THE BASOPHIL ADENOMAS OF THE PITUITARY BODY AND THEIR CLINICAL MANIFESTATIONS (PITUITARY BASOPHILISM)*

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Introduction. In a long since superseded monograph on the pituitary body and its disorders, published in 1912, a section was devoted to a group of cases which showed peculiar and sundry polyglandular syndromes. It was stated at the time that the term "polyglandular syndrome" implied nothing more than that secondary functional alterations occur in the ductless-gland series whenever the activity of one of the glands becomes primarily affected; and further, that the term, as employed, was restricted to those cases in which it was difficult to tell where the initial fault lay.

That a primary derangement of the pituitary gland, whether occurring spontaneously or experimentally induced, was particularly prone to cause widespread changes in other endocrine organs was appreciated even at that early day, and it was strongly suspected that this centrally placed and well protected structure in all probability represented the master-gland of the endocrine series. The multiglandular hyperplasias of acromegaly, so evident in the thyroid gland and adrenal cortex, were already known, and the no less striking atrophic alterations in these same glands brought about by the counter state of pituitary insufficiency were coming to be equally well recognized. But in spite of these hopeful signs, we were still stumbling blocks innumerable.

The usual method of progression has been somewhat as follows. A peculiar clinical syndrome has first been described by someone with a clarity sufficient to make it easily recognizable by others. This syndrome in course of time has been found to be associated either with a destructive lesion or with a tumefaction primarily involving one or another of the organs in question. These tumefactions have proved in most cases to be of an adenomatous character and it was finally recognized (first in the case of the thyroid) that adenomata of this kind were functionally active structures that produced hypersecretory effects. It then gradually came to be realized that the tumor need not necessarily be bulky but, quite to the contrary, striking clinical effects might be produced by minute, symptomatically predictable adenomas. So it is the degree of secretory activity of an adenoma, which may be out of all proportion to its dimensions, that evokes the recognizable symptom-complex in all hypersecretory states.

The pituitary adenomas. The anterior-pituitary body, as distinct from the neuro-hypophysis, is a compact of cellular elements of three recognizable sorts, divided by histologists, on the basis of their staining reactions, into two principal types: (1) those having a non-granular cytoplasm, and (2) those with a cytoplasm which is distinctly granular. Cells of the former type are known as neutrophil (chromophobe) elements and of the latter—the granular type—as chromophil elements of which there are two sorts: (a) those whose granules show an affinity for acid dyes (acidophil cells) and (b) those with an affinity for basic dyes (basophil or cyanophil cells). Each of these three cellular types—chromophobe, acidophil and basophil—is capable of producing its own peculiar adenomatous formations.

Whether these three types of cells are fixed in character or whether they represent different stages in activity of the same original cell is a matter of dispute. The most recent advocate of the unitarian view is Remy Collin of Nancy who, purely on anatomical grounds, presents a convincing argument to show (cf. Fig. 1) that the non-granular cell (cellule principale: mother-cell) represents the primitive stage of activity of an element which in the process of ripening acquires a granular cytoplasm that is primarily acidophilic (eosinophilic) but which may in turn become basophilic (cyanophilic). When the ripened granular cytoplasm comes to be discharged, little is left but the nucleus and membrane of the cell which may then either degenerate or, in a renewed cycle, once more pass through these same stages to be again discharged under proper stimulus. But if this is actually what takes place,
the fact that each of these varieties of cells is capable of forming adenomata whose elements appear to be of fixed rather than of a changing type is highly peculiar. What is more, one would naturally expect that adenomata composed of the non-granular mother-cells (*Hauptzellen; cellules principales*) would be more likely to show evidences of cell division than would adenomata composed of elements in the more advanced stages of secretory activity. But just the opposite occurs; the elements composing the common chromophobe adenomata rarely if ever show cell division, whereas those of a chromophil adenoma, whether acidophilic or basophilic, are frequently multinuclear (cf. Figs. 2b, 16, 29) and show numerous mitotic figures.4

Meanwhile, experimental pathology has provided us with some fairly definite facts concerning the function not only of the anterior pituitary considered as a whole, but, in turn, of its different cellular constituents. When its frequent association with a pituitary tumor came to be recognized, it was at first supposed that acromegaly was an expression of glandular deficiency and theoretically should be reproducible by experimental extirpation of the gland. This, however, in the majority of cases led to early death, at least of adult animals (chiefly dogs), whereas younger animals when hypophysectomized, though they might recover for long periods, ceased to grow and remained sexually infantile.

It had already been observed that tumors, grossly indistinguishable in situation and type from those associated with acromegaly, were of far greater frequency and provoked a syndrome, so far as its endocrinological manifestations were concerned, of a wholly different character. Individuals affected by these tumors when of adult age, instead of a tendency to overgrowth, showed on the contrary a tendency to become adipose, to lose their secondary sex-characters, and to become impotent, in company with recognizable atrophic changes in the sexual organs. When altogether comparable changes were seen occasionally to occur in animals (dogs) after incomplete experimental hypophysectomy, it became evident that the syndrome represented a deficiency state which was termed hypopituitarism; and this furnished an added reason to assume—what had already been conjectured—that acromegaly almost certainly represented the counter state of hyperpituitarism.5

The final experimental proof of the correctness of this assumption was delayed until Evans and Long,6 by daily parenteral injections of an alkaline anterior-lobe extract, succeeded in producing experimental overgrowth (gigantism) in the rat, an animal whose epiphyses do not close throughout

4 It would seem that the only possible way this question of fixity or changeableness of the elements composing pituitary adenomas could be conclusively answered would be by cultivating the cells of the different types to determine whether they breed true to their original form or whether their cytoplasm undergoes progressive alteration. Efforts in this direction have so far proved unconvincing owing largely to technical difficulties due to want of experience with the artificial growth of neoplastic tissues.
