THE ENDOCRINES IN THEORY AND PRACTICE

This article is one of a series on Endocrinology contributed by invitation

PITUITARY TUMOURS THEIR CLASSIFICATION AND TREATMENT

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Like the majority of animal pituitaries the human gland is composed of: (a) a large epithelial lobe or pars anterior; (b) a posterior lobe, which is composed of a specialized form of glial tissue—the pars nervosa; (c) the pars intermedia, which consists of epithelial cells similar to those found in the anterior lobe; and (d) a narrow epithelial investment of the stalk of the gland—the pars tuberalis—which covers the anterior surface of the stalk and is reflected on to the anterior part of the floor of the third ventricle. Theoretically tumours might arise from any of these constituent parts, but actually primary tumours are commonly found only in the anterior lobe and pars tuberalis. No primary tumours of the pars nervosa have been described, though this part of the gland is quite frequently the site of malignant metastases.

Sagittal section of normal pituitary gland and surroundings, showing site of: (1) origin of adenoma; (2a and 2b) suprasellar and intrasellar epidermoid tumour; (3) Rathke's pouch cyst; (4) meningioma of tuberculum sellae; (5) hydrocephalic distension of third ventricle.

Tumours of the Anterior Lobe

Histologically the anterior lobe is found to consist of three distinct types of cells. Some of them have a non-granular cytoplasm, and hence are called "chromophobe cells." Others—the chromophils—have their cytoplasm packed with granules, and according to their staining reaction these granular cells are further subdivided into eosinophils and basophils. Histological studies have suggested that the chromophobe cell is the mother cell of these two types, and that by a process of differentiation certain chromophobe cells may develop into eosinophils and others into basophils. This relationship can be easily understood from the following scheme.

By ordinary methods of staining it is impossible to decide which chromophobes will develop into eosinophils and which into basophils, but by staining the Golgi apparatus it is possible to recognize the two types of transitional chromophobe cell.

The adenomas can be composed of any of these cell types. Chromophobe, transitional, eosinophil, and basophil adenomas may all occur. These tumours of the anterior pituitary are among the most common in the body. Routine examination of the human gland shows that they occur in about 10 per cent. of adults, and Costello gives even higher figures (22.5 per cent.). Only a small percentage of these ever become clinically apparent, the remainder consisting of nodules too small to give rise to any clinical symptoms. All types of adenoma are uncommon in children, and in the adult the chromophobe type is the most common.

Chromophobe Adenoma

The available evidence does not suggest that the chromophobe cell secretes any of the hormones of the anterior

lobe. Hence the clinical symptoms of a chromophobe adenoma are the result of its pressure upon and ultimate destruction of neighbouring tissues. As the pituitary gland is enclosed in the bony sella turcica, which is covered by a strong dural diaphragm, any expanding lesion will compress and destroy the gland itself. In this manner the symptoms of hypopituitarism arise. The growth of the adenoma almost invariably produces an enlargement of the

sella turcica. Subsequent growth of the tumour leads to distension of the dural diaphragm. Finally, the diaphragm gives way and the growth extends freely into the cranial cavity. It may attain to a very large size and be found to occupy the whole of the interpeduncular space, and even occasionally to extend laterally into the temporal lobe. This upward extension results in compression of the optic chiasm, but because of the site of the tumour hydrocephalus and papilloedema are rarely produced.

Histologically such tumours are found to consist of cells with a non-granular cytoplasm. Most often the cells have a somewhat alveolar arrangement, with a delicate wide-meshed stroma. Occasionally they are arranged in flat sheets resembling a pavement epithelium—the so-called struma—or in masses suggesting a papilliform growth. Mitotic figures are rarely discovered, and though the local spread of the tumour and its histological appearance may suggest that it is malignant, metastases do not occur.

Eosinophil Adenoma

The eosinophil cells secrete a hormone which is necessary for the normal growth of the body. Their destruc-

tion leads to pituitary dwarfism, while tumours composed of this cell type are associated with gigantism or acromegaly. In addition, the tumour compresses and destroys the normal gland, and some symptoms may be the result of loss of function of the basophil cells and of the posterior lobe. The eosinophil adenoma tends to be somewhat smaller than the chromophobe one, but occasionally it shows the same upward extension. Such large adenomas have a tendency to haemorrhage and subsequent cystic formation.

On histological examination the cells show no definite arrangement. There is none of the alveolar arrangement seen so often in the chromophobe adenoma. Usually the only stroma is that carrying the blood vessels. Many of the cells may be multinucleated. With specific granule stains the cytoplasm of the tumour cells is found to contain an eosinophilic granulation. In some examples, more especially those of small size, every tumour cell is packed with these granules. In the larger tumours, however, a somewhat different appearance is often observed. Many of the cells appear to be chromophobes, though rather larger than similar cells in the normal gland. Eosinophil cells occur in small groups throughout the tumour, and cells in which only a few eosinophilic granules are present are also seen. In fact, all stages in the transition of the chromophobe to the mature eosinophil cell may be found. Such a tumour is in reality a transitional adenoma, and because, in its total bulk, it contains an excess of eosinophil cells over what would be found in the normal gland the symptoms dependent on hyperactivity of these cells are produced. In the majority of cases of acromegaly which exhibit signs of chiasmal compression these transitional eosinophil adenomas are present.

Basophil Adenoma

Unlike the other types of adenomas, tumours composed of basophil cells are usually small, and may only be discovered on serial section of the gland. Hence they do not usually produce visual symptoms through pressure on the optic chiasm. The largest basophil adenoma we have seen measured 2 cm. in greatest diameter. A number of these adenomas, but by no means all of them, are associated with Cushing's syndrome of hypertension and obesity, but, unlike the eosinophil adenoma, with its associated disturbance of growth, the relationship is not a constant one, and the relation of the tumour to the production of the symptoms is by no means clear.

Histologically there is much resemblance in structure to the eosinophil adenoma. There are the same lack of alveolar arrangement and the same scanty stroma. The cells are irregularly arranged, and binucleated and multinucleated forms occur. Around the blood vessels and along the strands of stroma they tend to be columnar. With specific stains they are found to contain a basophil granulation. Tumours composed of cells in various stages of transition from the chromophobe to the mature basophil also occur. In those patients in whom the presence of the adenoma is associated with Cushing's syndrome the basophil cells of the anterior pituitary, but not in the adenoma itself, show a curious degranulation and hyalinization of their cytoplasm. Adenomas appearing in the absence of the clinical syndrome are not associated with this cytoplasmic change.

Epidermoid Tumours (Craniopharyngiomas)

Tumours of epidermoid epithelial structure are found in relation to the pars tuberalis. Frequently these tumours arise above the diaphragm of the sella, but they may take origin within the sella itself. They are tumours of youth and early middle age, for over 75 per cent. of

them occur before the age of 40. When the normal pars tuberalis is examined one frequently finds small groups of squamous cells. These have been regarded as "cell rests," and it has been surmised that the epidermoid tumours arise from these islands of squamous cells. It is a curious fact, however, that the squamous cells are extremely rare in children, while they seem to become more frequent with age. It is possible, therefore, that they may represent a squamous metaplasia of the cells of the pars tuberalis rather than embryonic rests, and the tumours may also be of this nature.

Epidermoid tumours may be either solid or cystic. In the cystic form, which is the more common, a warty excrescence is usually found projecting into the lumen at the base of the cyst. Although the histological appearances of the tumour vary somewhat, it is always found composed of epidermal forms of epithelial cells. Some tumours have the usual histological structure of squamous epithelial growths, with cornification and the formation of epithelial pearls. Not uncommonly the histological picture is that of a basal-celled tumour, solid anastomosing masses of epithelium lying in a fibrous tissue stroma. This latter type may show much resemblance to the adamantinoma of the jaw. Fatty substances are frequently found in the stroma, and their calcification may lead to the recognition of the tumour on x-ray examination of the skull.

The frequent suprasellar origin of these tumours leads to an early development of hypothalamic symptoms, and later to those resulting from compression of the neighbouring chiasm and pituitary. They constitute a common cause of the syndrome of Fröhlich's dystrophia adiposogenitalis, and not infrequently give rise to diabetes insipidus.

Cysts of Rathke's Pouch

The true cyst of Rathke's pouch is somewhat rare, and is quite distinct from the epidermoid tumour or cyst. It is a pathological enlargement of the intraglandular cleft, which represents the end of Rathke's embryonic epithelial invagination from the stomodaeum. The cyst is lined by a single layer of columnar epithelium, often ciliated, which may be flattened by intracystic pressure. The lesion should be regarded not as a true neoplasm but rather as a pathological enlargement or distension of an embryonic vestige.

The cyst is intraglandular and intrasellar in origin. Its enlargement therefore destroys the gland. Rarely it attains sufficient size to protrude upwards into the cranial cavity and compress the optic chiasma.

Miscellaneous Tumours

A variety of tumours arise in the vicinity of the pituitary gland which closely simulate primary pituitary tumours in their effects. They may compress the gland and surrounding anatomical structures so as to produce hypopituitarism, bitemporal hemianopia, and similar "pituitary" symptoms. It is not possible here to do more than enumerate some of the more common lesions, such as meningiomas arising from the olfactory groove, anterior end of falx, or tuberculum sellae; gliomas of the optic chiasma; cholesteatoma, chordoma, and metastatic tumours in or near the pituitary. Though not neoplastic, aneurysm may constitute a tumour in the anatomical sense. The congenital saccular aneurysm arising from the internal carotid artery at the point of origin of its ophthalmic branch and those associated with the anterior communicating artery belong to the "pituitary tumour" group.

It should also be borne in mind that hydrocephalus from any cause, such as cerebellar tumour or chronic

adhesive meningitis, leads to distension of the third ventricle. The distended cyst-like third ventricle may act as a tumour in exercising injurious pressure upon the surrounding hypothalamic centres, the optic chiasma, the bony structure of the sella turcica, and the pituitary gland itself. Thus hydrocephalus secondary to disease elsewhere may give rise to Fröhlich's syndrome, to bi-temporal hemianopia, to stunting of growth, and to erosion of the sella turcica recognizable in *x*-ray studies.

(To be continued)

POST-GRADUATE TRAINING IN THE PRACTICE OF PREVENTIVE MEDICINE IN INDUSTRY*

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The words "post-graduate" and "preventive" have been deliberately included in the title of this paper for the following reasons. "Post-graduate" is used because it is essential that a sound basic training in medicine, surgery, and the medical sciences should precede concentrated study of the conditions and special human problems of health and disease which arise in industry. In industrial practice the medical man or woman will need to give detailed consideration to many matters which of necessity receive little, if any, attention in the already overloaded medical curriculum for qualification. Unless the would-be industrial medical officer takes advantage of the knowledge which is now available as a result of the experience and studies of others, he or she will have to acquire such knowledge and technique by experience at the expense of employees and of industry. This is the justification for proposing some form of post-graduate instruction.

"Preventive" is included because the efficiency and success of the industrial medical officer is directly proportional to the degree of fitness and standard of health he succeeds in maintaining in the population he serves, and inversely proportional to the size of his curative medical practice in industry. The industrial medical officer will best serve employees and employers by keeping men and women in an optimum state of fitness and freedom from disease and accident by taking endless pains to ensure that factors predisposing to unfitness or disease or accident are noticed, assessed, and promptly dealt with. The basic training for qualification enables the doctor to recognize disease, but the industrial medical officer must also be able to assess the degree of physical fitness of applicants and employees and their fitness for the particular work applied for, or on which they may be already engaged.

From our experience at the London School of Hygiene and Tropical Medicine and the contacts we have had with our past students, who, having taken the course for the Diploma in Public Health of London University, have proceeded to appointments wholly or partly connected with industry at home or abroad, I feel that the general teaching and practical instruction in the laboratory and the field now given by this School for the D.P.H. London and the Diploma in Tropical Medicine and Hygiene would, with some readjustment in respect of the allocation of time to certain subjects, admirably fit a medical man or woman for the industrial medical service.

Industrial Medicine in the D.P.H. London

I should like briefly to outline the course for the D.P.H., and to draw attention to the subjects which are of particular interest to industrial medical officers. To begin with, the course for the D.P.H. London is whole-time for one academic year, from October to July, or approximately nine months. It comprises teaching in the following subjects:

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Bacteriology Applied to Public Health.—This course includes immunology, uses of antitoxins and sera; serological tests; the bacteriological examination of foodstuffs, air, dust, soil, and sewage; the bacteriology of animal diseases communicable to man; and the study of diseases due to moulds and yeasts, etc.

Chemistry and Physics in Relation to Public Health.—Under this heading such matters are dealt with as water supply and its purity; analysis of air and its impurities; analysis of foods and beverages, adulterants, preservatives, and chemical poisons; disinfectants, disinfestants; poisonous substances occurring in trade processes, etc.

Parasitology as Applied to Public Health.—Including entomology, helminthology, and protozoology.

The Theory and Practice of Public Health Administration and the Principles of Sanitary Law.—Comprising administration; social insurance; control of food; legal procedure concerning offensive trades; infectious diseases, factories, and workshops; public education in health, etc.

Sanitary Engineering.—Including building sites and site planning; building construction; reading of plans; drainage, sewage, and refuse disposal; sanitation of houses, factories, workshops, and dairies; sanitary administration; sanitation of ships, etc.

Epidemiology and Vital Statistics.—Compilation and analysis of medical statistical data; reports and forecasts and methods of conducting special investigations, etc.

Medical Industrial Psychology.—Labour wastage; sickness absenteeism and methods of investigation of such problems in industry, etc.

Physiology Applied to Hygiene and Industry.—Physiological requirements in relation to age, sex, occupation, and environment; family hygiene, budgets, food; physical education and tests for fitness in children and adults; physiological principles of heating and ventilation; recent advances in first-aid measures; factors influencing human efficiency and fatigue in industry; the physiological rationalization of industrial work, etc.

Throughout the course for the D.P.H. the attention of students is drawn to current literature—the publications of the Medical Research Council, the Industrial Health Research Board, and the various official reports of the Ministry of Health and the Home Office Factory Department. In addition to the subjects mentioned above, the course includes some forty visits to institutions, works and factories, dairies, food factories, offensive trades, special industrial processes, the Port of London, and numerous clinics. Special lectures are given on industrial hygiene and medicine by industrial medical officers and medical officers from the Home Office Factory Department, and several visits are paid to the Home Office Industrial Museum. During the session the students are also required to attend a course in district work involving a large number of attendances of not less than three hours each, and also a course on infectious diseases and hospital management provided by the London County Council.

This is only a brief outline, but I think it is clear that a very large part of the course for the D.P.H. London concerns matters of immediate interest and practical importance to industrial medical officers. No doubt some modification in the form of expansion in certain directions and cutting down in others would be necessary in order to provide more instruction in subjects of special significance to the industrial medical service, as, for example, the attendance at factory and works clinics for clinical and administrative instruction under experienced industrial medical officers in place of district work and possibly the course on infectious diseases. I think, however, that this post-graduate course, which has already proved its value to those entering the public health service, may usefully form a basis for discussion when considering the type and scope of training best calculated to fit medical men and women for the work and responsibilities which face the medical officer in industry.

Industrial Physiology

I have been asked to deal more especially with our work at the London School of Hygiene and Tropical Medicine in the field of industrial physiology, and as time does not permit me to go into details I propose to outline very briefly our approach to the subject and its scope. In doing so I wish it to be clearly understood that I do not consider the training we could give in the