., medical officer, has taught us much about the care of stumps and the technicalities of limb fitting. Mr. W. Francis, the manager, and his staff have reduced the problems of the administration and documenting aspects of the study to a minimum. We have been greatly helped and impressed by the interest and co-operation of the limb fitters, and our own staff of physiotherapists, occupational therapists, and nurses have continued to render exceptional service, often in very difficult circumstances. We are also indebted to the surgeons in the region who have all followed our experiment in rehabilitation with interest and encouragement. But above all we have been encouraged by the remarkable achievements of the patients when put into a situation of positive encouragement and active rehabilitation.

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Clinical Endocrinology

The Hypothalamus

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Knowledge of the role of the hypothalamus has accumulated rapidly during the last two decades. Thus it is now apparent that this small area of the brain is an integrative centre for the neural control of pituitary function, temperature regulation, and food and water satiety, as well as taking part in the control of the cardiovascular system.

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Anatomy

The anatomical boundaries of the hypothalamus are not well defined, but anteriorly and below lies the optic chiasma and posteriorly its limits are the mammillary bodies and interpeduncular fossa. Laterally are the internal capsule and inferior part of the thalamus. Superiorly is the third ventricle; the lateral walls of the lower part of the ventricle form part of the hypothalamic area. Below, the hypothalamus extends downwards to join the pituitary stalk.

Embryologically, the hypothalamus, pituitary stalk, and posterior lobe of the pituitary are derived from an outgrowth

of the developing brain, so that they form one anatomical and functional unit. The anterior pituitary is formed from an outgrowth of the foregut, which comes into apposition with the neurohypophysis and develops vascular but not neural connexions with the hypothalamus. Within the hypothalamus certain groups of neurones can be recognized as "nuclei." In man the most easily identified are the supraoptic and paraventricular nuclei, which are responsible for the elaboration of vasopressin (anti-diuretic hormone) and oxytocin respectively. From these nuclei there are well-defined neural connexions with the posterior lobe of the pituitary through the axons forming the supraoptico-hypophysial tract of the pituitary stalk. Many afferent nerves pass into the hypothalamus from other areas of the brain, and these connexions are of great importance in regulating endocrine activity; nevertheless, the exact pathways are largely unknown.

Blood Supply

The substance of the hypothalamus and its nuclei are supplied by small branches from the arteries of the circle of Willis. Thus vascular lesions affecting the latter may give rise to hypothalamic damage. From a capillary plexus in that part of the ventral hypothalamus known as the median eminence loops of vessels run down the pituitary stalk to end in a capillary bed in the anterior pituitary, thereby forming a true portal system, which is the sole blood supply to the anterior pituitary. In contrast, the posterior pituitary has a separate arterial blood supply. It is the peculiar arrangement of vessels to the anterior pituitary which provides its functional connection with the hypothalamus.

Functions of Hypothalamus

CONTROL OF POSTERIOR PITUITARY FUNCTION

Studies in animals have shown that the posterior pituitary hormones vasopressin and oxytocin are actually produced by the neurosecretory cells of the supraoptic and paraventricular nuclei, whence they are transported down the axons of the supraoptico-hypophysial tract to be liberated at the nerve

endings in the posterior pituitary. In this sense, the posterior lobe acts merely as a storage organ and the hypothalamus is responsible for the secretion of the hormones. Removal of the posterior lobe of the pituitary or section of the stalk at a low level usually results in only a transient loss of vasopressin, so that diabetes insipidus is a temporary sequel. If the supraoptic nucleus is destroyed, however, permanent diabetes insipidus follows. The main factors which control the release of vasopressin are changes in the osmotic pressure of the plasma reaching the hypothalamus and changes in blood volume.

CONTROL OF ANTERIOR PITUITARY FUNCTION

There is now good evidence that neurohormones are secreted at nerve endings in the region of the median eminence, and that these substances pass down through the portal vessels to the anterior lobe causing the release of the various anterior pituitary hormones. From studies in animals hypothalamic releasing factors have been described for thyrotrophin, corticotrophin (ACTH), gonadotrophins (both follicle stimulating and luteinizing hormones), growth hormone, and melanocyte stimulating hormone. In the case of prolactin, which is responsible for stimulating milk secretion, the hypothalamus normally exerts an inhibitory influence, through a specific prolactin inhibitory factor.

At the present time the releasing factors for thyrotrophin, luteinizing hormone, and growth hormone have been characterized. They are all small polypeptides, the first being a tripeptide containing proline, histidine and pyroglutamic acid; the other two factors are decapeptides. Loss of any of these factors by lesions affecting the appropriate area of the hypothalamus will lead to secondary hypopituitarism in various degrees. In the case of prolactin, loss of the hypothalamic inhibitory factor will cause inappropriate lactation.

APPETITE, THIRST, TEMPERATURE, AND SLEEP

Experimental lesions or stimulation of certain areas of the hypothalamus give rise to appreciable changes in appetite. Bilateral lesions made in the ventromedial nuclei cause excessive appetite and obesity, whereas lesions in the lateral hypothalamus cause aphagia. The concept has therefore arisen of a ventromedial "satiety" centre and a lateral "feeding" centre. The exact mechanisms which regulate these centres are largely unknown.

Loss of vasopressin secretion leads to polyuria which in most cases results in severe thirst. There appear, however, to be centres separate from the supraoptic nucleus which determine the sensation of thirst. In animals, electrical stimulation of the hypothalamus lateral to the paraventricular nuclei gives rise to intense polydipsia, and lesions in various areas, especially the anterior hypothalamus, are followed by failure to drink (adipsia).

It has been known for many years that hypothalamic lesions can cause disturbances in body temperature. In some experiments bilateral lesions in the anterior part of the area caused hypothermia but the localization is not well defined. Probably certain areas of the hypothalamus are particularly sensitive to the temperature of the blood flowing through them and the body temperature can be regulated by the subsequent effector mechanisms of vasodilatation or shivering. The production of fever in response to infection is thought to be due to the effect of a pyrogenic substance from the leucocytes on the anterior hypothalamus.

Lesions in the hypothalamus are sometimes associated with increased somnolence, but probably the sleep rhythm is dependent on the activity of the reticular formation of the brain as a whole, and the hypothalamus includes only part of this formation.

Hypothalamic control of pituitary hormone secretion.

CARDIOVASCULAR SYSTEM

Studies in animals have shown that stimulation of parts of the lateral hypothalamus leads to a rise in blood pressure and stimulation of other areas results in a vasodilator response in skeletal muscle together with other features of the defence mechanism. There are, however, no clearly defined clinical counterparts to these experimental findings.

Clinical Manifestations of Hypothalamic Disorders

Much of the information described above has been derived from the classical neurological techniques of electrical stimulation and production of circumscribed lesions in animals. In man the localization of function within the hypothalamus may not be necessarily identical with these experimental findings, but there are several well-recognized clinical features which follow various destructive processes affecting the hypothalamic area.

DIABETES INSIPIDUS

Diabetes insipidus may result from a lesion situated at any level from the supraoptic nucleus to the posterior pituitary, but only when the nucleus itself is destroyed or the median eminence region of the ventral hypothalamus is damaged does permanent loss of vasopressin secretion result. Diabetes insipidus may be the only evidence of anterior hypothalamic damage or it may occur in association with other manifestations described below.

Diabetes insipidus must be distinguished from diabetes mellitus, and other causes of polyuria, such as chronic renal disease, hypokalaemia, hypercalcaemia, and nephrogenic diabetes insipidus. But perhaps the most difficult differentiation is from compulsive water drinking, or psychogenic polydipsia. In this condition the polyuria is a result of polydipsia which is itself a manifestation of a psychiatric disorder. Whether the excessive desire to drink is mediated from the higher centres through the thirst centre of the hypothalamus is not known. The differentiation from true diabetes insipidus is not always easy but can usually be made on the basis of the tendency to a low plasma osmolality, often a normal reaction to forced water deprivation, the continuation of excessive drinking after vasopressin administration, and the presence of a psychiatric disturbance.

ADIPSIA

Adipsia is a rare sequence of damage to the thirst centre in the anterior hypothalamus. Absence of the thirst mechanism in a fully conscious patient has been reported, together with other clinical evidence of hypothalamic disturbances, as a sequel to subarachnoid haemorrhage. Unless the patient is constantly exhorted to drink, severe dehydration occurs.

HYPOPITUITARISM

Hypopituitarism may result either from a primary disorder of the pituitary itself or from a lesion in the hypothalamus causing loss of any of the pituitary hormone releasing factors. Clinically, the distinction is not always apparent since large intrasellar pituitary tumours may extend into the hypothalamus, and, conversely, suprasellar tumours may compress the pituitary. If diabetes insipidus is also present it usually indicates a hypothalamic origin for the hypopituitarism. When more of the hypothalamic releasing factors become available, tests may be devised to distinguish the two types of pituitary deficiency.

DISTURBANCES OF PITUITARY HORMONE REGULATION

Even in the absence of clinical pituitary disorders there may be alterations in the hypothalamic regulation of pituitary hormone secretion. The well-recognized "feedback" control of ACTH secretion, for example, is centred in the hypothalamus rather than in the pituitary, and the normal depression of plasma cortisol levels produced by the administration of a powerful glucocorticoid such as dexamethasone may fail to occur with hypothalamic lesions. In addition, the normal nyctohemeral (diurnal) rhythm of ACTH secretion (as indicated by the levels of plasma cortisol) is often lost in the presence of hypothalamic damage. These tests may sometimes be useful in investigating hypothalamic disorders.

Precocious Puberty

In most children who develop puberty at an abnormally early age, no organic lesion can be detected. In about 8% of cases, however, there is a tumour of the hypothalamus, usually in the posterior part of the area, and the appropriate neuroradiological investigations should be carried out to determine this possibility.

Obesity

Undoubtedly lesions affecting the ventro-medial hypothalamus can give rise to an abnormally large appetite with resultant obesity. This type of obesity usually coexists with other evidence of hypothalamic disease, such as diabetes insipidus or hypogonadism. When this combination occurs it has been termed "Fröhlich's syndrome," but this name is now of historic interest only and should be avoided. Many children, particularly boys, suffering from obesity and delayed puberty without any other symptoms of hypopituitarism, are misdiagnosed as Fröhlich's syndrome. In most of these children no evidence of a suprasellar or pituitary lesion is found. Treatment consists of dietary restriction only and puberty eventually develops normally in almost all cases. Possibly the condition is due to a temporary functional hypothalamic disturbance but there is no definite proof of this suggestion.

Other Conditions

Anorexia nervosa, a psychiatric disorder resulting in loss of appetite, is associated with amenorrhoea due to low gonadotrophin secretion. Hence the disorder could be mediated through the hypothalamus, but again there is no direct proof of this possibility.

Somnolence sometimes accompanies hypothalamic disease, but often in the presence of a large tumour, such as a craniopharyngioma, particularly when there is obstruction to the third ventricle.

Disturbances of temperature regulation resulting in either hypothermia or hyperpyrexia may occur in the presence of tumours, surgical trauma, or even subarachnoid haemorrhage.^{1 2}

Galactorrhoea, or inappropriate secretion of milk, may result either from a prolactin-secreting tumour of the pituitary or by loss of the hypothalamic prolactin-inhibitory factor. Thus, after lesions of the pituitary stalk or in the presence of certain hypothalamic tumours, lactation may occur in the absence of pregnancy. Galactorrhoea which occasionally follows the use of chlorpromazine and other phenothiazine drugs or reserpine, is probably due to their suppressive effect on hypothalamic prolactin inhibitory factor.

When a hypothalamic lesion is suspected on clinical grounds a history of severe head injury, meningitis, or intracranial haemorrhage may be relevant. Plain radiographs of the skull are indicated to determine the presence or absence of changes in the appearance of the pituitary fossa. Calcification in the suprasellar

area may indicate the presence of a tumour, usually a craniopharyngioma. Further delineation of a hypothalamic tumour depends on special x-ray techniques such as radioisotopic brain scans, cerebral angiography, and pneumography. An electroencephalogram may occasionally provide confirmatory evidence but is rarely of much localizing value.

Nature of Lesions

Hypothalamic lesions are not always followed by clinical effects, presumably because bilateral destruction of a particular vital area is necessary before loss of function becomes apparent.

VASCULAR LESIONS

Severe vascular damage to the hypothalamus can follow a ruptured aneurysm of the circle of Willis.³ This may fairly often give rise to biochemical changes in pituitary function⁴ and much more rarely clinical disturbances, such as hypothermia and adipsia.²

TRAUMA

Severe head injuries or surgery affecting the hypothalamic area may lead to diabetes insipidus, disturbances of temperature control, obesity, and hypopituitarism. Crompton⁵ has shown that in many cases head injury causes haemorrhagic lesions of the anterior hypothalamus affecting the supraoptic and other nuclei. In some instances trauma results in transection of the pituitary stalk, thereby severing the neural connexions between the hypothalamus and posterior pituitary and, much less commonly, the vascular connexions with the anterior lobe.

INFECTIONS

Very occasionally basal meningitis due to tuberculous or virus infections may be followed by diabetes insipidus, temperature disturbances, a grossly excessive appetite, or hypopituitarism. Chronic granulomas, especially sarcoidosis, and histiocytosis may affect the hypothalamus usually as part of more generalized tissue disease.

TUMOURS

The commonest lesions to cause widespread hypothalamic damage are tumours, which may be primary or secondary.

Metastatic deposits in the area of the supraoptic nuclei from carcinoma of the breast or bronchus occur, resulting in diabetes insipidus. On rare occasions the hypothalamus is the site of a glioma, or more often the tumour arises from the optic nerve and invades the adjoining anterior hypothalamus. Much more common is a craniopharyngioma or a large pituitary adenoma which has extended to compress the hypothalamus.

Craniopharyngioma

This tumour comprises up to 13% of all intracranial neoplasms of childhood, though it may also manifest itself in adult life. It is a benign tumour arising not within the brain tissue but from the remains of the embryonic anterior pituitary (Rathke's pouch). Usually a cystic tumour, the craniopharyngioma is most often suprasellar in position and compresses the hypothalamus and optic chiasma. Sometimes there is obstruction to the third ventricle causing an internal hydrocephalus. Impairment of vision is a dominant clinical presentation often accompanied by various degrees of hypopituitarism, of which hypogonadism is the most common. As well as failure to develop puberty, retardation of growth often occurs and is due to the interference with the hypothalamic control of the secretion of growth hormone. Diabetes insipidus is present in about 30% of cases. In some instances, particularly with large tumours, obesity and somnolence are also part of the clinical picture. When there is internal hydrocephalus, symptoms of raised intracranial pressure such as headache and vomiting may be presenting features.

In about 60-70% of cases plain radiographs of the skull reveal suprasellar calcification. Full ophthalmological, neuro-radiological, and endocrinological investigations are required in all cases of suspected craniopharyngioma. The treatment is surgical decompression of the optic chiasma followed by intensive radiotherapy and the replacement of any hormone deficiencies. Useful recent reviews of the hypothalamus are provided by Sheehan,⁶ and the *British Medical Bulletin*.⁷

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Second Opinion, Please

Pulmonary Embolus

A DISCUSSION BETWEEN DR. W. DEWI REES AND DR. HOWARD JENKINS

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Case History

W.D.R.: I find assessing and treating other doctors' patients particularly difficult, especially when the problem posed is unusual. Such was the case when I was asked to visit a

53-year-old man, who was staying with his sister. The sister was slightly apologetic for asking me to visit as she considered him to be nervous person. Eight days previously he had been discharged from a teaching hospital and had come to Wales to recuperate. In hospital, he had been treated for swelling of the left leg. The swelling had been extensive and had reached